Lecture Notes for Internal Medicine

Weill Bugando School of Medicine

Bugando Medical Centre

Students Version

1st edition (2012)

Introduction

The following lecture notes are based on the topics described in the official curriculum of the Weill Bugando School of Medicine. The target audience for these lecture notes is medical students in their final 2 years of medical school. These lecture notes contain the basic concepts of internal medicine that every medical student should know by the time of graduation. They cover most of the major topic areas, but are far from comprehensive in scope. Students are still encouraged to consult one of the recommended textbooks of internal medicine for in depth explanations.

These lecture notes were written for use by the faculty and students of Bugando, but we hope that they are useful for faculty and students at other medical schools in East Africa. We have attempted to adapt these lecture notes and clinical cases to the diseases and resources that are commonly available at Bugando and in East Africa. In addition we hope that these notes provide a useful guide to the most essential learning points for any faculty asked to give a lecture on short notice.

We believe that the best setting for learning medicine is at the bedside of a patient, and that this material would be best taught at the bedside. These handouts can then serve as a useful reinforcement of key learning points for students. When an illustrative patient is not available, the teaching cases may be used to cover the most salient clinical details for each condition.

These lecture notes are focused on teaching algorithms for management of common problems with specific focus on differential diagnosis, diagnostic workup, treatment and natural history. Sessions on the physical examination of the major body systems are included with the expectation that these can be taught and modeled at the bedside. This will allow further instruction in communication skills and ethical standards of care.

These lecture notes are a labor of love that has been completed over the course of the past 5 years. Many people have contributed and we do not have space to thank them all. In particular we would like to thank our Vice Chancellor (Prof. Jacob Mtabaji), Hospital Director (Dr. Charles Majinge) , Dean (Prof. J.B. Kataraihya) and Department Head (Prof. Samuel Kalluvya). We would also like to thank all of the other members of our Department: Drs. Hyasinta Jaka, Dr. Rodrick Kabangila, Dr. Bahati Wajanga, Dr. Andrew Luhanga and Dr. Mubarak Janmohamed. This is a first edition and we hope these lecture notes will be improved with the contributions of additional editors in the 2nd edition.

Those who have prepared these notes have used a variety of resources. In particular, we have relied on:

- Swash M., Glynn M. *Hutchison's Clinical Methods: An integrated approach to clinical practice.* 22nd ed. Edinburgh: Saunders Elsevier; 2007. [for physical examination topics]
- Eddleston M, Davidson R, Brent A, Wilkinson R. *Oxford Handbook of Tropical Medicine.* 3rd ed. New York, NY: Oxford University Press USA; 2008. [for clinical topics]

Sincerely,

Drs. Robert Peck, Luke Smart and Riaz Aziz (The Editors)

History, Exam, and Procedures

Introduction to History Taking in Internal Medicine

Introduction

The medical history is the foundation of internal medicine. The answer to the patient's problem is in the history 90% of the time! The other 10% of the time, you will need to use investigations to help you figure the answer out.

Identification

Start your presentation with the patient's name, age, sex, home and referral status. Fore example: Luke Smart, 32 year old male, self referral to Bugando Medical Centre.

Chief Complaint (CC)

This is the main reason the patient came to the hospital. Ask the patient, "Why did you come to the hospital?" It is normally, one complaint, but can contain up to two or even three main complaints. State the duration of the complaint. For example: disturbance in breathing for two weeks.

History of Present Illness (HPI)

This should be a story about how the symptoms developed. Use the patient's own words as much as possible. Avoid medical terminology (like the word "angina") unless the patient actually uses that word. Usually a patient will say "chest pain" instead of "angina." Begin with the earliest symptoms related to the chief complaint and proceed chronologically. For example: "The patient described chest pain when walking up a hill four weeks ago. This resolved with rest and recurred with activity. Eventually the chest pain subsided and the patient began to experience shortness of breath when walking short distances. One week ago, the patient began to notice that they were short of breath when lying flat and began having swelling in his legs.

Review of Other Systems (ROS)

Review the systems that are not involved in the chief complaint. The system that is involved in the chief complaint should be reviewed within the HPI. Usually the ROS is done from head to toe (neurological, cardiovascular, pulmonary, gastroenterology, renal, genitourinary, and musculoskeletal). Review every system every time you take a history, but when you present the patient, only mention the ones that are important negatives and positives related to the chief complaint. For example, if the patient has abdominal pain, then the gastroenterology system will be reviewed in the HPI, and the cardiovascular, renal, and genitourinary systems ought to be specifically mentioned in the ROS. If you do not know which systems are relevant to the HPI, it is always better to include more information than less.

Past Medical/Surgical History (PMSHx)

This includes past admissions, chronic medical problems, medications, allergies, immunizations, prior surgeries, prior blood transfusions, and for women gynecological history. Any part of the PMHx related to the CC should also be mentioned in the HPI. For example, if the patient presents with chest pain that started one month ago and was admitted two weeks ago for this complaint, then it should be included in the HPI. One way to figure out if they have any chronic medical problems is to ask if they have ever gone to the clinic or if they are on any medication. For some past medical problems it is important to include more than just a diagnosis. For example, if the patient has IDS, then you want to include their baseline CD4 count, whether they are on ART, and if so how long. For

the allergy section, ask specifically what kind of reaction they had. If they don't remember what kind of medicine they had an allergy to, you can always try to figure out what medication it is by asking them why they were taking it. You can also ask if it was a pill or an intravenous medication. For women remember to include the last menstrual period.

Family/Social History (FSHx)

A complete social history includes marital status, number of children, the location of their home (region/village), type of home, number of children, occupation, level of education, alcohol use, tobacco use, illicit drug use, and sexual history.

Tobacco history should include how many cigarettes they smoke per day and how long they have smoked. This is reported in pack years. Pack years are equal to the number of packs per day multiplied by the number of years they smoked. If the patient smoked one pack per day for ten years, then they have a ten pack-year history of smoking. If they smoked 5 cigarettes per day for four years that is equal to ¼ pack x 4 years which equals one pack-year. Also report the type of cigarettes used. The alcohol history should include the type of alcohol, the amount per sitting, how many times per week, and the total number of years that the patient drank this much.

The sexual history should include the number of current partners (or the number of partners in the past month), the total number of past partners in the patient's life, any history of sexually transmitted infections, the age at first intercourse, and whether the patient uses protection when having sex.

The family history should include any inheritable diseases such as diabetes mellitus, sickle cell disease, and heart disease, as well as anything related to diseases that look like the chief complaint.

Summary #1

This is one sentence that **summarizes** the important parts of the history. Include identifying information, CC, a **very brief** description of the HPI plus essential details from the ROS, PMSHx, and FSHx. For example: "This is a 30yo new diagnosis of IDS, who presented with at 2 week history of difficulty breathing which was associated with chest pain, fever, weight loss, night sweats, and a TB contact."

Physical Exam

This is a brief overview of the physical exam. More detailed information about how to perform the different sections of the physical exam can be found in other lectures, and in Hutchison's.

Always start with the general exam. At the end of the general exam, report the vital signs. For example: "Ill appearing middle aged male, who was extremely wasted and lying in bed. The vital signs are temp of 37.3C, BP 105/70, pulse rate 105, O2 sat of 92%."

After reporting the general exam, report the systemic exam. Report the most affected organ systems first. If the patient presents with diarrhea, present GI first, then go on to other organ systems. Do a complete physical exam of each organ system every time you see a patient, but only report a detailed exam for the organ systems related to the chief complaint and for abnormal findings in other systems.

Each organ system ought to be examined in the same order: I. P. P. A. – inspection, palpation, percussion, auscultation. As a junior medical student, it is best to report "On inspection… on palpation… on percussion… on auscultation…" This way you will not forget any part of the examination and you will keep things in the correct order. The only exception to this rule would be for the central nervous system. Also for the cardiovascular exam we start out with the inverted J (check radial pulse, blood pressure, and JVP, then proceed to I. P. P. A. with the precordium and rest of the cardiovascular exam). Report the vital signs twice: once during the general exam, and then the appropriate vital signs for each of the organ systems that are investigated (e.g. you report BP and pulse with the CV exam even though they were already reported during the general exam).

Summary #2

This summary is **two sentences**. The first one is a repetition of Summary #1. The second sentence is a summary of the physical exam findings. You do not need to repeat the specifics of the exam findings if you are able to summarize them in a brief way. For example, if the patient has a respiratory exam with decreased tactile fremitus, stony dullness on percussion, and decreased breath sounds on auscultation, you can say that they have exam findings consistent with a pleural effusion.

Impression

Your impression should take into account the chief complaint and all abnormal findings on the history and physical. It should include every diagnosis that you think the patient DOES have. The differential diagnosis should include other possibilities, but not things that you are fairly certain the patient has. It is helpful if you explain your reasoning behind your impressions (e.g. I think this patient has IDS because they have wasting, fever, and candidal infection). You should give your reason for each impression and then give 3-5 good differential diagnoses for each impression.

Plan

Your plan should include both investigations and treatments (pharmacological and non-pharmacological). It is best to organize your plan by stating what investigations and treatments you want for each of your impressions, e.g. for IDS I want to send a cd4 count and get baseline ART labs (RFT, FBP, LFT); for TB I want to get sputum for afb, check FBP, and get a chest x-ray. This will help you in the future because your plan will be the same every time you see that diagnosis.

General Examination

Introduction

- The general examination is usually done in either sitting or lying position. Observation begins as soon as you see the patient (as they enter the room, or as they are lying in bed).
- Move from general observation to specific inspection of different parts of their body

Mental and emotional state

- What is their mental state? (confused, delirious, agitated, somnolent)
- What is their emotional state? (anxious, depressed, apathetic)

Physique

- Is appearance consistent with their age? (younger or older than stated age?)
- What is their body habitus? (tall, short, fat, thin, muscular, asthenic, wasted)
- Are there obvious deformities or scars? (kyphosis, scoliosis, pectus excavatum/carinatum)

Face

- Is there any asymmetry?
- Do they have any swelling? (general puffiness, parotid swelling)
- What is their color? (pale, red, bluish, facial plethora)
- Do they have any rashes? (telangiectasias, naevi, malar rash)
- Are their eyes or eyelids irregular?

Skin

- What is its color? (pallor, jaundice, central cyanosis, peripheral cyanosis)
- What is its temperature? (cool, pyrexia)
- What is its appearance? (dry, pitting edema, scratch marks, bruising, spider naevi)
- If there is edema, what is its distribution? How far up the leg does it go? How severe is it?

Hands/Feet

- What is the appearance of the fingers/joints? (redness, swelling, deformity, Dupuytren's contracture)
- What is the appearance of the nails? (clubbing, splinter haemorrhage, koilonychia)
- What is the appearance of the palms/pads? (Osler's nodes, laneway lesions, palmar erythema)
- Any abnormal movements? (hepatic flap, tremor)
    - Checking for hepatic flap: When the hands are arms are fully extended and the wrists extended with palms facing forward perpendicular to the ground, the patient will be unable to sustain the hands in extension and will periodically flap his hands.
- What is the appearance of their shins and feet? (hair loss, ulcers)

Neck

- Is there lymphatic swelling?
- Is there thyroid gland swelling?
- Are there abnormal pulsations of the neck vessels? (elevated jugular venous pressure, pulsus paradoxus)

- Checking for jugular venous pressure: have the patient lie at a forty five degree angle. Inspect the neck for the pulsations of the internal jugular vein. Measure its height from the level of the sternal angle. It should normally be less than 3 cm above the sternal angle.
- Checking for pulsus paradoxus: The systolic blood pressure normally decreases slightly during inspiration. Pulsus paradoxus is an abnormally large decrease in this normal variation. To check this, inflate a blood pressure cough as you normally would until you hear no sounds. Slowly deflate the cuff until you hear the first Korotkoff sound only during expiration and note the blood pressure. Continue to decrease the blood pressure until you hear the first Korotkoff sound during both inspiration and expiration. Subtract this from the first pressure. If it is greater than 10 mm Hg difference, then the patient has pulsus paradoxus.

Respiratory

- What is the quality of the voice? (strong, weak, hoarse)
- Are they breathless? If so, to what degree? (speaking in full sentences, speaking in one word sentences, unable to speak, dyspnoea, Cheyne-Stokes breathing)
- Are there any abnormal chest movements? (symmetri/asymmetric, subcostal, intercostal, supraclavicular, or suprasternal recessions)
- Are they using accessory respiratory muscles? (sternoclaidomastoid, intercostal)
- Are they coughing? (weak, dry, wet, productive sounding, or paroxysmal cough)
- What is the rate of respiration? (tachypnoea, apnoea)

Chest

- Observe chest, pulses, and body surface for abnormal pulsations
- Observe any breast irregularities (asymmetry, peau d'orange, gynaecomastia)

Gastrointestinal

- The patient should be supine with arms loosely by his or her sides, with head and neck supported by a pillow so that the abdomen can be relaxed.
- What is the shape of the abdomen? (general distention, localized distention, scaphoid)
- Is the umbilicus abnormally everted?
- Note any abnormal movements of the abdomen? (normal, abnormally still/silent, pulsations of the aorta, visible peristalsis)
- Are there any abdominal skin markings? (striae atrophica, striae gravidarum, purple striae, scars, prominent superficial veins, caput medusa, linea nigra)

Genitourinary

- Note any swellings or abnormal position of the testicles
- Note any testicular atrophy
- Note any loss of pubic hair

Basic Nervous System Exam

Introduction

This examination is best done in the sitting position except meningeal signs which require lying position and Coordination/Gate/Balance which require the patient to stand. In severely ill patients, the nervous system exam can be completed in the lying position

Always perform the neurological exam systematically so that you do not omit anything. Note any deficits and the anatomic site of the neurologic lesion. Always report all 6 parts of the nervous system examination – higher centers, cranial nerves, meningeal signs, motor/reflexes, sensation, coordination/gate/balance –even if you need to report that some part "could not be assessed." For more comprehensive neurological exam, refer to Hutchinson's

Higher Centers

- Mental State: Examination of the mental state overlaps with the field of psychiatry, and it includes examination of appearance, attitude, behavior, mood, affect, speech, language, thought process, thought content, perception, cognition, insight, and judgment.
- For the an internal medicine doctor, you should ***at the very least observe the level of consciousness and orientation***
- Level of Consciousness: In extremely ill patients consciousness can be quantified with the Glasgow Coma Scale (GCS). This is the sum of eye, verbal, and motor responses as below:

Eye Response	**Verbal Response**	**Motor Response**
4 = open spontaneously	5 = oriented, converses	6 = obeys commands
3 = open to verbal command	4 = disoriented, converses	5 = localizes to pain
2 = open to pain	3 = inappropriate response	4 = withdraws from pain
1 = no response	2 = incomprehensible sounds	3 = decorticate (flex) to pain
	1 = no response	2 = decerebrate (extend) to pain
		1 = no response

- Orientation: Check to see if the patient is oriented to person, place, and time. Do they know who they are (their name, age, date of birth), where they are (city, hospital, floor), and when it is (year, month, day, time)
- Speech: Do they have dysarthria, expressive aphasia, or receptive aphasia?
- Memory: assess both short term and long term memory.

Cranial Nerves

- CN I (Olfactory): Smell is testedwith pungent, non-irritant odors, each nostril separately. This is often omitted during a brief bedside exam.
- CN II (Optic): Test visual acuity with Snellen chart at 6m, visual fields (each quadrant one eye at a time) with fingers moving test.
- CN III, IV, VI (Oculomotor, Trochlear, Abducens): Have patient track with eyes as you trace an 'H' 1m away. Test smooth pursuit and nystagmus by tracing a '+'. Test pupils by shining light into eyes and checking for direct and symmetric reaction. Check accommodation by bringing finger close to their face between their eyes.

- CN V (Trigeminal): Check sensation to light touch and pin prick in all three branches of the trigeminal nerve on both sides of the face. If the patient is sedated or comatose, touch cotton to the corneal surface to illicit bilateral blink corneal reflex. Palpate masseter and temporalis muscles as patient clenches teeth to assess motor function.
- CN VII (Facial): Check movement of the upper face by having the patient raise their eyebrows and screw their eyes shut while you try to open their eyelids. Check movement of the lower face by having the patient smile, bare teeth, and hold air in the cheeks while you tap on them. You can also check taste with various solutions: 'sweet' with sugar, 'salt' with salt, 'sour' with a citric acid, and 'bitter' with quinine.
- CN VIII (Vestibulocochlear): Test hearing with different volumes of speaking (normal, whisper), and with rubbing your finger near their each ear individually. If a tuning fork is available, check Rinne and Weber tests. Check the vestibular function at the end of the neuro exam during the coordination, gait and balance assessment with the Romberg test, heel to toe walking, and Dix-Hallpike test.
    - Rinne test: strike the tuning fork and hold it near the external ear canal and then against the mastoid process. Ask the patient which is louder.
    - Weber test: place the base of the vibrating tuning fork on the vertex or forehead in the midline. Ask the patient whether the sound is heard in the midline or whether it is louder on one side
- CN IX (Glossopharyngeal): Test for motor function by having patient stick their tongue out. Test for taste on the posterior part of the tongue and gag reflex.
- CN X (Vagus): As the patient says 'ah,' confirm soft palate elevates and the uvula stays midline.
- CN XI (Accessory): Check strength as patient shrugs shoulders. Check for sternoclaidomastoid strength by placing hand on cheek and having patient turn their head against it.
- CN XII (Hypoglossal): Note any wasting, fasciculations, or tremor of the tongue

Signs of Meningeal Irritation

- Neck Stiffness: Passively but gently flex the patient's neck to see if they can touch the chest without pain.
- Kernig's Sign: With the patient supine on the bed passively extend the patient's knee on either side when the hip is fully flexed and look for patient spasm.
- Brudzinski's Sign: When forced flexion of the neck elicits a reflex flexion of the hips.

Motor/Reflexes

- Bulk: Note any muscle wasting, fasciculations, or hypertrophy and their distribution.
- Note any abnormal posture or abnormal movements (tremor, pseudoathetosis, myoclonus, chorea, ballism, athetosis, dystonia, tics, tetany, cramps).
- Tone: Move the limb passively back and forth at different rates. Note any hypertonia, hypotonia, rigidity, or spasticity .

Power

0 – Complete paralysis

1 – A flicker of contraction only

2 – Cannot resist gravity, but moves on the bed

3 – Resists gravity, but cannot resist examiner

4 – Resists gravity and examiner, but not normal

5 – Normal power

Deep Tendon Reflexes

0 = absent

1 = present (as a normal ankle jerk)

2 = brisk (as a normal knee jerk)

3 = very brisk

4 = clonus

- Superficial Reflexes
    - Abdominal reflex: with patient supine, drag stick across the abdomen from loin toward midline causing contraction
    - Plantar (Babinski) reflex: scratch the outer edge of the sole of the foot with a stick from the heel to the toe, and watch for flexion of the toes
    - Cremasteric reflex: Stroke the upper inner part of the thigh. Testicle moves upward.
    - Anal reflex: gently scratch skin on either side of the anus and it will contract

Sensory System

- Pinprick (small fibres/spinothalamic pathway): use a pin, start distal and move proximally.
- Temperature (small fibres/spinothalamic pathway): use cold metal.
- Light Touch (Moderately myelinated fibres/combined pathways): use finger or cotton.
- Vibration sense (large myelinated fibres/dorsal column pathway): use a vibrating tuning fork placed over bony prominences.
- Joint position sense (large myelinated fibres/dorsal column pathway): Test a finger and toe on each limb. Move it up or down and asking the patient to tell you which direction you moved it.
- Two Point Discrimination: Normally 2mm separation can be recognized as separate stimuli on the finger tips, but only 1cm separation on the bottoms of the toes

Coordination, Gait, and Balance

- Coordination: Test when concerned about cerebellar injury
    - Finger to nose test: ask the patient to touch his nose and then the tip of your finger, held at arm's length in front of the patient's face using their index finger.
    - Rapid alternating movements: have patient to tap your palm with the tips of the fingers of one hand, alternating in pronation and supination
    - Heel-shin test: with the patient is supine, place the heel of one foot on the opposite knee and slide the heel down the shin towards the ankle
- Gait: by having the patient walk at a brisk pace and observing any changes in arm swing, poor posture, lurches, asymmetry, change in breadth of base, floppiness, involuntary movements, pain, or ataxia. Then have patient walk heel to toe with their eyes first open, then closed.
- Balance/Stance: test with the Romberg's test.
    - Romberg's: Standing with feet firmly together, have the patient close his or her eyes and see if balance worsens (do they sway or fall).

Cardiovascular System Exam

Introduction

The entire CV examination is best performed with the patient sitting at 45 degree in cardiac position.

Inspection of the Hands

This would normally be done and reported as part of the general examination unless ONLY a focused cardiovascular examination is done. Especially note any, cyanosis, finger clubbing, warmth of extremities, signs of infective endocarditis.

Arterial Pulses

- **Rate**: Palpate the right radial artery. Note tachycardia (>100 bpm) or bradycardia (<60bmp).
- **Rhythm**: Note whether the rhythm is regular (no missed or extra beats) or irregular. If there is sinus arrhythmia, the heart rate will slow slightly whenever the patient breaths out.
- **Character**: Palpate the right carotid artery on the neck at the angle of the right mandible. Assess the volume (increased/decreased). Check for symmetry between the right and left side, and for delay between the brachial and femoral pulses.
- **Synchronicity**: Is the radial pulse synchronous with both the contralateral radial pulse and the femoral pulsation?
- Radial, brachial, carotid, femoral, popliteal, and pedal pulses commonly assessed.

Blood Pressure

- Blood pressure should be checked first in the sitting position in both arms. If you are concerned about hypovolemia, check the blood pressure and pulse in standing, sitting, and lying positions
- Patient must be sitting with feet flat on the floor with blood pressure cuff above the elbow, with the width of the cuff being at least 40% of the circumference of the arm.
- Place the bell of the stethoscope over the brachial artery on the ventral surface of the elbow.
- Inflate the blood pressure cuff until the pulse is totally occlude; slowly deflate the cuff and listen for the appearance of the Korotkoff sounds:
    - Phase 1: the first appearance of sound = the systolic blood pressure
    - Phase 2 and 3: increasingly loud sounds
    - Phase 4: abrupt muffling of the sounds
    - Phase 5: disappearance of the sounds = the diastolic blood pressure

Examination of the neck vessels

- Jugular Venous Pressure: Measure its height from the sternal angle. Normally it is less than 4cm vertically above the angle.
    - Kussmaul's sign: paradoxical rise in jugular venous pressure during inspiration
- Waveform of Jugular Venous Pulse
    - "a" and "v" waves separated by "x" and "y" descents
    - Giant "a" wave: forceful contraction against a stenosed tricuspid valve or non-compliant hypertrophied right ventricle
    - Cannon "a" wave: atrial systole against a closed tricuspid valve caused by atrial-ventricular dissociation (complete heart block)
    - Giant "v" wave: sign of tricuspid regurgitation

    - Prominent “x” and “y” descents: constrictive pericarditis
- Waveform of the carotid pulse
    - Tardus et parvus: the carotid pulse is slow and small
    - Biphasic pulse: two systolic peaks
    - Alternating pulse: alternating high and low systolic peaks
    - Paradoxical pulse: More than 10mm Hg decline in systolic blood pressure during inspiration

Inspection

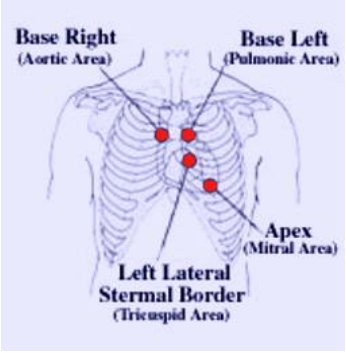
Look for any precordial hyperactivity, any bulging of the chest wall on one side or the other, as well as any traditional marks or scars.

Palpation

Place your right hand on the patient’s left chest with the butt of the hand at the sternum and the fingers extending into the axilla

- Apex beat: the lowest most lateral point at which the cardiac impulse can be palpated. Normally located superior to the 5th intercostals space and medial to the midclavicular line.
- Double Thrust: A palpable 3rd and 4th heart sound
- Left Parasternal Thrust: Thrust appreciated just to the left of the sternum
- Thrill: Palpable vibrations on the chest wall

Auscultation



Technique

- Diaphragm of the stethoscope for high-pitched sounds
- Bell of the stethoscope to hear the low-pitched sounds.
- Place the stethoscope in the four primary areas.

Sounds

- 1st sound (S1) – closing of the mitral and tricuspid valves
- 2nd sound (S2) – closing of the aortic and pulmonary valves. Split S2 occurs during inspiration.
- 3rd and 4th sounds (S3, S4)
    - Low frequency sounds. Occur during diastole after S2. Either one is called a ‘gallop.’
    - Best heard with the bell of the stethoscope
- Systolic clicks and opening snaps are abnormal
    - Early systolic click – can occur with aortic stenosis right before the ejection murmur
    - Late systolic click – mitral valve prolapsed
    - Early diastolic snap – mitral stenosis
- Heart murmurs: Defined by four qualities: loudness, quality, location, and timing
    - Loudness: graded on scale from 1 to 6
        - 1 = Barely audible
        - 2 = Somewhat audible
        - 3 = Audible
        - 4 = Audible with thrill

        - 5 = Audible with the edge of the stethoscope on the chest
        - 6 = Audible without using a stethoscope
    - Quality: the frequency. This can be low-pitched, medium pitched, or high-pitched.
    - Location: where is it best heard? Use one of the four main areas.
    - Radiation: what direction does the sound travel to? (neck, axilla, back?)
    - Timing: describes what phase of diastole or systole the murmur is heard
        - Systolic: midsystolic, pansystolic, late systolic
        - Diastolic: early diastolic, mid-diastolic, or presystolic
        - Continuous: audible in both phases of the cardiac cycle
- Innocent murmurs: always mid-systolic, rarely greater than grade 3
- Positioning/Maneuvers: Some murmurs are louder when the patient is positioned differently
    - Lying on the left side: helps with mitral regurgitation
    - Inspiration: helps to hear tricuspid regurgitation
    - Leaning forward: helps to hear aortic regurgitation or pulmonic regurgitation
- Friction and venous hums
    - Best heard in maintained expiration with the patient leaning forward
    - High-pitched scratching noise audible during any part of the cardiac cycle and over any part of the left precordium
    - Hyperkinetic venous hum can be heard at the base of the heart, and is particularly common in infants and usually disappears when lying flat

Other organs to examine during a focused cardiac exam

- Auscultation and percussion of the lung bases to look for pulmonary edema
- Palpation of the liver to examine for tender hepatomegaly or, hepatojugular reflux
- Examine extremities for edema.

Respiratory System Exam

Inspection

- Surface appearance (skin, spine, and rib cage)
    - Skin: Are there any scars, lesions, or lumps?
    - Spine: do they have any kyphosis or scoliosis?
    - Rib cage: is it normal or barrel shaped with increased anterior-posterior diameter?
- Movement
    - Is the degree of expansion normal?
    - Are the movements symmetrical or asymmetrical? If asymmetrical, is it from congenital deformity, trauma, or other?
    - Are there intercostals recessions?
- What is the respiratory rate and rhythm? (normal, tachypnea, bradypnea, hyperpnea, dyspnea, apnea, kussmaul's breathing, Cheyne-Stokes breathing)

Palpation

- Do you feel any lymph nodes? If so, note the region (supraclavicular fossae, cervical, axillary), size of the lymph nodes, and the feeling of the lymph nodes (firm/soft, tender/nontender, mobile/fixed).
- Note any areas of swelling or tenderness
- Note the position of the trachea: Feel with your second and fourth fingers on each edge of the sternal notch. Use the 3rd finger to assess its position. (midline, deviated to the right or left)
- Note the apical impulse of the heart, both its location (is it displaced from the 5th intercostals space, midclavicluar line?) and its quality (is it bounding, is there a heave)?
- Note any asymmetry during chest expansion: Face the patient and place the fingertips of both hands on either side of the lower ribcage, so that the tips of the thumbs meet in the midline in front of – but not touching – the chest. Observe the position of the thumb as with each breath.
- Check tactile fremitus: Place the hands on the front of the chest with one hand on each side of the sternum. Have the patient say "nane, nane" or "nyama, nyama" and feel for any abnormalities. Repeat on the back of the chest. Not any increased, decreased, or asymmetrical fremitus.

Percussion

- Note any hyperresonance (increase in resonance) or dullness (reduction in resonance) as well as any pain or tenderness on percussion.
- Place middle finger of the left hand on the part to be percussed and press firmly against the surface of the chest.
- Use the tip of the right middle finger to strike the distal interphalangeal joint of the left hand
- Move your right hand at the wrist
- Make sure the right middle finger is bent so that it strikes the left finger at a right angle in a tapping motion
- Percuss on the two sides of the chest, moving back and forth between the
- Percuss over the clavicles, then three of four areas on the anterior chest wall, in the axillae, and three or four areas on the back of the chest

Auscultation

- Use correct technique
    - Use the diaphragm of the stethoscope (not the bell)
    - Ask the patient to take deep breaths through an open mouth
    - Listen in comparable positions on each side and compare them to each other
- Describe the breath sounds?
    - Intensity (loudness): normal, loud or diminished
    - Quality (vesicular, bronchial).
- Are there any added breath sounds (wheezes, crackles, stridor, pleural rub)
- Are there any abnormalities in vocal resonance?
        - Use correct technique
        - Have the patient repeat a phrase such as “nani-nani”
        - Listen with the stethoscope to the sound of the vibrations being transmitted from the vocal cords into the chest.
        - Compare each point with a corresponding point on the other side of the chest.
        - Determine if there is increased resonance (louder, clearer sounds)
    - Whispering pectoriloquy: when vocal resonance is so loud, that you can clearly hear a whispered phrase with your stethoscope at the chest wall
    - Aegophony: the nasal, bleating sound that the voice has when you listen overtop of a consolidation while a person speaks

Remember that palpation, percussion and auscultation of the lungs should be performed and reported in all 7 lung areas on both right and left sides.

1. Supraclavicular (anterior)
2. Supramammary (anterior)
3. Inframammary (anterior)
4. Axillary
5. Suprascapular (Posterior)
6. Intrascapular (Posterior)
7. Infrascapular (Posterior)

Gastrointestinal System Exam

Introduction

- Prepare the patient: position them supine and expose the patient's abdomen from the xyphoid to the symphysis pubis. Make sure to inspect the genitals after the abdomen.
- Describe your findings according to the nine sections of the abdomen: Right and left hypochondrium, epigastrium, right and left lumbar, umbilical, right and left iliac, hypogastric/suprapubic.

Inspection

- Shape: Is it distended (generalized/local, symmetric/asymmetric) or sunken (scaphoid)
- Umbilicus: Is it abnormally everted?
- Movements of the abdominal wall.
    - Is the movement absent or markedly diminished?
    - Is there visible pulsation of the abdominal aorta in the epigastrium?
    - Is there visible peristalsis of the stomach or small intestine?
- Skin, veins, and pigmentation of the abdomen.
    - Skin:
        - Smooth and shiny with marked abdominal distention
        - Striae atrophica/gravidarum: white or pink wrinkled linear marks
        - Purple striae: purple linear marks
    - Veins: Is there a Caput medusae? (distended veins around the umbilicus)
    - Pigmentation: is there a linea nigra, striae purpura, striae atrophica?
- Groin, penis, and scrotum: Note any swelling or abnormal position.

Palpation

Mould the hand to the abdominal wall. Use gentle firm pressure. Ask the patient to take a deep breath to make detection of organs easier. Use a logical sequence to avoid missing anything.

- Left kidney: Not normally palpable unless it is low in position or enlarged. If the lower pole is felt, it is rounded firm swelling between the right and left hands (bimanually palpable) and can be pushed from one hand to the other
- Spleen: Not normally palpable, unless it is enlarged two to three times its size
    - Minor enlargement: firm swelling with smooth, rounded borders
    - Considerable splenomegaly: firm swelling, beneath left subcostal margin, in the left upper quadrant of the abdomen, moves downwards on inspiration, is not bimanually palpable, upper border cannot be felt, notch sometimes felt in the lower medial border
- Right kidney: Lower pole is commonly palpable in thin patients, smooth, rounded swelling which descends on inspiration and is bimanually palpable.
- Liver
    - Describe the enlargement of the liver as centimeters of enlargement below the costal margin (use a ruler if possible).
    - Determine how the surface of the liver feels (Soft, smooth, and tender OR firm and regular, OR hard, irregular, panless and nodular)
    - Does the liver pulsate?

- Gallbladder: The normal gallbladder cannot be felt.
    - Distended gallbladder feels like a firm, smooth, or globular swelling with distinct borders just lateral to the edge of the rectus abdominis near the tip of the ninth costal cartilage
    - Sometimes it is felt in the hypochondrium, but occasionally may be found in the right lumbar area or even as low as the right iliac region
    - It moves with respiration
- Signs of the liver and gallbladder
    - Murphy's sign: ask the patient to take a deep breath in, and palpate for the gallbladder in the normal way. At the height of inspiration the breathing stops with a gasp as the mass of an acutely inflamed gallbladder is palpated which is exquisitely tender
    - Courvoisier's Law: in the presence of jaundice a palpable gallbladder makes gallstone obstruction of the common bile duct unlikely
- Urinary bladder: Normally not palpable.
    - When patient has urinary retention, the bladder feels like a smooth, firm, regular oval-shaped swelling in the suprapubic region with the dome of the bladder reaching as high as the umbilicus in severe cases
    - Do not confuse with uterine and ovarian pathology in women
- Aorta: Use your fingertips (this is one of the few times you are allowed to do so). Note the width of the aorta.
    - Note any palpable lymph nodes around the aorta. They can only be felt if they are enlarged and are rounded, firm, often confluent fixed masses in the umbilical region and epigastrium along the left border of the aorta
- Common femoral vessels: Just below the inguinal ligament at the midpoint between the anterior superior iliac spine and the symphysis pubis
    - Note the strength and character of the pulsation
    - Compare the right side to the left side
    - Note any inguinal lymph nodes
- Confusing Findings in Abdominal Palpation
    - Stool filled colon
    - Sigmoid colon: firm tubular structure, 12cm long, in the left iliac fossa, parallel to the inguinal ligament
    - Caecum: in the right iliac fossa, soft, rounded swelling, indistinct borders
    - Transverse colon: palpable in the epigastrium, softer and larger than pelvic colon, distinct upper and lower borders and convex anterior surface
- Rectus abdominis muscle belly, between the tendinous intersections
    - See if this contracts when the patient flexes the abdominal muscles
- Abdominal Masses: Make sure it is not a normal structure or an enlarged organ.
    - Note the site
        - Anterior to the abdominal wall: the mass will be appreciated even when the patient flexes their abdominal muscles
        - Within the abdominal cavity: the mass will not be appreciated when the patient flexes their abdominal muscles
        - Can you feel the superior edge of the mass, or does it disappear above the costal margin?
        - Can you feel the inferior edge of the mass, or does it disappear into the pelvis?

    - Note the size and shape
    - Note its surface, edge, and consistency (hard/soft, irregular/regular, nodular/smooth, round)
    - Note its mobility and attachment
        - Does it move downward with inspiration?
        - Can it be moved by palpation?
        - Does it have side to side mobility?
    - Note whether it is bimanually palpable
    - Note whether it is pulsatile. Does this pulsation come from the mass or is it transmitted by the mass?
- Feel for any guarding
    - Involuntary reflex contraction of the muscles of the abdominal wall
    - Determine if this is truly involuntary, or if it is voluntary contraction
- Feel for rigidity
        - Board-like abdomen
- Feel for rebound tenderness
    - Palpate slowly and deeply over the abdomen
    - Release the palpating hand, and observe to see if the patient experiences severe pain

Percussion

Define the boundaries of abdominal organs and masses

- Liver
    - Start anteriorly, at the 4^{th} intercostal space in the midclavicular line.
    - The note should be resonant because you are over the lung at this height.
    - Move vertically downward the chest wall as you percuss
    - The note will become dull at about the intercostal space as you move over the liver
    - The dullness extends down to the lower border at or just below the right subcostal margin
    - Normal liver height is 12cm to 15cm
- Spleen: Normally not able to discern splenic size based on percussion. Percussion is used to confirm splenic enlargement as it protrudes into the abdominal space.
- Urinary bladder: Normally not able to find with percussion. Can be dull to percussion just over the pubic bone when the bladder is enlarged from urinary retention.
- Other Masses: Use percussion and the change from resonance to dullness to measure the size of masses in the abdomen.
- Findings on percussion of the abdomen
    - Shifting dullness:
        - lie the patient supine
        - Place your fingers on the longitudinal axis on the midline near the umbilicus and begin percussion moving your fingers laterally towards the right flank
        - When dullness is first detected keep your fingers in that position and ask the patient to roll on their left side
        - Wait a few seconds for any peritoneal fluid to redistribute
        - Percuss again starting at the place that you stopped

        - With ascites, this place should now be resonant rather than dull
        - Continue to percuss back towards the midline until you find the area of dullness again (this confirms that fluid did actually shift)
    - Fluid Thrill
        - Lie the patient supine
        - Place one hand flat over the lumbar region on one side of the abdomen
        - Ask an assistant to put the side of their hand longitudinally and firmly in the midline of the abdomen (this will dampen any movement that is transmitted through the fat of the abdominal wall itself)
        - Flick or tap the opposite lumbar region
        - If the patient has ascites, a fluid thrill or wave is felt by the detecting hand held flat on the lumbar region

Auscultation

- Bowel Sounds: normally intermittent, low or medium-pitched gurgles interspersed with an occasional high-pitched noise or tinkle.
    - Abnormal bowel sounds
        - Excessive or exaggerated sounds
        - Frequent, loud, low-pitched gurgles
        - High pitched tinkles occurring in a rhythmic pattern with peristaltic activity
        - Silence
    - Succussion splash
        - place the patient supine and place the stethoscope over the epigastrium
        - roll the patient briskly from side to side
        - if the stomach is distended with a fluid, a splashing sound will be heard
        - Can be normal up to three hours after a meal
- Vascular Bruits: listen for turbulent flow
    - Listen lightly above and to the left of the umbilicus for the aorta
    - Listen over the iliac fossae for the iliac arteries
    - Listen over the epigastrium for the celiac and superior mesenteric arteries
    - Listen laterally in the mid-abdomen for the renal arteries
    - Listen over the liver for increased blood flow in liver tumors

The Groins

- Inspection
    - Ask patient to cough and observe for expansile impulse in the inguinal canal
    - If a mass is present, does it extend into the scrotum?
    - If there is a hernia present, observe the relationship of the hernia sac to the pubic tubercle
- Palpation
    - Ask the patient to cough loudly and feel for an expansile impulse in the inguinal area
    - Palpate along the femoral artery for enlarged inguinal lymph nodes
    - Examine any lumps in the groin with the patient both supine and erect
    - If swelling is present in the groin or scrotum, is it tender or nontender?
    - If a hernia sac is present, determine whether it is reducible

- Auscultation
    - If there is a sac protruding into the inguinal canal or scrotum, listen for bowel sounds

The Anus and Rectum

- Correctly position the patient: have them lie in the left lateral position
- Inspection: Separate the buttocks, inspect perianal area and anus. Note perianal skin abnormalities, erythema, weeping skin, white skin, anal skin tags, anal warts (sessile or pedunculated papillomata with red base and white surface), holes, dimples, pus or granulation tissue, anal fissures, perianal hematomas (bluish swelling), tender/red/fluctuant swelling, deformations of the outline of the anus, ulcerations, or prolapsed tissue.
- Palpation (the digital rectal exam)
    - Place lubricant on the gloved index finger of the right hand
    - Place the pulp of the finger (not the tip) flat on the anus
    - Press firmly and slowly, flexing the finger in a slightly backwards direction
    - Feel the tone of the sphincter. Normally it grips the finger firmly
    - Feel for the shallow groove just inside the anal canal which marks the dividing line between the external and internal sphincter
    - Push the finger into the rectum
    - Sweep the finger through a 360 degree circle at 2,5 , and 8cm inwards
    - Repeat this as the finger is withdrawn
    - Feel for thickening or irregularity of the wall of the canal
    - Feel anteriorly in men for the rectovesicular pouch, the seminal vesicles (normally not palpable), and the prostate
    - Feel for any boggy, hard, or irregular swelling
    - Feel the each lateral lobe of the prostate and the median sulcus and determine whether it is rubbery and firm or abnormal (boggy, hard, irregular, nodular)
    - In women feel for the cervix, the pouch of Douglas
    - Inspect the finger after withdrawing

Common Procedures

Procedure Documentation

Before you begin **stop and confirm**: correct procedure, correct site, no contraindications. After you finish, document the procedure in the patient's file: date, time, procedure, indication, site, technique, quantity and quality of specimen, complications.

"25/12/2008 – 10AM. A lumbar puncture was performed to rule out meningitis. A 20g needle was inserted at L2-L3 using sterile technique. 5mL of clear fluid was removed, normal pressure. A dipstick of the fluid revealed negative leukocyte esterase. No complications occurred."

Lumbar Puncture (LP)

Indications: Diagnostic (ruling out meningitis, sub-arachnoid hemorrhage, demyelinating disorders) or therapeutic (ex. cryptococcal meningitis) Patient presents with 2/4 of the following symptoms should have an urgent LP performed: (1) fever (T>38.0) (2) headache (3) altered mental status (GCS<14) and (4) neck stiffness/Kernig/Brudzinski's sign!!! (Fever + headache alone are an indication for LP if MPS is negative or patient already treated for malaria).

Contraindications: Skin infection over puncture site, increase intracranial pressure due to a mass (papilledema, CT scan with mass), bleeding disorders

Technique:

- Position the patient in either the lateral decubitus or upright sitting position. In both positions the patient's spine should be straight and as flexed as possible with forehead bent toward the knees. **Positioning is very important for LP**.
- Identify the puncture site. Palpate the top of the iliac crest and the vertebral interspace located at the same level (L4-L5). Palpate L3-L4, L4-L5 and L5-S1 and mark the interspace that is most open. Conus Medullaris is at L1-L2.
- Sterilize the puncture site around your mark.
- Using a sterile 20g needle (or spinal needle) and sterile gloves, enter at the middle of the interspace. Advance the needle slowly toward the umbilicus and parallel to the ground.
- Once CSF is obtained, estimate the opening pressure based on the flow rate. Collect fluid in at least 3 separate bottles/tubes. Only the 2nd bottle needs to be sterile to be sent for microbiology. Describe the appearance of the fluid in each bottle/tube.
- Place one drop of CSF on a urine dipstick and record results.
- Send the 1st tube to chemistry (1mL) for total protein and glucose. Send the 2nd bottle (5mL) to microbiology for gram stain, culture, sensitivity and AFB (if indicated). Send the 3rd bottle to hematology for cell count and differential.

Complications: Post LP Headache (common, treat with caffeine), nerve root injury (shooting pains, transient), tonsillar herniation/spinal hemorrhage (rare but severe)

Thoracentesis

Indications: **1) Diagnostic**: should be performed for any patient with a moderate-large pleural effusion who have not had a previous diagnostic thoracentesis. **2) Therapeutic**: for patient with

respiratory distress due to large pleural effusion and for patients any patient with moderate-large exudates effusion

Contraindications: Small pleural effusions (<1cm on lateral decubitus film), skin infection over the puncture site, bleeding disorder

Technique:

- Position the patient. Have them sit on the edge of their bed while leaning forward over a bedside table. This posterior approach reduces the risk of lung injury.
- Identify the puncture site by reviewing the CXR and percussing the level of the effusion. Mark a puncture site 1-2 intercostal spaces below this level at the midline (in line with tip of the scapula). **Do not enter below the 8th intercostal space** to avoid the abdominal organs**.**
- Sterilize the puncture site.
- Using a sterile 16 or 18g needle attached to a sterile syringe (5 or 10mL) and sterile gloves, insert the needle at the puncture site **above the rib** to avoid the neurovascular bundle below the rib. Insert the need slowly while drawing back on the syringe. Stop inserting the needle when fluid starts to flow.
- Withdraw 5-10mL of fluid into the syringe for a diagnostic tap. Send 1mL to chemistry for total protein and 4-5mL to microbiology for gram stain, culture, sensitivity and AFB. Also send serum for total protein at same time. Consider sending fluid for cytology if concerned for malignancy.
- For a therapeutic tap, remove the needle but leave the plastic cannula in place and attach it to IV tubing and a urinal bag. Never drain more than 1 liter at a time to prevent reexpansion edema. If more than 1 liter needs to be removed, clamp the IV tubing and wait 4-6 hours before draining another 1 liter. This process can be repeated several times if necessary.
- An urgent CXR should be ordered post procedure if air is aspirated or the patient develops cough, shortness of breath or chest pain.
- Note: Patients with empyema or loculated pleural effusion should have chest tubes or surgical drainage.

Complications: Pneumothorax (common but usually mild, if signs of tension pneumothorax consider immediate needle decompression), hemothorax

Paracentesis

Indications: **1) Diagnostic**: Should be performed on any patient with ascites detectable by examination who has not had a previous diagnostic paracentesis or when concerned for spontaneous bacterial peritonitis. **2) Therapeutic**: **Only** for patients with severe respiratory distress or abdominal compartment syndrome due to massive ascites

Contraindications: Acute abdomen, skin infection at puncture site, pregnancy. Bleeding disorders are generally not a contraindication to paracentesis.

Technique:

- Position the patient either sitting up in bed or lying in the left lateral decubitus position.
- Identify the puncture site. Use either 2cm below the umbilicus (lower risk of bleeding) or McBurney's point in the LLQ (to prevent cecal perforation). Avoid the lateral border of the rectus abdominis muscle. Confirm by percussion that there is fluid at the puncture site.
- Sterilize the puncture site.

- Using a sterile 22g needle (18g for therapeutic paracentesis) attached to a sterile 5-10mL syringe and sterile gloves, enter the skin at the puncture site while pulling the skin 2cm caudal in relation to the deep tissue (**Z line tract approach)**. This helps to skin leakage after the procedure. Advance the needle slowly while drawing back on the syringe. Stop advancing the needle when fluid is obtained.
- For diagnostic tap, remove 5-10mL of fluid in the syringe. For therapeutic tap, remove the needle and attach the plastic catheter to IV tubing and a urine bag. Drain 2-6L as necessary to remove the patient's symptoms.
- Send 1mL to chemistry for albumin and total protein. Send blood for albumin at the same time. Send 5mL to microbiology for gram stain, culture, sensitivity and AFB (if indicated). If concerned for SBP, send 1mL to hematology for cell count and differential. Consider sending fluid for cytology if concerned for malignancy.

Complications: Bowel/bladder perforation, hemorrhage, hypotension (if too much fluid withdrawn), skin leak

Arthrocentesis

Indications: Any patient with a joint effusion who has not had a previous arthrocentesis and whose effusion is not obviously due to osteoarthritis.

Contraindications: Skin infection at the puncture site

Technique

- This is for knee aspiration, which is the easiest
- Identify the puncture site. Place the knee in the extended position (with patient lying supine) and palpate the joint line and the lateral border of the patella. Move 1cm lateral and 1cm inferior from this point.
- Sterilize the puncture site.
- Using a 22g needle attached to a sterile 5-10mL syringe and sterile gloves, slowly advance the needle downward at a 45 degree angle. Draw back on the syringe while advancing until fluid is withdrawn (usually after 1-1.5cm). Remove 10mL. An 18g needle may be necessary to remove the fluid if it is purulent.
- Send 1mL to chemistry for glucose. Send 1mL to hematology for cell count and differential. Send 5mL to microbiology for gram stain, culture, sensitivity and AFB (if indicated). Send 1mL to histopathology to evaluate for crystals.

Complications: Rare.

Cardiology

Congestive Cardiac Failure (CCF)

A complex syndrome caused by a structural or functional abnormality in the cardiac muscle that impairs its ability to function as a pump and meet the metabolic needs of the body. Characterized by shortness of breath, fatigue and signs of fluid retention.

Decreased cardiac output triggers the baroreceptors in the the LV, carotid sinus and the aortic arch . This leads to stimulation of the cardio-respiratory centre in the brains, increased ADH release (causing peripheral vasoconstriction and increases renal salt and water absorption) and increased sympathetic stimulation (activating renin - angiotension system, promoting more water retention and peripheral vasoconstriction). These lead to LV dilatation and hypertrophy (poor ejection fraction), increased peripheral vascular resistance (high afterload) and retention of fluid(high preload).

Most patients present with left heart failure which can progresses to right heart failure. The most common cause of right heart failure is left heart failure but it can also be caused by pulmonary hypertension (cor pulmonale) or disease that effect the RV>LF (like EMF). Heart failure can be either compensated (when the patient is stable) or decompensated (when the patient suddenly gets worse)

Etiology of CHF

Systolic Dysfunction (inability to expel blood)

- Hypertension*
- Ischemic heart disease
- Idiopathic cardiomyopathy (like HIV)*
- Valvular disease*
- Alcoholic cardiomyopathy
- Drug-associated cardiomyopathy
- Myocarditis

Diastolic Dysfunction (abnormal filling)

- Hypertension
- Fibrosis
- Ischemia
- Aging process
- Constrictive pericarditis (like TB)*
- Restrictive pericarditis (like EMF)*
- Hypertrophic cardiomyopathy

* The most common causes in our setting

The New York heart association (NYHA) functional classification

- Class I- no limitation in physical activity
- Class II- slight limitation of physical activity (fatigue, SOB)
- Cass III- marked limitation of activity(comfortable at rest but slight exertion causes symptoms)
- Class IV- symptoms at rest

Diagnosis

- History and clinical examination
- Echocardiography -wall thickness, cavity dimensions, ventricular function (systolic and diastolic), can reveal underlying aetiology
- ECG-Commonly abnormal, Q waves, ST/T changes, LVH, arrhythmias and axis change
- Chest Xray - Cardiomeglay, pulmonary congestions (upper lobe diversions, fluid in the fissures, Kerley B lines, pleural effusions)

Framingham Criteria for CHF

- Validated CHF with 2 major criteria or 1 major and 2 minor
- Major : PND or orthopnea, Elevated JVP, Pulmonary rales, S3, Cardiomegaly on chest xray.
- Minor :peripheral edema, night time cough, dyspnea on exertion (DOE), pleural effusions,HR > 120, weight loss > 4.5 kg in 5 days with diuresis

Causes of CHF exacerbation/decompensation: FAILURE

F: forgot to take medication, ran out of medication

A: arrhythmias (especially atrial fibrillation)

I: ischemia / infarction / infection

L: lifestyle (poor diet)

U: up-regulation (high cardiac output states i.e. pregnancy, thyroid)

R: renal failure (fluid overload)

E: embolism / endocarditis

Treatment

- Counseling
    - Weight loss in obese patients, dietary sodium restriction (< 2 grams a day), fluid restriction, administration of oxygen if needed, exercise as tolerated for class I and II
- Vasodilator therapy: mainstay of chronic therapy; reduces mortality
    - ACE inhibitors (1st line) – but must follow renal function
    - Hydralazine (rarely used)
- Beta-blockers: for chronic therapy in patients with non-valvular CHF; not acute, decompensated heart failure; reduces mortality
    - Carvedilol (best), metoprolol, atenolol
- Digoxin
    - for Class II-III
    - improves symptoms, does not reduce mortality
- Diuretics
    - Loop diuretics (lasix) for diuresis are the primary treatment of decompensated heart failure but do not reduce mortality
    - Aldactone – useful in chronic therapy of patients with Class III-IV; reduces mortality but also greatly increases risk of hyperkalemia in patients who are also taking ACE inhibitors.

Chest Pain

Chest pain is a common symptom and may be a manifestation of cardiovascular or noncardiovascular disease. Full characterization of the pain with regard to quality (squeezing, tightening, pressing, burning), quantity, frequency, location, duration, radiation, aggravating or alleviating factors and associated symptoms can help to distinguish the cause. All patients presenting to a hospital with severe or persistent chest pain should have a full set of vital signs, an ECG, and a CXR. *****The life-threatening causes that must be considered and ruled out in all patients with severe, persistent chest pain.***

Cardiac Causes

Angina/Myocardial infarction **

- Substernal pressure +/- radiation to neck, jaw, Left arm
- Duration usually > 1 minute and < 12 hours for angina
- Associated with dyspnea, diaphoresis, nausea/vomiting
- Worsened with exertion, relieved with rest or nitroglycerin
- Infarction is same as angina except increased intensity and duration
- ECG: look for ST elevations or depressions, T wave inversions

Pericarditis/Myocarditis **

- Sharp pain radiation to trapezius
- Aggravated by respiration, relieved by sitting forward
- Listen for pericardial friction rub
- ECG: look for diffuse ST elevations and PR depressions

Aortic Dissection **

- Sudden onset of tearing chest pain, knife-life pain
- Radiation to back
- Usually severely hypertensive (can become hypotensive)
- Asymmetric blood pressure in arms and asymmetric pulses bilaterally
- Widened mediastinum on CXR, new aortic insufficiency murmur

Pulmonary Causes

Pneumonia **

- A very common cause of chest pain in our settings
- Pleuritic in nature
- Associated with dyspnea, cough, fever, sputum production
- Presents with fever, tachycardia, crackles on physical exam
- CXR should show an infiltrate

Pneumothorax **

- Sharp, pleuritic pain +/- shortness of breath
- Unilateral hyperresonance and decreased breath sounds on one side
- Confirmed by CXR

Pulmonary embolism **

- Pleuritic, sudden onset
- Associated with tachypnea, tachycardia, hypoxemia
- ECG can show T wave inversions V1-V4, RAD, S1Q3T3
- Pulmonary hypertension
- Dyspnea, exertional pressure
- Hypoxemia, Loud P2 sound on heart exam, right sided S3 &S4

GI causes

Esophageal reflux

- Substernal burning, worsened with lying down
- Acid taste in mouth

Peptic ulcer disease

- Epigastric pain
- Hematemesis or melena
- EGD with *H. pylori* test

Biliary disease

- With RUQ pain, nausea/vomiting
- Aggravated by fatty foods
- Needs RUQ ultrasound, liver tests

Pancreatitis

- Epigastric or back discomfort
- Increased amylase and lipase, has risk factors

Musculoskeletal and other Causes

Costochondritis

- Localized sharp or dull pain, tenderness to palpation

Herpes zoster

- Intense unilateral pain often precedes rash, dermatomal rash and sensory findings

Cervical spine disease or arthritis

- Precipitated by motion, asts seconds to hours
- X-rays to confirm

Ischemic Heart Disease (IHD)

Definition

Due to insufficient oxygen supply to the heart. When the oxygen demands of the heart are greater than the amount of oxygen that can be delivered to the heart, ischemia occurs. This is usually caused by a narrowing of the coronary artery either due to plaque accumulation or vasoconstriction. If left untreated it can lead to an infarct (i.e. necrotic, dead tissue).

Pathophysiology

Most commonly IHD is due to atherosclerotic plaque build-up. Over time this causes narrowing of the coronary arteries. This narrowing prevents adequate oxygen supply from reaching the heart and ischemia occurs. This narrowing can either completely occlude an artery causing a STEMI or it can partially occlude one or many arteries usually leading to either unstable angina or an NSTEMI.

Predisposing conditions

Diabetes, HTN, and smoking are all risk factors for atherosclerotic plaque formation, which puts someone at increased risk for ischemic heart disease and a myocardial infarction.

Epidemiology

IHD is much less common in East Africa than it is in the US and Europe. This is likely because the population of East Africa is younger (due to shorter life spans) as well as less diabetes mellitus, hypercholesterolemia and number of cigarettes smoked by smokers.

Symptoms

Patients usually present complaining of chest pain and/or SOB. The chest pain is usually a squeezing pain that often radiates to arms or neck. It can be worsened by exercise and improves with rest or nitroglycerin. Other symptoms include: diaphoresis, nausea, vomiting, palpitations, or lightheadedness.

Anytime a patient has SOB or chest pain, IHD or an MI need to be on the differential

Many times patients, especially women, present with atypical symptoms when they are having an MI. Abdominal pain is a common complaint for women having MIs.

If a woman over 40yrs old comes in with risk factors for ischemic heart disease, include that on your differential even if her symptoms may not be typical

Signs

On physical exam, look for signs of ischemia, heart failure, or atherosclerotic disease

- Signs of ischemia: S4, new MR
- Signs of heart failure: elevated JVP, crackles in lung bases, S3, hypotension, cool extremities
- Signs of atherosclerotic disease: carotid or femoral bruits, decreased distal pulses

Diagnosis

Primarily made via ECG. Key changes on ECG include: ST elevation, ST depression, T wave inversion, or new LBBB. If patient is having a STEMI, the leads with the ST elevation tell you where the infarct has occurred.

- Lead I and aVL: lateral MI (left circumflex is affected)
- Leads II, III, and aVF: inferior MI (right coronary artery is affected)
- Leads V3-V6: anterior MI (LAD if affected)
- Leads V1-V2: septal MI (either distal LAD, left circumflex or right coronary are affected)

Management

This can be divided into care that needs to be given immediately and long term care that will continue after the patient leaves the hospital.

Immediate care

Aspirin 300mg PO STAT, heparin (1000 IU/h), atenolol 50-100 mg PO STAT (goal PR of 60-70), isosorbide mononitrate (ISMN) 20mg PO STAT then BD, morphine prn for pain, O2, and simvastatin 40mg PO

Post-MI care

Aspirin 75 PO OD, clopidogrel 75mg PO OD, atenolol 50-100 mg PO OD, simvastatin 40mg PO OD, captor peril 25 mg PO BD, and you can add ISMN if needed

Valvular Heart Disease

Valvular heart disease involves outflow obstruction or incompetence of one of four valves of heart. The distribution of disease varies greatly based on population and risk factors. The most valvular diseases are Rheumatic, Congenital or Degenerative. **Most common cause of valvular heart disease in Tanzania is Rheumatic heart disease.**

Aortic Stenosis

- **Pathophysiology**: LV hypertrophies in order to overcome outflow obstruction but this compensatory change becomes maladaptive and leads to LV dilatation and CCF
- **Etiology:** 1) rheumatic, 2) calcification of normal valve in elderly, 3) calcification/fibrosis of congenital bicuspid valve
- **Symptoms**: **Mnemonic- Aortic Stenosis Complication** - Early symptoms of Angina, Serious later complication of Syncope and finally the late presentation of Congestive heart failure.
- **Exam:** AS is a harsh crescendo/decrescendo midsystolic (ejection) murmur. It is heard loudest at in the Aortic area (RUSB) with radiation to the carotids. It is heard best with the diaphragm when the patient sits forward. When loud enough it can be heard all over the precordium. The phase during systole which the murmur peaks can help to determine the severity of the disease. An Early- peaking murmur is usually a less stenotic valve where as a late peaking murmur is a more severe stenosis. This occurs because as the valve become more stenotic it takes the left ventricle longer time to generate enough pressure to overcome the stenosis. AS is associated with a narrow pulse pressure (due to lower cardiac outputs), Left ventricular hypertrophy (shifting of the apex beat) and pulsus parvus et tardus (weak and slow upstroke of the carotid pulse indicating flow limitations seen in AS). As the AS progresses the valve will become progressively become less mobile and stenotic causing the S2 to be quieter or even absent. If there is significant delay in the closing of the Aortic valve compared to the pulmonary valve there may be splitting of the S2
- **Investigations :** Severity graded by echocardiogram and symptoms
- **Management: As** symptoms develop prognosis becomes worse and presence of Syncope/CCF/Angina are poor predictors. Surgery is definitive treatment. Medical therapy to releve symptom. Control HTN. Avoid vasodilators (nitrates) and beta-blockers in severe AS.

Aortic Insufficiency/Regurgitation

- **Pathophysiology**: In diastole, blood flows from aorta into LV due to incompetence of aortic valve which increases End Diastolic Volume and Stroke Volume. These changes eventually lead to dilatation of the LV and CCF.
- **Etiology:** 1) rheumatic fever, 2) endocarditis, trauma, connective tissue disease, congenital bicuspid aortic valve, HTN
- **Symptoms:** angina / CCF
- **Exam:** High pitched early diastolic murmur. Starts immediately after the second heart sound and fades away in mid diastole. The murmur radiates from the aortic area to the left lower sternal edge, where is best heard. To Auscultate use the diaphragm of the stethoscope with the patient sitting forward in expiration. The Murmur is associated with a wide pulse pressure (fall in diastole pressure due to the regurgitating blood) and displacement of apex beat.
- **Treatment**: definitive is surgical. Medical therapy includes hydralazine, ACE inhibitors for severe disease and digoxin for CCF.

Mitral Stenosis

- **Pathophysiology:** Stenosis of the mitral valve results in outflow obstruction from the LA to LV and therefore high atrial pressures. These elevated pressures lead to atrial dilatation and often atrial fibrillation. Elevated atrial pressure causes elevated pulmonary pressures and pulmonary symptoms.
- **Etiology:** most common rheumatic heart disease, congenital
- **Symptoms**: SOB, palpitations, dyspnea on exertion, atrial fibrillation or features of CCF.
- **Exam:** Loud S1, low- pitch rumbling mid diastolic murmur. It is best heard at the apex beat with the bell of the stethoscope while the patient lying on the left side.
- **Treatment:** Surgery required if patient symptomatic. Can use beta blockers. Existence of atrial fibrillation OR prior systemic emboli require anticoagulation

Mitral Regurgitation (RHD in 30% of cases, often secondary to ischemia)

- **Pathophysiology**: abnormal coaptation of mitral leaflets creates a regurgitant orifice and a resultant regurgitant volume creating a volume overload of the LA
- **Etiology:** 1) rheumatic heart disease, 2) endocarditis, ischemia, connective tissue
- **Symptoms**: pulmonary edema, progressive shortness of breath, fatigue
- **Exam**: high-pitched, blowing, pansystolic murmur at apex, radiates to axilla. Murmur increases with handgrip and decreases with valsalva. Brisk carotid upstroke
- **Treatment:** surgery in symptomatic severe cases , decrease afterload with ACE inhibitors, hydralazine. Decrease preload with diuretics

Acute Rheumatic Fever and Rheumatic Heart Disease

Acute Rheumatic Fever

Definition

It is a nonsuppurative consequence of a pharyngeal infection by group A Beta hemolytic streptococcus (Strep pyogenes). It commonly occurs 2-3 weeks after throat symptoms in 3-6% of the cases due to immune cross reactivity between the bacteria and the connective tissue. This is disease of the poor, the overcrowded and the poorly housed. The presence of severe disease tends to reflect recurrent episodes of acute rheumatic fever. In most patients with carditis, if the recent attacks could be prevented they would eventually lose their murmur and the heart would return to normal or near normal.

Worldwide an estimated 10-20 million people get acute RF yearly. Rheumatic heart disease is the most common cause of valvular heart disease in the world. Most common in children ages 4-9 years old, but adults can get acute rheumatic fever also.

Diagnosis:

Generally a clinical diagnosis with laboratory confirmation is needed.

Clinical diagnosis:

Jones Criteria: 2 major criteria OR one major + 2 minor criteria **AND** evidence of recent streptococcal infection.

Major Criteria

- Carditis: Occurs in about 50% of the cases and is the most serious manifestation of RF. It may affect only the endocardium, or it can affect all layers of the heart (pericardium to the endocardium). This acute presentation is different from the later sequelae of rheumatic heart disease (mitral stenosis). Congestive heart failure symptoms tend to represent advance disease.
- Arthritis: Occurs in 80% of the cases. Migratory polyarthritis usually of large joints. each affected joint inflamed for less than one week and typically over 6 joints involved
- Chorea: also called Sydenham chorea or St. Vitus dance is seen in 10% of the patients. It's abrupt, purposeless, nonrhythmic, involuntary movements, usually worse on one side. Chorea can occur up to 8 months after strep infection
- Subcutaneous nodules: Firm, painless, non inflamed, variable in size, symmetric when multiple and located over bony surfaces or near tendons, appear earlier in course of ARF and usually only in patients with carditis. This presentation is rare.
- Erythema marginatum: pink, evanescent, non-itchy rash on trunk and limbs, but not on face. Heat brings lesions out. Seen in < 5% of the cases.

Minor criteria

- Fever
- Arthralgia
- Previous rheumatic fever or rheumatic heart disease

Laboratory Diagnosis

- Increase titres of antistreptolysin O**(ASO, most common antibody test used) or strep antibodies
- Positive throat culture for Group A beta-hemolytic strep
- Recent scarlet fever

**Antibodies are better than culture because the culture is often negative. Antibody titer usually peaks at 4-5 weeks after pharyngitis. Cannot use titers as indicator of disease activity after initial illness.

Treatment

- **Acute treatment**: Oral penicillin 500mg BD-TDS for 10 days, or Benzathine benzylpenicillin 1.2 million IM once. Use erythromycin 40mg/kg/day divided in 2-4 doses or a cephalosporin if PCN allergic Treat even if no pharyngitis at the time of diagnosis; culture family contacts and treat if positive
- **Secondary prophylaxis**: Benzathine benzylpenicillin 1.2 million units every 2-4 weeks for approximately 5 years. If penicillin allergy use erythromycin 250mg PO BD. Lifelong prophylaxis is recommended for patients with carditis and residual heart disease.
- **Anti-inflammatory drugs**: These act to suppress the immune response. Aspirin 20-25mg/kg PO QDS 3-6 weeks if no cardiac involvement. For mild carditis 3 months and 6 months for severe carditis. In these severe cases prednisolone 0.5mg/kg QDS can be given for 2 weeks.
- **Heart failure:** as standard
- **Chorea:** Sodium Valproate 10mg/Kg PO BD or haloperidol for 3 months.

Rheumatic heart disease

Rheumatic heart disease occurs 10-20 years after original attack. This is why the peak incidence of rheumatic heart disease is 15 – 30 years of age (since the peak age for acute rheumatic fever is at 4-9 years of age). Probably develops in over 50% of patients with initial carditis due to acute rheumatic fever. Severe rheumatic heart disease usually only occurs after multiple episodes of acute rheumatic fever. Recurrent episodes of inflammation lead to chronic fibrosis and then calcification of the valves. This is why antibiotic prophylaxis after a first episode of acute rheumatic fever is so important.

Pathophysiology

Tiny nodules gather on the valve leaflets in acute rheumatic fever. Over time fibrin deposition occurs and valves thicken or fuse (fibrosis). Another proposed mechanism is acute inflammation causing adhesion of commisures and then degenerative sequelae. A subclinical inflammatory process caused by the stress of chronic turbulent flow due to the deformed valve contributes to the progression of stenosis. With time there is a gradual loss of valve area.

Valve findings and when they occur

Mitral stenosis is most common finding, followed by aortic stenosis. Some studies suggest that over 70% of MS is caused by RHD. Even though stenosis occurs 10-20 years after infection symptoms may be delayed as late as 40 years. If antibiotic treatment is not adequate in ARF (not available vs. more virulent strains causing earlier adhesion of leaflets), onset of symptoms often occurs earlier.

When does the patient need an intervention?

Symptoms drive the need for intervention. Can do closed or open commisurotomy, percutaneous balloon valvulotomy, or valve replacement. Mitral valve replacement should occur in symptomatic patients (NYHA Class III-IV) with severe mitral stenosis

Complications of rheumatic heart disease

- Congestive heart failure: Mortality is related to patient's functional status.
- Atrial fibrillation: occurs in over 45% of mitral stenosis patients
- Pulmonary HTN: mean survival without surgery 2.4 years
- Thromboembolic events: mostly occur in patients with atrial fibrillation, but can happen in normal sinus rhythm in patients with mitral stenosis
- Bacterial endocarditis

Infective Endocarditis (IE)

Infection of the endothelium of the heart, usually but not always limited to the valves. Either subacute (often due to *Strep viridians*) or acute (less common, often due to *Staph aureus*).

Pathophysiology: Infection of the valves with bacteria (or rarely fungi) causes injury to the valve and valvular regurgitation. The bacteria on the valve can form a mass or vegetation. Parts of this can embolize. Immune complexes form with the bacteria. Infection of the endothelium causes 1) persistent bacteremia, 2) valvular disfigurement (with vegetations/regurgitation), 3) septic emboli and 4) immune complex phenomenon.

Predisposing conditions

- **Abnormal valve**: prior endocarditis, h/o rheumatic heart disease, valvular heart disease, congenital heart disease, prosthetic valves. Low virulence organisms such as *Strep viridans.*
- **Abnormal risk of bacteremia (valves may or may not damaged)**: poor dentition, tooth extraction (or other GI/GU procedures breaking mucosal barriers like endoscopy), IV drug use, hemodialysis (organism tend to be more virulent such as *Strep. Pneumoniae or Staph Aureus*). In our settings post-partum pelvic infection and an acute pyomyositis are important are important sources.

Symptoms

- Persistent bacteremia causes fevers, weight loss, night sweats, fatigue. (Nonspecific symptoms).
- Valvular disfigurement can cause symptoms of CCF.
- Septic emboli may cause stroke, renal or renal infarcts, infected joints and pulmonary emboli.
- Immune complex phenomenon can cause arthritis or glomeruonephritis.
- Remember: **Fever + regurgitant murmur = IE until proven otherwise**

Signs

- General - Finger clubbing, Splenomegaly, pallor (anaemia)
- New regurgitant murmurs due to valvular disfigurement- AR and MR are most common.
- Septic emboli : Strokes, acute limb ischaemia, embolic abscesses or mycotic aneurysms, Janeway lesions - nontender, hyperpigmented macules on palms or soles, subconjunctival hemorrhage.
- Vasculitic events (Due to immune complexes formed)
- Splinter hemorrhages in nailbed
- Roth spots (retinal hemorrhage + pale center)
- Osler's Nodes (tender nodules on tips of fingers and toes)
- Glomerulonephritis

Diagnostic studies

- 3 sets of blood cultures from different sites, ideally >1 hour apart, should be drawn before starting antibiotics! In some resource limited settings, obtaining 2 sets of blood cultures may be more feasible.
- Echocardiogram- Floating vegetations seen on affected valves
- FBP with differential, ESR, rheumatoid factor, creatinine, urinalysis
- EKG (to assess for conduction abnormalities)

- Urinalysis to detect renal failure (Microscopic heamaturia and proteniuria)

Modified Duke Criteria

Major

- Sustained bacteremia by organism known to cause endocarditis (at least 2 cultures positive)
- Endocardial involvement documented by either vegetation or new valvular regurgitation seen on echocardiogram

Definitive: 2 major OR 1 major + 3 minor OR 5 minor

Possible: 1 major +1 minor OR 3 minor

Minor

- Fever >38.0 C
- Predisposition (like rheumatic heart disease)
- Embolic phenomena (arterial emboli, septic pulmonary infarct, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, laneway lesion)
- Immunologic phenomena (glomerulonephritis, Osler's nodes, Roth spots, + rheumatoid factor
- Blood cultures that don't meet criteria (only 1 positive)

Microbiology

- Native valve endocarditis, *Strep viridans, Staph aureus and Enterococcus* most common
- The organisms that cause endocarditis are different in:
    - IV drug abusers – *Staph aureus* most common
    - Prosthetic valve endocarditis - *Staph epidermidis* most common <6mo after surgery
    - Immunosuppression – fungi more common

Treatment

- Empiric antibiotics, adjust according to organism and sensitivities, continue for at least 6 weeks after last positive blood culture
- Start with penicillin 1.2g IV 4hrly + gentamicin 60mg BD
- If acute onset add in staph Aureus cover (like Flucloxacillin)
- Surgery may (rarely) be necessary if refractory CCF, persistent/refractory bacteremia, invasive infection, prosthetic valve, fugal infection

Endocarditis Prophylaxis:

Patients with h/o rheumatic heart disease, previous endocarditis, unrepaired congenital heart disease and valve replacement when undergoing dental procedures.

Antibiotics used: amoxicillin 3g PO 60 min prior to procedure OR Clindamycin 600mg if PCN allergy or > 1 course of penicillin in the last mont use of antibiotics.

Arrhythmias (emphasis on Atrial Fibrillation)

Definition: Abnormality in cardiac conduction that can manifest as either change in rate or rhythm

Types and etiologies

Bradyarrhythmia: any rhythm that results in a ventricular rate of less than 60 beats per minute.

Sinus bradycardia: sinus rate of less than 60 beats/minute. Has normal P wave configuration consistent with origin in sinus node area. Etiology: increased vagal tone, hypothyroidism, ischemia, medication such as digoxin, beta blockers, calcium channel blockers

AV Block

- 1st degree: conduction delay within AV node, with prolonged PR interval on ECG > 200 msec. Etiology: medication, CHF, ischemia, electrolyte abnormalities. No therapy needed.
- 2nd degree Type I (Wenckebach): progressive PR interval prolongation before a blocked or dropped beat. Etiology: medication, electrolyte abnormalities, ischemia. If symptomatic, can give atropine.
- 2nd degree Type II: abrupt AV conduction block without evidence of PR prolongation. No change in PR interval and then sudden dropped beat. Etiology: ischemia, conduction system disease. Need pacemaker.
- 3rd degree: dissociation of atrial beats and ventricular beats. Atrial impulses fail to conduct to the ventricle. And ventricle is beating on its own with a slower rate. Etiology: medication toxicity, ischemia, infiltrative disease (sarcoid, amyloid), Lyme disease, Chagas disease. Need pacemaker.

Tachyarrhythmia: any rhythm with a rate in excess of 100 beats per minute

- **Narrow Complex Tachycardia or Supraventricular** (narrow QRS < 120 msec)
    - Sinus Tachycardia. Etiology: pain, fever, hypovolemia, hypoxia, anemia, anxiety, thyroid disease; rate not greater than 220-age
    - AV nodal reentrant tachycardia (AVNRT): reentrant circuit using AV node and accessory pathway, rate can be > 150.
    - Atrial flutter: macro-reentry usually within right atrium (atrial rate is 300 and usually conducts 2:1 for HR = 150)
    - Atrial fibrillation: see below for more
- **Wide Complex Tachycardia** (wide QRS > 120 msec)
    - Ventricular tachycardia: monomorphic (QRS all the same size) or polymorphic Etiology: ischemia, cardiomyopathy, structurally abnormal heart, prior MI

Atrial Fibrillation

Definition: Most common arrhythmia for which patients seek treatment. This is an irregularly irregular rhythm in which the atria depolarize chaotically and are not able to properly contract. The ventricular response to an irregular atrial beat is also irregular and sometimes rapid (i.e. rapid ventricular response).

Types

- *Valvular* atrial fibrillation: usually associated with rheumatic heart disease due to MS or MR with left atrial enlargement; *the most common type in our setting*
- *Isolated* atrial fibrillation: secondary to another illness (hyperthyroidism, PNA, PE, etc.)
- *Lone* atrial fibrillation: age < 65, no history of stroke or HTN, no structural heart disease
- *Paroxysmal* atrial fibrillation: intermittent (less than 24 hours)
- *Persistent* atrial fibrillation: lasts > 7 days or requires cardioversion
- *Chronic* atrial fibrillation: atrial fibrillation is the predominant rhythm
- *paroxysmal, persistent, and chronic afib have the same risk of stroke

Pathophysiology

Commonly originates from ectopic pacemakers in atria around the pulmonary veins. The loss of atrial contraction then leads to heart failure. This loss of atrial contraction also leads to stasis and clots in left atrium which further leads to thromboemboli (like stroke)

Causes and Risk factors of Atrial Fibrillation:

Acute atrial fibrillation:

- Cardiac: heart failure, hypertensive crisis, ischemia, myocarditis
- Pulmonary: acute pulmonary disease or hypoxia (PNA), pulmonary embolus
- Metabolic: high catecholamine states (stress), infection, post-op, pheochromocytoma,
- Thyrotoxicosis
- Drugs: alcohol, stimulants

Chronic atrial fibrillation:

- Age, hypertension, ischemia, valvular disease*, cardiomyopathy, hyperthyroidism, obesity

History: Ask about prior symptoms and onset, history of rheumatic heart disease, symptoms of thyroid disease, alcohol abuse, and prior digoxin use. Symptoms include fatigue, syncope, chest pain, palpitations. Severe symptoms include acute pulmonary edema. Many patients have no symptoms at all. Most symptoms are related to rapid ventricular rate. Look for

Signs: There are 2 important signs of atrial fibrillation are: Irregularly irregular pulse. A pulse deficit of > 10 (The “pulse deficit” = heart rate – pulse rate). Make sure to do thorough cardiac and pulmonary exams

Evaluation

- ECG
- CXR
- Echocardiogram to look for valvular disease, presence of thrombus, left ventricular function
- Thyroid function tests (TSH), creatinine

Treatment

- If patient is hemodynamically unstable, consider electrical cardioversion in the ICU (consider heparin drip if doing cardioversion)
- If low TSH and symptoms of hyperthyroidism, do complete thyroid workup (T3/T4, thyroid ultrasound) and treat atrial fibrillation as below
- *Rate Control (goal heart rate 60-80) – best treatment for most patients

    - Beta blockers (atenolol, propranolol)
    - Calcium channel blockers (verapamil)
    - Digoxin for heart failure patients if blood pressure is low or if severe valvular heart disease is present (but beware of renal dysfunction)
- Rhythm Control – used only for severely symptomatic patients
    - Amiodarone
- *Anticoagulation to reduce risk of stroke. Give in patients with valvular heart disease, prior stroke, or any two of the following (older > 65, hypertension, diabetes, or congestive cardiac failure). Consider simultaneous peptic ulcer disease prophylaxis.
    - Warfarin (goal INR 2.5)
    - Aspirin (if monitoring of INR is not feasible) – technically an antiplatelet drug
- *Thromboembolism prevention: Keeping the INR 2-3 with warfarin reduces risk of stroke by 66% in patients with above risk factors. Always monitor for risk of bleeding.

Introduction to Hypertension

Definition

HTN is simply defined as a persistently abnormal elevation in blood pressure, < 140/90mmHg. HTN is not diagnosed unless BP is elevated on multiple occasions (at least 2-3) or if the patient is complications of HTN (as with patients admitted with hypertensive emergency). We treat HTN because it is a major risk factor for stroke, MI, CCF, CKD, retinopathy and peripheral vascular disease. The risk of hypertensive complications increases continuously throughout the BP range.

Physiology of HTN

HTN is caused by a combination of cardiac output, peripheral vascular resistance and sodium retention (regulated by the renin-angiotensin system). The latter 2 factors are more important. All treatment of HTN targets these factors.

Epidemiology

HTN is a growing problem in sub-Saharan Africa. Early studies indicated HTN was rare in Africa but several recent studies have shown that the prevalence of HTN is now 5-15% (higher in urban areas). One from Tanzania indicated that HTN occurs in 22% of males and 18% of females in Dar es Salaam and 13% of both men and women in rural areas (Edwards et al., 2000)! The average blood pressure in this group was higher than studies from America and Europe!

Types of HTN

- Essential (Primary) HTN – most common (95%) and due to a combination of genetic, environmental factors (salt intake, weight, exercise etc) and age. Usually develops after the age of 30 but can develop earlier.
- Secondary HTN – HTN due to other causes. All patients < 30yo with HTN and those with HTN no sufficiently controlled on 3 drugs should be assessed for these conditions.
    - Renal – most common; can be related to CKD or renal artery stenosis
    - Cushing's syndrome – hypercortisolemia
    - Conn's syndrome - hyperaldosteronemia
    - Coarctation of the Aorta
    - Pheochromocytoma – catecholamine producing tumor
    - Hyperthyroidism or hypothyroidism.

Degrees of HTN

- Mild (Grade 1) = 140-160/90-99mmHg
- Moderate (Grade 2) = 160-180/100-109mmHg
- Severe (Grade 3) = > 180/110mmHg
- Hypertensive Urgency – severe HTN but no end organ damage
- Hypertensive Emergency – severe HTN with end organ damage
    - Usually does not occur unless sudden increase in DBP to < 130mmHg. Was called malignant HTN in the past.
    - Signs of end organ damage can include encephalopathy (confusion with severe HA), blurry vision/retinal hemorrhage, angina, pulmonary edema, aortic dissection and acute kidney injury

Symptoms/Signs

Most patients with HTN are asymptomatic! Symptoms and signs develop only with complications of HTN or in cases of secondary HTN. The only reliable sign of HTN is the blood pressure.

Measuring the BP **– The blood pressure cuff must be large enough so that the bladder of the cuff encircles the arm + 30%!** If the cuff is too small the blood pressure will be falsely elevated.

Diagnosis

HTN is diagnosed if BP is elevated on 3 separate occasions. Once the diagnosis of HTN has been made the following steps tests should be ordered:

- Cr, electrolytes, RBG, cholesterol, ECG, fundoscopy in all patients
- TSH, Renal US (with dopplers), urinary catecholamines/VMA/cortisol, serum renin/aldosterone, CXR, Echo if looking for cause of secondary HTN

Other important concepts

"Burnt out" HTN – Occurs in patients who have had severe, long standing HTN but have now progressed to CCF (usually with dilated ventricles) with decreased systolic function and a blood pressure that is now normal or low.

Treatment of Hypertension

Treatment of Chronic HTN

When to Treat?

- See new WHO guidelines for Prevention of Cardiovascular Disease!
- In general, any patient with severe (Grade 3) HTN and/or signs of complications (stroke, CKD, CAD, CCF, retinopathy etc) should be started on antihypertensive treatment immediately
- Patients with mild to moderate (Grade 1-2) HTN should be given 3 months to see if they respond to behavioral modification first. If BP remains >140/90 they should then be started on antihypertensives.

Counseling

- lose weight (>5kg) if overweight by BMI > 25
- reduce salt intake – no added salt in cooking or at table
- increase physical activity
- Smoking cessation!
- Reduce alcohol intake (<3 units/day)

Patient should also be counseled that, if they start antihypertensives, they will likely need to take medications every day for life to prevent complications. They need to take the medication even if they feel well. If they have side effects they should come directly to see the doctor and not stop the medications until they are seen.

Which drug to start with?

- For most patient, bendrofluazide 5mg PO OD is the best first drug as it is cheap, easy to take and very effective in Africans.
    - Use with caution in patients with DM and gout as bendrofluazide can cause hyperglycemia and hyperuricemia.
- CCBs (like Nifedipine or amlodipine) are all very effective in Africans and is a good first antihypertensive if you want to lower the BP rapidly (as in hypertensive urgency)
- For patients with DM or CCF and a normal or stable creatinine, ACE inhibitors (like captopril or lisinopril) are the best first antihypertensive.
- In patient with CAD, beta blockers are the best first antihypertensive as they reduce the risk of death from CAD
- Of note, most antihypertensives take 2-4 weeks to reach maximal effect so it is good to wait 1 month before increasing the dose of a medicine or adding another one.

What to do if the first drug doesn't work?

- 2/3 of patient with hypertension will require at least 2 drugs to control their hypertension and 1/3 will require 3 drugs
- Always titrate your first drug to its maximum dose first before adding another drug.
- Monitor for side effects
    - ACE inhibitors – monitor creatinine
    - Thiazide diuretics – monitor electrolytes
    - Beta blockers – monitor heart rate

- If the BP remains elevated despite maximal dose of a first drug, add another drug and then titrate this to its maximal dose. Whatever you start with, either thiazides or CCB are good second drugs in most African patients.

What is the goal BP?

- In most patients the goal BP is < 140/90
- In patients with DM or CKD we use a goal BP of < 130/85

Treatment of Hypertensive Urgency and Emergency

In any patient with BP > 220/120 ("Very Severe Hypertension"), assess for signs of end organ damage and consider admission to the hospital. Hypertensive emergency usually does not occur unless DBP > 130. Keep in mind that urgency is much more common than emergency

Signs of End Organ Damage

- Hypertensive Encephalopathy (confusion, headache)
- Acute retinal hemorrhage (sudden onset of blurry vision, massive hemorrhage on ophthalmoscopy)
- Myocardial ischemia or infarction (chest pain, ECG changes)
- Pulmonary Edema (shortness of breath, CXR with pulmonary edema)
- Acute Kidney Injury (recent onset of oliguria or anuria, elevated creatinine, blood on UA)

Treatment Goals

If Hypertensive Urgency (no signs of end organ damage)

- Aim to lower MAP by 25% over 2-3 days using oral medications
- Start with Nifedipine 20mg BD and add other meds as necessary

If Hypertensive Emergency (+ signs of end organ damage)

- Aim to lower MAP by 25% over 1-2 hours using IV medications
- Currently we are using IV Hydralazine drips titrated to goal BP
- Labetalol drips (+ other meds) are better when available
- Once the BP improves, patients can be transitioned to oral medications

Shock & Hypotension

Hypotension is state of **low blood pressure** with systolic blood pressure <90 mmHg (relative hypotension with >30mmHg below baseline, or mean arterial pressure <65.

Shock is a physiologic state characterized by a significant reduction of systemic tissue perfusion ("**decreased perfusion**"), resulting in decreased oxygen delivery to the tissues & organ injury (e.g. brain, kidneys, liver, etc)

Types of Shock:

1. Hypovolemic* – due to loss of fluid or blood
2. Cardiogenic* – due to decreased cardiac contractility
3. Septic* - due to infection
4. Anaphylactic – due to allergic reaction
5. Obstructive – due to decreased blood flow to the left ventricle as in cardiac tamponade or PE
6. Endocrine - Adrenal Insufficiency, pituitary failure etc

* The 3 most common types of shock

Etiology & Pathophysiology

- Shock is due to inadequate blood pressure.
- Low blood pressure is due to inadequate cardiac output or low peripheral resistance.
- Low cardiac output is caused by a problem with heart rate or stroke volume
- Heart rate abnormalities: too fast (tachycardia), too slow (bradycardia).
- Stroke Volume abnormalities: failure to receive (preload), failure to eject (contractility & afterload), inadequate volume
- Low peripheral vascular resistance is due to inappropriate vasodilatation.

Clinical presentation: Cardinal findings in all shock presentations

- Hypotension – Absolute (systolic blood pressure <90 mmHg) or relative (a drop in systolic blood pressure >40 mmHg), which is why a patient may be in shock with a high or normal blood pressure.
- Oliguria –From shunting of renal flow to other vital organs, intravascular volume depletion, or both.
- Change in mental status – A continuum from agitation→confusion/delirium→ obtundation/coma.
- Cool, clammy skin – Compensatory peripheral vasoconstriction redirects blood from the periphery to the vital organs (heart, brain, splanchnic). However, in early distributive shock or terminal shock the skin may be flushed or hyperemic skin due to failure of compensatory vasoconstriction
- Metabolic acidosis – Increased lactate production from anaerobic metabolism when shock progresses to circulatory failure and tissue hypoxia, along with decreased clearance of lactate by the liver, kidneys, and skeletal muscle.

Once the diagnosis of shock has been made, the most important next step is to quickly determine the type of shock. In low-resource settings, this is usually done based on history and physical examination. Some basic investigations may be helpful.

History

Look for underlying causes, try to classify type of shock. Often limited due to confusion or obtundation.

- History of bleeding? Trauma? Hematemesis? Hematochezia? Melena? If so => hypovolemic shock
- History of coronary artery disease? Valvular heart disease? CCF? If so => cardiogenic shock
- History of fever? Pneumonia? Meningitis? => septic shock

Remember that patients may have more than 1 type of shock, for example hypovolemic + septic.

Examination

- General: Ill-appearing? Pale? Confused? Lethargic? Unresponsive? Temperature >38°C or <36°C?
- Neurologic: Meningismus? Focal neurologic deficits?
- Cardiac: Tachycardic (HR>100)? Hypotensive (SBP<100)? Dizziness? Orthostatic hypotension? S3? Murmurs? Extremities warm/well-perfused or cold/blue? Capillary refill brisk or slow? Chest pain?
- Pulmonary: Evidence of pneumonia? Using accessory muscles of respiration? RR>30? Oxygen saturation <95%?
- Gastrointestinal: Abdominal pain? Tense/rigid abdomen (may indicate perforated viscus, hemorrhage, peritonitis)? Rebound? Guarding? Melena or blood on rectal exam?
- Renal: Flank tenderness (pyelonephritis)? Urine output <0.5 mL/kg/h or <30 mL/h?

Diagnostic studies

- Basic chemistry tests (Na, K, Cl, HCO3), Renal function tests, Liver enzymes
- Glucose, arterial blood gas/lactate (if possible)
- Full blood picture (leukocytes & bandemia in sepsis)
- Type and cross
- Septic work up (CXR, blood culture, sputum microscopy culture & sensitivity, urine dipstick, microscopy, culture & sensitivity)
- ECG, cardiac enzymes & echocardiogram.
- Ultrasound – focused assessment with sonography for trauma (FAST)

Management

In schock, the management depends entirely on the type of schock!!! Shock is ALWAYS an emergency and must be treated rapidly.

Direct at most likely underlying cause; see other topics (GI bleeding, fever, meningitis, pneumonia, MI, etc). Usually need:

- **2 large IV cannulas – 18 gauge (green) or greater**
- **Aggressive colloid (NS or LR) fluid resuscitation for hypotension – especially in hypovolemic + septic shock (may require > 10L!!!)**
- **Packed red blood cells if bleeding/hypovolemic shock**
- Foley catheter and monitoring of urine output
- Frequent monitoring of vital signs

- Intubation if in respiratory distress
- Stop any antihypertensives or diuretics. If pressors (dopamine, epinephrine, neosynephrine, etc), if shock is present despite aggressive fluid resuscitation and pressors are available
- If septic: search for source & start empiric antibiotics based on likely type of infection. Give IV fluids
- If hypovolemic: IV fluids, check electrolytes, fix underlying condition (e.g. diabetic ketoacidosis), send for type & crossmatch for urgent transfusion if hemorrhage (hemorrhage is the most common cause of hypovolemic shock).
- If cardiogenic: IV fluids may be harmful, IV lasix and or dopamine may help, fix the underlying problem (e.g. valve replacement).
- If outflow obstruction suspected: IV fluids, urgent ECG, CXR to confirm, thrombolysis for PE, chest tube for tension pneumothorax, percardiocentesis for tamponade.
- If anaphylactic: IV fluids, subcutaneous epinephrine 0.3ml 1:1000 solution if severe, antihistamines, & corticosteroids may help.
- If adrenal insufficiency: give hydrocortisone 100mg TDS x 5/7

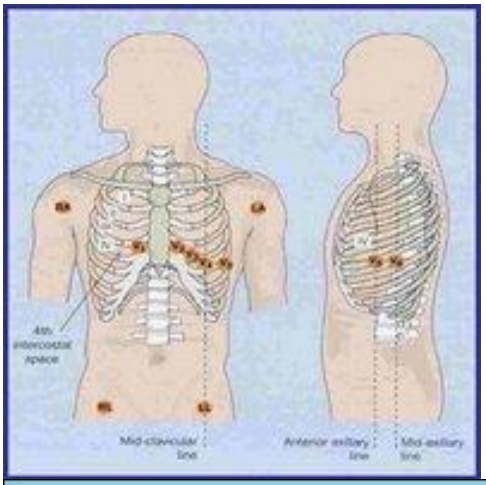
Introduction to Electrocardiograms (ECG/EKG)

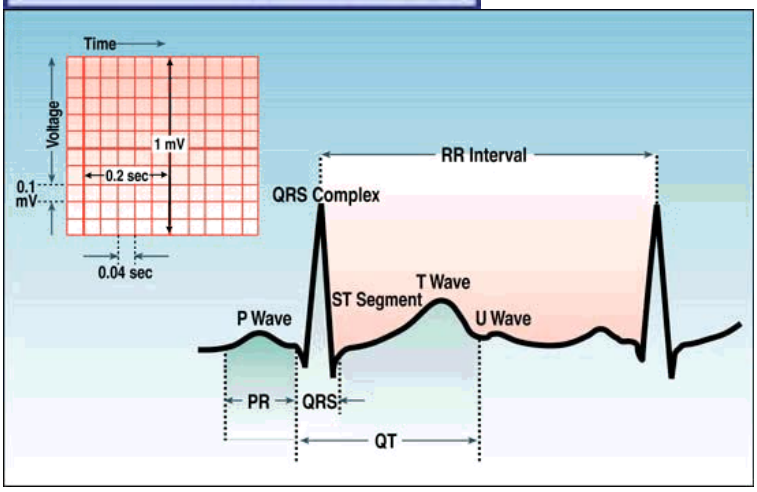
Indications

- Any patient with severe or persistent chest pain should have an EKG to rule out myocardial ischemia or infarction.
- Any patient with irregular cardiac rhythms or abnormal rate should have EKG to determine the type of arrythmia.
- EKGs are also useful in patients with CCF, patients with unexplained shortness of breath (like pulmonary embolism) etc.

How to Perform

Place leads on the patient as seen in diagram:





Basic EKG Interpretation:

**You Must have a systemic approach (FOLLOW SAME PROCESS EVERY TIME).

- **1. RATE**
- **2. RHYTHM**
- **3. AXIS**
- **4. INTERVALS**
- **5. CHAMBERS**

Some Basic Measurements

--one small box is 1mV

--one small box is 40ms (0.04 sec)

- **6. ST CHANGES AND Q WAVES**

1. Rate

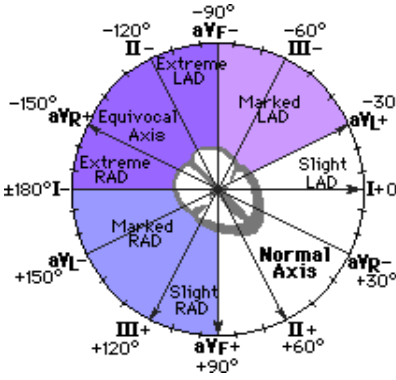
- normal is 60-100
- bradycardia is less than 60
- tachycardia is greater than 100
- Calculate Rate by looking at R waves
- Memorize: 300—150—100—75—60—50
- 300 divided by total number of big boxes

2. Rhythm

- Is the patient in sinus rhythm or not?
- Is the R-R interval regular or irregular?
- Is there a P for every QRS and a QRS for every P?
- Is the P upright in II and downward deflection in V1?

3. Axis

- What is the direction of the depolarization of the ventricle?
- Figure this out by looking at the QRS complex in the limb leads or the frontal plane.
- Normal is –30 to 90.
- Right Axis is greater than 90.
- Left Axis is less than –30.
- Positive complex in I and II means axis is in the normal range.



4. Intervals

- What is the PR interval – normal is less than 200ms (0.2 sec) one big box
- What is the QRS interval – normal is less than 100ms
    - incomplete block is 100-120ms
    - complete block is greater than 120ms
- What is the QT interval – this is rate dependent but should be less than ½ of RR interval.

5. Chambers

- What size are the atria?
    - LAE – look for biphasic P in V1 or notched P in II
    - RAE – look for tall P in II (>2.5mV)
- What size are the ventricles?
    - RVH – look for large R in V1 (R>S in V1)
    - LVH – many different criteria
        - S in V1 + R in V5 > 35mV OR
        - R in aVL + S in V3 >28 in men and >20 in women OR
        - R in aVL >= 11Mv

6. Look for ST Segments and Q Waves

Renal

Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD)

Acute Kindey Injury

Definition

- Increase in the serum creatinine concentration from baseline (>26 mmol/L within 48 hours)
- Percentage serum creatinine increase >50%
- Oliguria of less than 0.5 mL/kg per hour for more than six hours (or <500mL/day for an adult). Normal UOP is approximately 1mL/kg/hour = 1500mL/day for a 60kg adult.

History

- ***Consider these things for all patients. Remember, kidney injury in the hospital is often tied into another problem (infection, heart failure, medications).***
- *decreased or no urine output, flank pain, edema, hypertension, or discolored urine? Hesistancy, frequency?
- *weakness and easy fatiguability (from anemia), anorexia, vomiting, diarrhea, mental status changes or seizures, and edema?
- *fever, cough, dysuria? Bleeding (i.e. melena, blood per rectum)?*new/changed doses in medications?
- Does the patient have medical problems that pre-dispose to CKD (i.e. HIV, diabetes, HTN)

Exam

- Vital signs (including orthostatics), CVA tenderness, Prostate exam

Investigations

- Urinalysis, including microscopic analysis of centrifuged sediment to look for cells.
- BUN and creatinine. Calculated FENa if urine electrolytes available.
- Electrolytes if available
- Abdominal ultrasound (rule out obstruction, assess size and echotexture of kidneys).
- Monitor urine output (UOP). Strongly consider catheterization, especially in setting of enlarged prostate or full bladder on exam.

	Etiologies	U/A, sediment, Indices
Prerenal*	Hypovolemia (bleeding, diarrhea) Systemic vasodilation (infection) Decreased cardiac output (heart failure) Renal vasoconstriction (ACEI, NSAIDS, cirrhosis) Large vessel (thrombosis, embolism, dissection)	Bland (no cells) FEna<1% BUN/Cr>20 (in mg/dL)
Intrinsic	**Acute Tubular Necrosis (ATN)*** Ischemia: prolonged pre-renal Toxins: drugs (aminoglycosides), pigments (rhabdo), protein Contrast induced	Pigmented granular "muddy brown" casts (~75% of cases) FENa>2% (except in pigment and contrast types)
	Acute Interstital Nephritis Allerigc: sulfa, b-lactams, NSAIDs, traditional meds Infection: pyelonephritis Infiltrative: sarcoid, lymphoma, leukemia	WBCs, WBC casts, +/- RBCs +eosinophils in abx induced (~90%) +lymphs in NSAIDs

	Renovascular (small vessel) HUS/TTP, DIC, pre-eclampsia, HTN crisis*, endocarditis	+/- RBCs
	Glomerulonephritis*	**Dysmorphic RBCs & RBC casts**
Post	Bladder neck: BPH, prostate CA, schisto* Ureteral: malignancy, LAD, nephrolithiasis Tubular: precipitation of crystal	Bland US will show dilation of the renal pelvis

*** Most common causes AKI in our setting.**

Treatment Options

- Consider fluid boluses if you think the patient is dehydrated and has prerenal AKI.
- Goal UOP to at least 100mL/hour (but listen to lungs to assess for fluid overload)
- If patient is bleeding, check PT/INR; consider blood transfusion.
- Monitor for uremia (i.e. mental status changes, vomiting), and electrolyte drerangement
- Stop all nephrotoxic agents, such as NSAIDs or aminoglycosides, and adjust meds to GFR.

Indications for urgent dialysis:

- **A**cid-base disturbance (academia)
- **E**lectrolyte disorder (usually hyperkalemia)
- **I**ntoxication (methanol, ethylene glycol, lithium, salicylates)
- **O**verload of volume (pulmonary edema)
- **U**remia (pericarditis, encephalopathy, severe bleeding)

Signs and Sxs of Uremia	
General	Nausea, anorexia, malaise, fetor uremicus, metallic taste, pruritis, uremic frost
Neurologic	Encephalopathy (change in mental status, decreased memory and attention), seizures, neuropathy
Cardiovascular	Pericarditis, HTN, volume overload, CHF, cardiomyopathy, hyperlipidemia, accelerated atherosclerosis
Hematologic	Anemia, bleeding (due to platelet dysfunction)
Metabolic	Hyperkalemia, hyperphosphatemia, acidosis, hypocalcemia, secondary hyperparathyroidism, osteodystrophy

Chronic Kidney Disease (CKD)

Definition: 3 months of reduced GFR and or kidney damage (abnormal pathology, blood/urine markers, or imaging)

Etiologies: Most common etiologies include diabetes, HTN, HIV, glomerulonephritis, polycystic kidney disease, drug-induced, multiple myeloma, progression of AKI (like severe obstruction)

KDOQI Stages of CKD		
Stage	**GFR**	**Goals**
1	>90 *	Dx/rx of underlying condition and comorbidities; slow progression; cardiovascular risk reduction
2 (mild)	60-89	Estimate progression
3 (moderate)	30-59	Evaluate and treat complications

4 (severe)	15-29	Begin preparation for renal replacement therapy (dialysis)
5 (kidney failure)	<15 or on dialysis	Dialysis if uremic

*** with proteinuria**

Complications

- Anemia – due to decreased production of erythropoietin (+ other factors)
- Hyperkalemia – due to decreased potassium excretion
- Hyperphosphatemia / Hypocalcemia – due to decreased phosphate excretion and binding of phosphate to calcium
- Acidemia – due to decreased H+ excretion
- Low Vit D 1,25 / Secondary Hyperparathyroidism / renal osteodystrophy – decreased activation of Vit D causes hyperparathyroidism and painful breakdown of bones
- Edema – due to decreased sodium excretion and hyperaldosteronism
- Uremia - due to decreased excretion of urea and other toxins

Treatment

- Control risk factors for progression of CKD (ex: tight glycemic control if diabetic)
- BP control, goal <130/80, start with an ACEI as first line medication (nephroprotective)
- Monitor for and treat complications: iron +/- erythropoietin to maintain hgb 7-10, low potassium diet / potassium binders, phosphate binders, give Vit D1,25, lasix for edema, dialysis or renal transplant for uremia
- Avoid Nephrotoxins

Estimating the Glomerular Filtration Rate (GFR) using the Cockroft & Gault equation:

Creatinine Clearance (ml/min) = 1.23 x ((140-age) x weight (kg)) / Creatinine (umol/l))

For women = 1.04 x ((140-age) x weight (kg)) / Creatinine (umol/l))

Nephritic & Nephrotic Syndromes

Introduction

Both nephritic syndrome and nephrotic syndrome occur with injury to the glomerulus of the kidney. Either syndrome can be caused by a number of different diseases processes. If you can identify the clinical syndrome as either nephritic or nephrotic, then you have narrowed the etiology of the glomerular disease. This is often the best you can do in a setting where kidney biopsy is not available.

	Nephrotic Syndrome	Nephritic Syndrome
Clinical Picutre	• **Heavy proteinuria (UA 3+ or 4+)** • Minimal hematuria • Generalized oedema (lower extremities, periorbital, ascites, pleural effusions) • Hypoalbuminaemia • Hyperlipidaemi • Normal blood pressure on diagnosis, eventually will progress to HTN	• **Hematuria (recurrent, macroscopic, with red blood cell casts)** • Mild to moderate proteinuria • Oedema • Pyuria • Hypertension on diagnosis
Etiology	• Focal segmental glomerulonephritis • Minimal change nephropathy • Membranous nephropathy • Deposition diseases: amyloidosis, light chain deposition, and fibrillary-immunotactoid disease • Fabry's disease • Other: Diabetes mellitus, leprosy, malaria, drugs, systemic erythematosus	• Postinfectious glomerulonephritis (including poststreptococcal) • Subacute bacterial endocarditis • Lupus nephritis • Antiglomerular basement membrane disease • IgA nephropathy • ANCA small vessel Vasculitis (Wegener's granulomatosis, microscopic polyangiitis, Church-Strauss syndrome) • Membranoproliferative glomerulonephritis • Mesangioproliferative glomerulonephritis
Diagn	• Definitive diagnosis is by renal biopsy • If biopsy not available, must use clinical signs/symptoms, UA, age, sex • Difficult to be certain without biopsy	
Treatment	• Diuretics for oedema ○ Start with Bendrofluazide 5mg daily ○ Add Furosemide 40mg-120mg daily • Lipid lowering agent for hyperlipidaemia • Treat any skin infections early and vigorously • If clots develop use anticoagulants • Attempt high protein diet • Use ace-i to slow proteinuria	• Use ace-I if there is a component of proteinuria and the creatinine is stable • Consider corticosteroid therapy or other immunosuppressive agents (although benefit depends on histologic type)

Specific Treatments	• Minimal Change Disease and Focal Segmental Glomerulosclerosis
	  ○ Prolonged steroids with taper
	• Diabetic Nephropathy
	  ○ Control blood sugar
	  ○ Control blood pressure
	  ○ Use ace-i
	• Others
	  ○ Treat with cytotoxic agents or disease specific treatment
		• Poststreptococcal glomerulonephritis and subacute bacterial endocarditis
		  ○ Supportive care
		  ○ Treat infectious aetiologies
		• Others
		  ○ Treat with some combination of steroids, cytotoxic agents, and plasmapheresis

Treatment in Africa

Minimal Change Disease

Minimal change disease is more common in children than in adults but it is important to attempt the diagnosis of minimal change disease as this is the most treatable form of nephrotic syndrome since it will frequently respond to steroids. Minimal change disease has the usual findings of heavy proteinuria, no red blood cells in the urine. It usually has a normal urea, creatinine, and blood pressure. In addition the proteinuria in minimal change disease is often selective: it will only be albumin. Begin treatment with 60mg of prednisolone daily. You can begin tapering once the proteinuria has resolved (usually within 10-20 days). The oedema usually takes another couple of weeks to resolve. When tapering the prednisolone, aim to stop it by 3-6 months. Some patients will not respond to steroids. You can say they are nonresponders if there is no improvement after two full months of steroids. At that point, you can taper and stop the steroids since they will only cause side effects and will not benefit the patient. Up to 50% of patients who respond will have a relapse within the first year of treatment. Repeat the original regimen for their first relapse.

Focal Segmental Glomerulosclerosis (FSGS)

FSGS is the most common type of nephrotic syndrome in adults in Africa. Some of these patients will also respond to steroids, but much fewer than in minimal change disease. They usually require much longer courses of steroids for improvement (6-9 months).

Prognosis of Nephrotic Syndrome

The 10% of adult patients with minimal change disease have a relatively good prognosis since many of them will respond to steroids. For most other causes of nephrotic syndrome, they will likely progress to renal failure and uremia. Membranoproliferative glomerulonephritis will spontaneously remit in about 1/3 of patients, and another 1/3 will have relapsing nephrotic syndrome with normal renal function if they can get the appropriate treatment. The final 1/3 will progress to renal failure despite treatment.

Hematuria & Schistosomiasis

Hematuria

Definition: blood in the urine (macroscopic = grossly visible; microscopic = only visible with microscope).

Diagnosis

- Check urine dip:
- + blood, +RBCs suggests true hematuria
- +blood, -RBCs suggests myoglobinuria (such as from rhabdomyolysis)

Three important questions:

1. How old is the patient?
    - patients older than 50 years have much increased risk of malignancy (bladder, renal, prostate
    - these patients should be evaluated with urine CYTOLOGY and imaging (CT or IVP)
2. Are there any clues from the history or physical exam?
    - concurrent pyuria and dysuria, consider UTI
    - recent URI, consider post-infectious glomerulonephritis
    - family history of renal disease, consider hereditary nephritis, polycystic kidney disease, sickle cell disease
    - unilateral flank pain radiating to groin, consider ureteral obstruction (kidney stone, clot, cancer)
    - hesitancy/dribbling, consider BPH
    - history of bleeding disorders or bleeding from multiple sites, consider DIC
    - cyclic in a woman, consider menses or endometriosis
    - living in endemic area, consider Schistosomiasis haematobium
    - sterile pyuria with hematuria, consider renal TB
    - elevated creatinine consistent with renal failure
3. Is the bleeding from glomerular or extraglomerular source?
    - glomerular = RED BLOOD CELL CASTS on microscopy
    - also see dysmorphic RBCs and protein >500mg/day
    - glomerular causes include IgA nephropathy, Alport syndrome, thin BM disease, post-infectious glomerular nephritis
    - extraglomerular = only RBC and clots

Schistosomiasis

Schistosomiasis is caused in humans by infection with the mammalian blood flukes or trematodes S. mansoni, S. japonicum, S. haematobium and occasionally S. mekongi and S. inercalatum. S. haematobium causes genitourinary disease. The rest of the species cause intestinal/hepatic disease; of these species S. mansoni is the most common in Africa but S. intercalatum is also present. S. japonicm and S. mekongi are only found in Asia.

Life Cycle

Transmission occurs when humans are exposed to water infested with the intermediate snail host. Schitosome cercariae released from the snails penetrate human skin and enter blood vessels, pass through the lungs into the liver and from there mature into adults. The adults mate and start producing eggs, some of which pass into the urinary tract where they are then passed through the urine back to the outside world. Other eggs embolize in the blood to various sites such as the lung, liver and CNS where they stimulate a strong immune response causing immunopathological disease.

Clinical Features

Egg-induced chronic granulomatous inflammation and subsequent fibrosis can affect many organs:

- Hepatic disease: often occurs in the left lobe. Features include portal hypertension, hepatospelnomegaly, ascites, esophageal and gastric varices.
- Intestinal disease: chronic inflammation of the bowel may cause intermittent blody diarrhea with tenesmus, pseudopolyp formation, hypoalbuminemia, anemia.
- Genitourinary disease: classically “terminal hematuria”, schistosomiasis can causes macroscopic and microscopic hematuria, frequency and dysuria; chronic fibrosis and calcification of bladder can lead to hydroureter and hydronephrosis; chronic inflammation can lead to squamous cell carcinoma of bladder; immune complex deposition can also lead to proteinuria, nephrotic syndrome
- Pulmonary disease: Rare. Embolizing eggs can cause arteritis and pulmonary blood flow obstruction leading to pulmonary HTN.

Management

Chronic disease can be treated with praziquantel 40mg/kg po as a single dose or 20mg/kg PO BD for 1 day. Cure rate is around 70%. Some patients require a second dose.

Electrolyte & Acid-Base Disorders

Hyponatremia

An excess of water relative to sodium, almost always 2/2 elevated ADH (appropriate vs inappropriate).

History & Physical Exam

- The patient may be asymptomatic or may present with confusion, lethargy, muscle cramps or nausea. Hyponatremia can progress to seizures, status epilepticus
- On physical exam look for signs to help assess volume status (vital signs, orthostatics, JVP, skin turgor, mucous membranes, peripheral edema); careful mental status assessment

Workup

- Measure plasma osmolality, BUN and creatinine, uric acid
- Urine osmolality generally not helpful because almost always >300 (although Uosm <100 generally seen in primary polydipsia)
- Now try to determine if the patient has *hypovolemic hyponatremia, euvolemic hyponatremia* or *hypervolemic hyponatremia*

Etiology and Treatment

Hypovolemic hyponatremia: From renal losses (diuretics, salt wasting nephropathy, cerebral salt wasting, mineralcorticoid deficiency) or extrarenal losses (GI losses, third spacing, inadequate intake, insensible losses). Treat with volume repletion with normal saline.

Euvolemic hyponatremia: From SIADH (can be triggered by pulmonary processes, intracranial disorders, certain drugs), endocrinopathies (glucocorticoids deficiency or hypothyroidism), psychogenic polydipsia, low solute diet, or reset osmostat. Treat SIADH with free water restriction +/- loop diuretics, and treat underlying cause. If this doesn't work treat with hypertonic saline.

Hypervolemic hyponatremia: From CHF, cirrhosis, nephritic syndrome, and advanced renal failure. Treat with diuretics and free water restriction.

Remember: Avoid rapid correction of hyponatremia as it can lead to central pontine myelinolysis (spastic quadriplegia, dysarthria, dysphagia). Be especially cautious if you suspect that the patient is chronically hyponatremic. If the pt is asymptomatic, aim for Na correction at a rate of <= .5 mEq/L/h. If they are symptomatic they will need initial rapid correction of Na (2meq/l/hr for the first 2-3 hours) util their sxs resolve. Do not correct the Na more than 10-12 mEq/L/day.

Hypernatremia

A deficit of water relative to sodium (Na >145 mEq/L)

History & Physical Exam

- Pts may report thirst and oliguria or polyuria (depending on the etiology) as well as mental status changes, weakness, focal neurologic deficits and seizures.
- Physical exam may reveal doughy skin; you want to check their volume status (vital signs, orthostatics, JVP, skin turgor, mucous membranes, peripheral edema)

Workup

- Check BUN, creatinine, Uosm, and UNa

Etiology and Treatment

Hypovolemic hypernatremia:

- renal H2O losses: Uosm 300-600, UNa >20; can be due to loop diuretics, osmotic diuresis
- extrarenal H20 losses: Uosm>600, UNa <20; caused by diarrhea, insensible losses (fever, exercise)
- treat the underlying causes and replace free water deficit with hypotonic salne, D5W or oral water depending on volume status. Correction should occur gradually over 48-72 hours to precent neurologic damage secondary to cerebral edema.

Euvolemic hypernnatremia:

- central diabetes insipidus: caused by ADH *deficiency*, Uosm <300-600; etiologies include congenital, trauma/surgery, tumors, infiltrative disease of hypothalamus or posterior pituitary, idiopathic, hypoxia, encephalopathy, anorexia
- nephrogenic diabetes insipidus: caused by ADH *resistance*, Uosm <300-600; etiologies include drugs (lithium, amphotericin, demeclocycline, foscarnet, cidofovir), metabolic (hypercalcemia, severe hypokalemia, protein malnutrition, congenital), tubulointerstitial (postobstructive, recovery phase of ATN, PCKD, sickle cell, sjogrens, amyloid, pregnancy
- Seizures or exercise: Uosm >600; increased intracellular osmoles -> H2O shift -> transient elevation in serum sodium
- Central DI can be treated with desmopressin while nephrogenic DI is treated by treating the underlying cause; you can also try sodium restriction with a thiazide

Hypervolemic hypernatremia:

- Hypertonic saline administration (eg. Cardiac arrest resuscitation with NaHCO3)
- Mineralcorticoid excess: usually presents as mild hypernatremia caused by ADH suppression
- treat with D5W and a loop diuretic

Hypokalemia

Serum potassium is <3.5 mEq/L

Etiology

- Transcellular shifts: Insulin. B-agonists, alkalosis, periodic paralysis (Ca channelopathy), acute increase in hematopoiesis (megaloblastic anemia txd with B12, AML crisis)
- GI losses *plus* metabolic acidosis: diarrhea, laxative abuse, villous adenoma
- Renal potassium losses: diuretics, primary mineralocorticoid excess or sevondary hypoeraldosteronism, DKA, RTA, hypomagnesemia

History & Physical Exam

- May present with nausea/vomiting, fatigue, muscle weakness or cramps, ileus, hyporeflexia, paresthesias, flaccid paralysis

Workup

- 24 hour or spot urine potassium can help differentiate renal from GI losses

- EKG may reveal T-wave flattening, U waves, and ST depression followed by AV block and subsequent cardiac arrest

Treatment

- Potassium repletion: KCl 4 mEq po q4-6h if non-urgent, KCl 10 meq/h IV if urgent; recheck K frequently
- beware of excessive potassium repletion if transcellular shift is the cause of hypokalemia
- treat underlying cause
- replete Mg as necessary

Hyperkalemia

Serum potassium >5 mEq/L

Etiologies

- Transcellular shifts: acidosis, insulin deficiency, B-blockers, dig toxicity, massive cellular necrosis (tumor lysis, rhabdo, ischemic bowel) hyperkalemic period paralysis (Na channelopathy)
- Decreased GFR: any cause of oligo- or anuric acute renal failure or any cause of end-stage renal disease
- Normal GFR but with decreased renal K excretion: CHF, cirrhosis, nephropathy (diabetic, HIV), chronic interstitial nephritis, primary adrenal disorders, drugs (NSAIDS, ACEI/ARBSm potassium sparing diuretics, bactrim), systemic disorders that cause tubulointerstitial disease (sickle cell, SLE, amyloid)
- Iatrogenic (over-repletion of hypokalemia)

History & Physical Exam

- pts may be asymptomatic or may present with nausea, vomiting, weakness, paresthesias, palpitations
- PE may reveal areflexia, flaccid paralysis, paresthesias

Workup

- Verify hyperkalemia with repeat blood draw (unless already have high index of suspicion)
- Check EKG: findings may include tall peaked T waves, PR prolongations, wide QRS, loss of P waves and eventual progression to sine waves, v fib and cardiac arrest!

Treatment

- values of >6.5 mEq/L or EKG changes (especially PR prolongation or wide QRS) require immediate treatment
- calcium gluconate 1-2 amps IV for cardiac cell membrane stabilization
- insulin 10U IV with 1-2 amps D50W to transiently drive K into cells
- Bicarbonate 1-3 amps to transiently drive K into cells
- B2 agonist (albuterol) to transiently drive K into cells
- Kayexalate 30-90 g po/pr to decrease total body K
- loop diuretic (lasix 40 mg IV) to decrease total body K
- dialysis

Gastrointestinal

Acute and Chronic Diarrhea in Adults

Definitions

- Diarrhea: 3 or more loose or fluid stools per day
- Acute Diarrhea: less than 4 weeks. Major causes are infectious agents, toxins, and drugs.
- Chronic Diarrhea: loose stool more than 4 weeks. Can be with or without increased frequency

History

Onset (sudden or gradual), duration, pattern (during fasting, day or night), characteristics, volume, relieving factors, fecal incontinence, fever, weight loss, pain, exposures, travel history, dietary history, antibiotic use, contact with diarrhea, immunopression, family history and risk factors for HIV infection.

Acute Diarrhea with Blood

Bacillary dysentery (shigellosis): Caused by Shigella dysenteriae: children mostly affected. Person to person contact or ingestion of contaminated food. Severe cases: bloody diarrhea with fevers, dehydration, rash. Treatment: ampillicin in severe disease.

Enterohaemmorrhagic Ecoli: Produces vero cell cytotoxin. Most common Ecoli O157:h7. Inflammatory, hemorrhagic colitis, can be complicated by HUS syndrome. Occur in summer mostly, contaminated food. First watery diarrhea, then blood in 2-3 days with vomiting, abdominal pain, decreased platelets, renal failure. No antibiotics indicated.

Camplyobacter Enterocolitis: C jejuni, C.Coli . Contact with animals, poultry. Self limiting disease, usually lasts 5-7 days. Fever, abdominal pain, watery diarrhea followed by blood

Yersinia enterocolitis: yersinia enterocolitica

Salmonella entercolitis: salmonella typhimurium. Among wild and domesticated animals, *associated with malaria and HIV. Nausea vomiting, headache, fever, malaise, diarrhea (watery then bloody), abdominal pain.*patients with schistosomiasis are prone to salmonella bacteremia. When severe, Typhoid: systemic illness. Treatment: supportive, if severe: ciprofloxacin, amoxicillin, chloramphenicol

Amoebic dysentery: entamoeba histolytica, parasite. Fecal oral transmission. Asymptomatic or fulminant colitis with perforation in severe infection. Abdominal pain, increasingly bloody diarrhea. Treatment: metronidazole x 5 days, then diloxanide furoate x 10 days. Extraintestinal manifestations: liver abscess.

Trichuriasis (whipworm): trichuris trichuria. Colonize the colon after ingestion of fecally contaminated soil. Can have vomiting, abdominal distention, blood diarrhea, weight loss. Treatment: albendazole

Causes of Acute Watery Diarrhea (without blood)

Entertoxigenic EColi (ETEC): This is probably the most common cause of non-bloody diarrhea in adults.

Viruses (Rotavirus, Norovirus etc): Rotarvirus is most common cause of non-bloody diarrhea in children and can occur in adults (though less common.

Cholera: vibrio cholera. Causes severe dehydration from voluminous diarrhea, described as rice stool, vomiting, can lead to electrolyte imbalance. Rare but life-threatening. Occurs in outbreaks.Treatment: supportive

Clostridium perfringens: More common in Uganda. 2 types of disease simple diarrhea or nectroic enterocolitis

Giardia: Giardia intestinalis. Infection follow ingestion of cysts in fecally contaminated water. Watery diarrhea is most common symptoms, usually resolves in 2-4 weeks, accompanied with abdominal pain, weight loss

Causes of Chronic Diarrhea

Infections

- Giardia, E. histolytica, stongyloidiasis, cryptosporidium
- Clues as to etiology: Ingestion of stream water (Giardia), undercooked beef (Ecoli O157:H7), undercooked chicken (campylobacter, salmonella), shellfish (norovirus, vibrio).
- HIV related diarrhea – Cryptosporidium, Cyclospora, Isospora
- Tuberculosis of ileocecal area
- Intestinal works/flukes: common in Asia

Medications

- Increased secretion, increased gut motility, change in bacterial flora in the gut and inflammation.
- Common medications: antibiotics, lactulose, NSAIDs, HIV medications

Malabsorption

Impaired absorption of nutrients and fat. Intraluminal mucosal or obstructive malabsorption may cause steatorrhea. Symptoms include voluminous pale, greasy, foul-smelling stools, flatulence, abdominal distention, low albumin, anorexia, weight loss, nutritional deficits, glossitis, anemia. Diarrhea improves with fasting.

- Bile salt deficiency: decrease synthesis: liver disease (cirrhosis)
- Pancreatic insufficiency: most commonly from chronic pancreatitis
- Mucosal abnormalities
    - Celiac sprue: intestinal reaction to gliadin in gluten. Loss of villi and absorptive area. Can present with iron deficiency anemia, rash
    - Tropical sprue: treat with antibiotics, b12/folate replacement
- Whipple's disease: infection with T. whipplei
- Lactulose intolerance
    - Symptoms: bloating, flatulence, epigastric discomfort with eating
    - Treat: lactose free diet, lactase enzyme replacement

Inflammatory

Presents with fever, bloody stool, abdominal pain (acute or chronic). Inflammatory bowel disease: crohn's disease or ulcerative colitis. Ischemic colitis, diverticulitis, colon cancer, lymphoma

Secretory

- No change in diarrhea with fasting, nocturnal diarrhea is frequently described
- Hormonal diarrhea: gastrin (Zollinger-Ellison), thyroxine, serotonin (carcinoid)
- Neoplasm: carcinoma, lymphoma, villous adenoma.

Motility

- Irritable bowel syndrome: recurrent abdominal pain > 3 months with constipation and/or diarrhea
- Hyperthyroidism

Diagnosis

Diagnosis based mostly on history

Treatment

Acute Diarrhea

- Assess for severe dehydration, fever, duration < 5 days, stool with mucus or pus, blood in stool, abdominal pain
- If no to above: then observe, conservative management, oral hydration
- If yes to any of above:
    - begin IVF for dehydration
    - then check stool for fecal leukocytes and culture
    - if infectious etiology: treat according to symptoms and guide therapy through stool culture, for severe illness can give empiric antibiotics, quinolones such as cipro
    - avoid anti-diarrheal medication for bloody diarrhea, risk of toxic megacolon

Chronic Diarrhea

Asses for any culprit medications and lactulose intolerance. For chronic diarrhea, all patients should have rapid test for HIV and stool culture/fecal leukocytes sent. Discontinue any possible culprit medications that may be causing diarrhea.

- negative fecal leukocytes->secretory diarrhea
- positive fecal leukocytes->inflammatory diarrhea (inflammatory bowel disease)
- if diarrhea decreases with fasting->malabsorptive process

Abdominal Pain and Peptic Ulcer Disease

Abdominal Pain

Definition

Abdominal pain describes a broad general process with numerous etiologies. Prompt diagnosis and treatment is crucial for abdominal emergencies. It is important that, as a student, you should learn the differential diagnoses for abdominal pain in different regions of the adomen.

History and Physical Exam

Ask about onset, location, severity, character, radiation, and exacerbating or relieving factors, related symptoms (nausea, vomiting, diarrhea, constipation, flatulence, melena, hematemesis, fever, dysuria, hematuria, chest pain, shortness of breath). Clarify the exact sequence of pain and other symptoms. Physical exam should be thorough and you should examine all four quadrants. All female patients should get a pelvic exam if complaining of lower abdominal pain.

An abdominal xray is a good imaging test to start with for severe abdominal pain or abdominal pain with associated nausea/vomiting. You can order an abdominal x-ray.

Causes of abdominal pain

- **Right upper quadrant pain**: acute hepatitis, liver abscess, duodenal ulcer, appendicitis (high appendix), gallbladder rupture, acute cholecystitis, pyelonephritis.
- **Right lower quadrant pain**: acute appendicitis, duodenal ulcer, pyelonephritis, kidney stone, acute pancreatitis, inflammatory bowel disease, Yersina enterocolitica infection, biliary peritonitis
- **Left upper quadrant pain**: acute pancreatitis, perforated gastric ulcer, splenic rupture, splenic infarct, perinephric abscess, pyelonephritis
- **Left lower quadrant pain**: diverticulitis, inflammatory bowel disease, kidney stone, appendicitis
- **Mid-lower abdominal pain**: perforated appendix, perforated sigmoid diverticulum, large bowel obstruction, colitis.
- **Epigastric pain**
    - generalized pain: typhoid, TB peritonitis, early appendicitis, small bowel obstruction, gastroenteritis, peptic ulcer disease, pancreatitis, duodenal ulcer
    - generalized pain and rigidity (very concerning): perforated gastric ulcer, perforated duodenal ulcer, perforated gallbladder, bowel perforation, ruptured ectopic pregnancy
    - general pain with circulatory shock (very concerning): intrabdominal hemorrhage, ruptured aortic aneurysm, dissecting aortic aneurysm, ruptured ectopic pregnancy, mesenteric ischemia
- **Other causes of abdominal pain**: TB peritonitis, typhoid
- **Less common causes of abdominal pain**: pneumonia, malaria, sickle cell crisis, uremia, thyroid disease, Pott's disease, acute porphyria, tabes dorsalis, diabetic ketoacidosis
- Women with abdominal pain*: (always consider these with lower abdominal pain):-* ovarian torsion, ovarian cyst, ectopic pregnancy, threatened abortion, twisted or inflamed fibroid, dysmenorrheal

Peptic Ulcer Disease

Definition: Mucosal defects of the GI mucosa of the stomach or duodenum. Men and women are at equal risk. The prevalence of PUD is higher in regions where the infection rates of HPylori are higher such as in sub-Saharan Africa.

Pathophysiology: Normally they gastric acid is suppressed by a negative feedback loop. Meal → gastrin mediated acid secretion→ release of somatostatin → inhibition of further gastric acid. In PUD there is too much gastric acid. In addition there is disruption of the protective mucosal barrier. H. pylori and NSAIDs both can disrupt the mucosal layer. H. pylori also decreases somatostatin secretion.

Signs/Symptoms

- Wide range of presentation from asymptomatic iron deficient anemia to perforation
- Epigastric abdominal pain: relieved with food (duodenal) or worsened with food (gastric)
- Usually dull pain, but may be sharp or burning. Can be associated with nausea/vomiting.
- Gastric outlet obstruction can occur with duodenal ulcers
- Can present with upper GI bleed if ulcer is actively bleeding
- NSAID ulcers can present has painless bleeding

Etiology

* H.Pylori infection: 90% duodenal ulcers, 70% gastric ulcers, NSAID use, Gastrinoma (Zollinger-Ellison), alcohol, malignancy, Stress related (ICU patients, stroke, ventilator dependence, immunocompromised) * = most common

Diagnosis

History and physical are helpful. Ask about NSAID, asa, alcohol use, history of Hpylori infection and weight loss. Full blood panel will evaluate for iron deficiency anemia. Upper endoscopy is the preferred method for diagnosing peptic ulcer disease, can also get tissue sampling to evaluate for malignancy and Hpylori. Hpylori can also be detected by urea breath testing and serology. Hpylori stool antigen is useful in detecting eradication after antibiotic therapy.

Treatment

- stop NSAID or aspirin use for at least 3-4 weeks
- start acid suppression with PPI (proton pump inhibitors) such as omeprazole, intial dose can be 20 mg once a day and can be increased to 40 mg twice day for bleeding ulcers
- acid suppression can also be done with H2 blockers on prn basis with ranitidine
- sulcrafate acts by coating mucosal surface without blocking acid secrtion and can be used with PPI
- Hpylori: can treat with omeprazole, amoxicillin or clarithromycin, and metronidzole for 14 days.
- lifestyle changes: stop alcohol and tobacco use
- critically ill patients in ICU should get acid suppression therapy prophylaxis to prevent stress ulcers: usually ranitidine 150 mg BD

PUD Complications

GI bleeding, gastric outlet obstruction, perforation, pancreatitis.

GI Bleeding

- **Hematemesis** is upper gastrointestinal bleeding from site proximal to the ligament of Treitz.
- **Hematochezia**: bright red blood per rectum from rapid upper gi bleed, or very distal lower gi bleed.
- **Melena**: lower gi bleeding that is black in color and has distinct odor. Can be anywhere in gi tract.

Etiology

UGIB: Esophageal Varices (either due to cirrhosis or schistosomiasis) and Peptic ulcer disease (Hpylori, NSAIDs) are most common causes of hematemesis in our settings. Other causes: Esophagitis/gastritis, Mallory-Weiss tears, Arteriovenous malformations, tumors and erosions, Erosive esophagitis (in HIV patients consider CMV, HSV, candida), Dieulafoy's lesions (submucosal artery), gastric vascular ectasis. Aortic-enteric fistula.

LGIB: The most common cause of LGIB is UGIB with passing of blood in stool. Other causes include diverticulosis, angiodysplasia, colitis (infectious or ischemic), AVMs, colon cancer, anorectal disorders.

Signs/Symptoms

- *Acute* upper GI bleed: Will see bright red bloody vomitus. With stasis of blood in stomach, patient will vomit coffee ground like material. As the blood passes through the GI tract, the patient will produce dark, tar like stool called melena and this often time suggest an upper GI source but can also be from other intestinal lesions. Hematochezia (bright red blood per rectum) is more often a lower GI source, however a very rapid upper GI source can produce this. Patients are often hemodynamically unstable.
- *Chronic* slow upper GI bleed can present with hemoccult postive brown stool and chronic iron deficiety anema.
- General: nausea, epigastric pain, syncope, lightheadedness, dizziness, fatigue

Evaluation

- First determine if bleed is acute or chronic. If the bleed is acute, first *evaluate hemodynamic stabiligy.* Check blood pressure and heart rate. Ask about lightheadedness, syncope, dizziness. Check orthostatic vital signs, will be positive is patient with significant blood loss.
- ask about number of bleeding episodes, most recent episode, abdominal pain, weight loss, use of asa, NSAIDs, alcohol, cirrhosis, risk factors for schistosomiasis
- check full blood panel
- do rectal exam to look for bright red blood, melena or hemoccult positive brown stool
- check creatinine
- check PT/PTT/INR for coagulopathy
- may need to place nasogastric tube for localization: if you pull out fresh blood-> acute and active upper GI bleed, if you pull out coffee ground like material -> recent upper GI bleed,
- if you pull out non bloody bilious material -> does not exclude upper gi bleed, may be lower

Management

- establish IV access: 2 large bore IV's or central line placement

- start IV fluids with normal saline if blood pressure is low (if you suspect esophageal variceal bleed, start normal saline cautiously)
- cross match blood and administer packed red blood cells if needed
- place foley catheter to closely moniter urine output, decrease urine output is sign of hypoperfusion, bleeding
- start PPI (proton pump inhibitor), omeprazole 40 mg bid
- correct any coagulopathies, consider giving vitamin K if signs of liver disease. For severe bleeding give vitamin K 5 mg IV stat
- upper/lower endoscopy if available

Liver Disease

Classify by duration of abnormalities: acute (< 6 months) or chronic (>6 months). Liver disease is common in Africa and accounts for high mortality and morbidity. The liver acts as a filter for the blood coming from the portal circulation and is exposed to many microbes and toxins. **Common causes of liver disease in Africa include: viral hepatitis (acute and chronic), cirrhosis (secondary to alcohol and schistosomiasis), and hepatocellular carcinoma.**

Function of the liver

Connected to to the gut by the billary system and portal venous system and to the systemic circulation by the hepatic arteries and veins. Its main functions include

- Metabolism of proteins, carbohydrate, fats and vitamins.
- Storage of glycogen, vitamins and minerals
- Detoxification and inactivation of endogenous and exogenous substances
- Secretion of bile
- Synthesis of coagulation factors.

Examination of the Liver

- Size -normal size is 12cm. Upper border defined by percussion which is normally at the 5th Intercostal space and lower border below the costal margin in the midclavicular space.
- Edge -Regular or irregular
- Surface - Smooth, nodular
- Consistency - Hard or soft or firm
- Pulsatile or not
- Bruit - present or not and position
- If a mass is identified within the live, define its margins , is it fluctuant?

Laboratory Evaluation

- ***Liver (synthetic) function tests:*** PT/PTT, bilirubin, albumin
- Inflammatory/injury tests (liver enzymes): AST/ALT
- Used to determine the following if the liver disease is primary or secondary, due to parenchymal or extrahepatic biliary obstruction, and how progressed the disease has become.
- Due to large reserve, tests may be normal in early liver disease.

AST, ALT: intracellular enzymes released secondary to necrosis/inflammation. ALT more specific for liver than AST (also found in heart, skeletal muscle). ALT > AST more likely viral hepatitis or fatty liver. AST: ALT ratio > 2:1, suggets of alcoholic hepatitis. Increased LDH suggests ischemic or toxic hepatitis.

Alkaline phosphatase: enzyme bound in hepatic canicular membrane. Also inbone and intestines. If from liver GGT will also be increased. High alk phos in biliary obstruction or intrahepatic cholestasis.

Albumin: marker for liver protein synthesis. Decreases in chronic liver disease

Prothrobmin Time (PT): depends on synthesis of coagulation factors. Increased levels found in severe acute injury or chronic injury. Best guide to the prognosis in acute hepatitis.

Bilirubin: product of heme metabolism in liver. Direct/conjugated bilirubin high in obstruction. Indirect/Unconjugated high in hemolysis and decreased conjugation by the liver.

Patterns of Liver Injury

- *Hepatocellular:* marked increase in AST and ALT +/- increased bilirubin(indirect++) in severe forms. AST and ALT > 1,000 is indicative of severe viral hepatitis, acetominophen toxicity or ischemic hepatitis
- *Cholestasis*: increased alk phos and direct bilirubin +/- mild increases in AST and ALT
- *Jaundice*: a clinical sign when bilirubin levels are high > 2.5 mg/dl, if hyperbilirubinemia is conjugated, should see increase in urine bilirubin
- *Fulminant liver failure*: high AST/ALT, alk phos, bilirubin, PT with hepatic encephalopathy.

Clinical Presentation:

1. ***Signs of Cirrhosis: (ie signs of liver dysfunction)*** Jaundice, clubbing, palmer erythema, easy bruising, asterixis, spider nevi, gynecomastia, loss of body hair, testicular atrophy
2. ***Signs of Portal Hypertension:*** splenomegaly, ascites, caput medussae (distended abdominal veins)

Of note, cirrhosis will present with both #1 and 2 whereas schistosomiasis will present with only #2.

Types of Liver Injury

Prehepatic causes

F.malaria, HUS, sepsis, pneumococcal pneumonia, sickle cell disease

Hepatic causes

Viral Hepatitis:

- **Acute**: From asymptomatic to fulminant liver failure. Encephalopathy < 8 wks = poor prognosis.
- **Chronic**: From subclinical persistent to progressive with cirrhosis +/- hepatocellualr carcinoma.
- Signs and symptoms: Anorexia, malaise, nausea, vomiting, fatigue, myalgia, headache, low grade fevers, RUQ pain, jaundice , dark urine/pale stools. Increased AST/ALT first, bilirubin rises later in disease course. Prolonged PT = severe disease
- *Hepatitis A*: fecal oral transmission, serologies: acutely anti HAV IgM, past infection is IgG. Can be a mild illness in children. No chronic carrier state. Treatment is supportive
- *Hepatitis B*: most common in Tanzania, parenteral and perinatal -transmission. Serologies: hep B surface antigen positive = infection. Hep B surface antibody positive: immune to infection. Hep B E antigen positive: high infectivity rate. High rate of progression to hepatocellular cancer. Treatment: in Tanzania is supportive. Can have co-infection with Hep D (needs hep B in order to infect).
- *Hepatitis C:* parenteral transmission (particularly IV drug abuse). Serology: anti Hep C antibody positive. Treatment: pegylated interferon, ribaviron
- *Hepatitis E:* fecal oral transmission. More common in southeast asia. Increased mortality in pregnancy. Serology: IgM anti HEV
- EBV, CMV

Alcoholic Hepatitis

- Usually an acute exacerbation of symptoms in a patient with chronic and excessive alcohol ingestion from.
- **Signs/Symptoms**: RUQ pain, nausea, vomiting, low grade fever, jaundice, leukocytosis, AST: ALT ratio > 2:1, tender hepatomegaly
- **Treatment**: stop alcohol, supportive. If severe injury with hepatic encephalopathy, can treat with steroids x 1 month with taper

Vascular Hepatitis

- Ischemic hepatitis: "shock liver" from severe hypotension (low cardiac output state) from septic shock, cardiogenic shock, AST/ALT > 1000
- Congestive hepatitis: from any cause of right sided heart failure -> passive congestion leading to ischemia and necrosis of liver
- Budd-Chiari Syndrome: occlusion (thrombosis) of the hepatic veins leading to sinusoidal congestion and portal hypertension -> passive congestion and ischemia of liver, necrosis of hepatocytes

Toxin induced Hepatitis

- Paracetomol- usually ingestion > 10 grams to cause clinical syndrome but can occur at 2-6 grams in malnourished and alcoholics. 4-12 hours after ingestion: nausea, vomiting,diarrhea, abdominal pain, shock. Treatment: n-acetylcysteine
- Isoniazid, rifampin, fluconazole, phenytoin
- HIV medications: zidovudine, didanosine, nevirapine
- All statins for hyperlipidemia (stop drug is AST/ALT reaches 3-4 x upper limit)

Genetic Causes of Liver disease

- Hemochromatosis: iron overload with deposition in liver, heart, pancreas. Signs/symptoms: bronze skin coloring, arthritis, CCF, hepatomegaly, cirrhosis. Diagnosis: increased iron saturation (iron/TIBC x 100% > 45%), increased ferriton.
- Wilson's Disease: copper overload. Signs/symptoms: neurological manifestatinos (copper toxicity in brain), movement disorder, psychiatric, Kayser-Fleischer rings (copper deposits in cornea). Diagnosis: low serum ceruloplasmin.

Biliary origin

Primary biliary cirrhosis: autoimmune destruction of intrahepatic ductsPrimary sclerosing cholangitis: cholestasis with fibrosis, stricturing of intra and extra hepatic ducts

Portal Hypertension

Definition

It is established by determining the pressure difference between the hepatic vein and the portal vein. A pressure gradient of greater than 10 mmHg is seen in portal hypertension, and complications can occur when the pressure gradient is greater than 12 mmHg.

Etiology

Most common etiologies in Tanzania for portal HTN are schistosomal portal fibrosis and cirrhosis: other causes include splenic and portal vein thrombosis.

Schistosomiasis

***Pathophysiology in liver disease**:* NON cirrhotic, peri-portal fibrosis of the liver caused by inflammatory response to schistosomal eggs. PRE-sinusoidal portal hypertension.

***Clinical features of hepatic disease**:* often occurs in the left lobe. Most common feature is portal hypertension, severe hepatosplenomegaly, ascites, esophageal or gastric varices. Liver enzymes usually normal with few stigmata of cirrhosis

Diagnosis: history of exposure, eggs in urine or feces.

Treatment: high rate of reinfection so total cure is difficult and retreatment is often necessary. Praziquantel effective against all schistosome species, cure rate is 70%.

Complications Portal Hypertension:

Esophageal Varices

- Pathophysiology: Occurs from development of portal-systemic collateral channels through esophageal veins
- Signs/symptoms: upper GI bleed, high mortalitiy
- Treatment: IV access, packed red blood cells, somatostatin analogues or esophageal balloon if available, endoscopy with banding if available
- Prevention of upper GI bleed in patients with portal HTN is non-selective beta blockers (titrate to goal heart rate less than 25% of baseline). Want to decrease portal pressures to < 12 mmHg. Nitrates can be added if necessary.
- Other sources of GI bleeding: hemorrhoids, rectal varices

Ascites

- Definition: abnormal accumulation of fluid within the peritoneal cavity.
- Pathophysiology: portal hypertenion leads to leakage of fluid into peritoneum, thus leads to a decrease in plasma volume and this leads to sodium retention (via aldosterone).
- Signs/Symptoms: abdominal distention, abdominal discomfort
- Evaluation: physical exam findings of shifting dullness. Abdominal ultrasound will detect fluid if > 100 cc. Paracentesis
    - Paracentesis: diagnostic is indicated in all patients with new ascites, signs of infection (abdominal pain, fever, leukocytosis, acidosis), coagulopathy is not a contraindication

    - SAAG (serum-ascites albumin gradient): if ratio is > 1.1-> portal HTN as etiology of ascites (cirrhosis, schistosomiasis, heart failure, budd chiari) .
    - If ratio is < 1.1 -> peritonitis (TB), peritoneal cancer, pancreatitis
- Treatment:
    - decrease sodium intake (less than 2 grams a day)
    - diuretics: combination of spironolactone and lasix (can increase slowly until goal diuresis of 1 liter a day is obtained)
    - therapeutic paracentesis (large volume): If diuretics are not working and respiratory compromise present. Moniter blood pressure during procedure since removing a lot of fluid can result in hypotension. In most cases, therapeutic paracentesis is not indicated as the benefit is only temporary since the ascites will usually recur almost immediately.
- Complications: spontaneous bacterial peritonitis, > 250 neutrophils on diagnostic tap or positive gram stain, needs IV antibiotics

Splenomegaly

Definition

Splenomegaly is defined as the presence of a palpable spleen in the left upper quadrant of the abdomen. A health spleen measures 11cm in length and lies between the 9th and 11th ribs on the left hand side behind the ribs.The spleen needs to be swollen to twice its normal size in order for it to be palpable. The presence of splenomegaly implies an active inflammatory process for which the underlying course must be determined. However in young children who are otherwise healthy splenomegaly may be due to chronic, asymptomatic *Plasmodium falciparum* malaria.

Three Main Functions of the Spleen

- Filter damaged cells from the blood
- Antibody production
- Provides protection against infection by the process of phagocytosis.

Pathophysiology of splenomegaly

- Phagocytosis of abnormal red cells (haemoglobinapathies).
- Proliferation of the splenic tissue -particular the plasma cells as a result of antigenic stimulation leading to antibody production
- Portal Hypertension- Common in the context of chronic *schistosoma mansoni* infection or Hepatitis B
- Space occupying lesions within the splenic capsule - usually an abscess.
- *Acute splenomegaly* - Tender ,usually the result of a febrile illness -Malaria , septicemia.
- *Chronic splenomegaly*-More firmer and fibrous. Likely due to HIV, Hyper- reactive splenomegaly, malignancy and portal hypertension.

Examination

The size of the spleen should be expressed in centimeters below the left costal margin and should be measure diagonally from the left mid-clavicular line to the tip of the spleen. This is important to indicate the extend of the pathology but also in clinical monitoring of the patients where the spleen is likely to shrink with treatment,

When examining it is important to differentiate the spleen from an enlarged left kidney or any other palpable masses. ***There are 5 clues on physical examination that can differentiate splenomegaly from other abdominal masses.***

1. Spleen moves downwards with respiration and medially with respiration
2. Spleen has a palpable notch on its medial border
3. If the spleen is enlarged it is not possible to delineate its upper border which is covered by the lower ribs
4. The enlarged spleen does not have a band of colonic resonance over it whereas the enlarged kidney does. The spleen is dull to percuss.
5. The spleen is not palpable bimanually in the loin where is kidney can be.

Causes of Massive Splenomegaly

Massive splenomegaly is defined as splenomegaly > 10-12cm below the costal margin. There are only a limited number of diseases that cause massive splenomegaly.

- Infectious: Hyperreactive malarial splenomegaly, visceral leishmaniasis, schistosomiasis,
- Malignancies: lymphoma, CLL, myeloproliferative disorders (PRV, myelofibrosis)
- Reactive: haemoglobinopathies
- Congestive: portal hypertension

Clinical approach to splenomegaly

Splenomegaly is not a diagnosis but a presentation of an underlying pathology. Look for HIV wasting, anaemia, Lymphanopathy, Ascities, Stigmata of chronic liver disease

Examination

- Determine size - Centimeters below the left costal margin (mid-clavicular line) as measure diagonally toward the umbilicus.
- Is it tender (acute infection/infarction)
- Is the spleen soft (acute) or firm (chronic)?
- Shoulder pain - Perisplenitis may be due to splenic infarct.abcess
- Low grade fever and a murmur may indicate Infective endocarditis
- Asses for any ascities and the liver

Investigations

- Blood film for malaria - Interpret with caution especially in high endemic areas
- Full blood picture, liver function test, HIV test, Sickle cell test, blood cultures
- Pheirpheral blood smear to asses cell morphology
- Sputum for fast acid bacilli, bone marrow culture if salmonellae is suspected, Lymph node aspiration/biopsy
- Abdominal USS(periportal fibrosis in schistosomiasis) , echocardiogram is infective endocarditis is suspected.

Nutritional Deficiencies

Definitions

Macronutrient deficiencies – insufficient intake or excessive loss of carbohydrates, proteins or fats leading to either wasting, stunting or both

Micronutrient deficiencies – insufficient intake or excessive loss of vitamins and minerals leading to the syndromes defined below

Causes of weight loss and malnutrition

The syndrome of malnutrition can be a primary compliant or secondary to another illness. The primary reason for malnutrition is a negative balance between dietary intake and physical needs. There are three major underlying factors: lack of food, infectious disease, and caring practices for dependents. These elements seldom occur in isolation and they often reinforce each other.

Infections: malnutrition is both a cause and a consequence of infection. The malnourished become immunosuppressed and so the infections last longer and are more severe. Infections can lead to malabsortion and diarrhea (Giardia, Strongyloides). Infections deplete body stores of vitamin A, C, E. Infection create iron deficiency (hookworm, HIV, tuberculosis)

Measuring malnutrition

Malnutrition is assessed by a combination of clinical features and body measurements.

Indicators used are: wasting (decreased body mass index), stunting (decreased height fore age), wasting and stunting combined (weight for age). BMI = weight (kg) / height (m^2). If <18.5 then there is an increased likelihood of illness

Specific Nutrient deficiencies and their signs/symptoms

Nutrients	Source	Function	Sign/symptoms during deficiency
Iron	Heme-iron = blood, flesh animals Non-Heme iron = green leafy plants, eggs, milk (poorly absorbed but enhanced by vitamin C)	Carries oxygen in hemoglobin	Iron-deficiency anemia (heavy blood loss, hook worms, poor intake)
Iodine	Soil, iodized salt, avoid itrogenenic cassaca and cabbage	Formation of thyroid hormones	Hypothyroidis or multi-nodular goiter in adults (cretinism in infants)
Vitamin A	Animal products (liver), red and yellow fruits	Cell differentiation, rhodopsin production in retina	blindness
Vitamin D	Animal products (liver)	Stimulates intestinal calcium absorption, bone formation	Malabsoption of ca, rickets in children, osteomalacia in adults
Vitamin K	Dark green vegetables	Enables clotting factors	Easy bruising, bleeding

Thiamin (vitamin B1)	Yeast, unrefined cereals, grains, absent in polished white rice	Carbohydrate metabolism, CNS function	Beri-beri: Dry: mixed sensory and motor peripheral neuropathy Wet: high-output RHF
Riboflavin (vitaminB2)	Meat, dairy, fish, eggs	Oxidative metabolism	Angular stomatitis, glossitis, cracking and peeling skin
Niacin (precursor tryptophan)	Eggs, dairy, meat	Glycolysis, fatty acid metabolism, respiration	Pellagra (dermatitis, diarrhea, dementia)
Folate	Green leaves, nuts	DNA synthesis	Macrocytic anemia
Vitamin B6 (pyridoxine)	Animal products, nuts	Protein metabolism, formation of neurotransmitters	Peripheral neuropathy, sideroblastic anemia
Vitamin B12 (cobalamin)	Animal products, absorption requires intrinsic factor	DNA synthesis, degradation of fatty acids	Pernicious anemia, macrocytic anemia, glossitis, peripheral neuropathy
Vitamin C	Citrus fruits, vegetables (baobab, mangoes, oranges)	Formation of protein cross-links in collagen, anti-oxidant	Scurvy (gum bleeding, bruises, poor wound healing)

Treatment of malnutrition

- Whenever possible, use the gastrointestinal tract for feeding (maintains integrity, no atrophy)
- Moniter for refeeding syndrome in severely malnourished patients – hypoPhos, hypoK, hypoMag, heart failure exacerbation, arrythmias, glucose intolerance (treat with small, frequent meals, frequent lab checks and cardiac monitoring)
- Replace GI losses with IV fluids (GI losses = diarrhea, vomiting)
- Treat any underlying infections

If patients has signs/symptoms of specific nutritional deficiency, replace that nutrient orally

Infectious Disease

Introduction to Antibiotics

Beta Lactams

- All have beta-lactam ring
- Inhibit bacterial growth by inactivating enzymes in cell wall synthesis, bind to Penicillin Binding Proteins (PBPs) , usually transpeptidases.

Classes of Beta Lactams

- Penicillins: Effects gram positives without beta-lactamase, mainly strep and staph.
- Anti-staphylococcal penicillins (Methicillin, Oxacillin, Nafcillin, Cloxacillin, Dicloxicillin) bulky hydrophobic R group prevents beta-lactamase from cleaving beta-lactam ring.
- Amino-penicillins (Ampicillin, Amoxicillin) amino group makes drug more hydrophilic, allowing passage through GN cell wall, so covers Gram negatives and Enterococcus.
- Extended-spectrum Penicillins (Carbenicillin, Ticarcillin, Piperacillin, Azlocillin, mezlocillin) much broader gram negative coverage, but must be given at high doses. Effective against Pseudomonas.
- Carbapenems (i.e. Imipenem) Gram positives and negatives, resistant to beta-lactamase, but limited CNS penetration.
- Monobactams (i.e. Aztreonam) only effective against Gram negatives.
- Beta-lactamase inhibitors (i.e. Clavulanic acid, Sulbactam, Tazobactam) inhibit beta-lactamase, these drugs have gram-positive, gram negative, and anaerobic activity.

Resistance to Beta Lactams

- Decreased penetration (outer membrane of Gram negative bacilli = effective barrier)
- Alteration of target site (altered PBPs in pneumococci, MRSA, gonococci, enterococci)
- Inactivation by bacteria (beta-lactamase, now extended-spectrum beta lactamase)

Adverse Effects

- Allergy:
    - Immediate (within 60 minutes) urticaria, angioedema, bronchospasm, anaphylaxis
    - Accelerated (1-72 hours) urticaria
    - Late (>72 hours) rash, serum sickness (rash, fever, arthritis, adenopathy), drug fever
- Derm: morbilliform, erythema multiforme (target lesions), Stevens Johnson Syndrome (mucosal involvement), exfoliative dermatitis
- Other: neurotoxicity (LOC, hyperreflexia, seizures), drug-induced lupus, diarrhea, AIN
- PCN allergy has 15% cross-reaction with cephalosporins, NO cross-reaction with aztreonam

Cephalosporins

Related to beta-lactams, and contain a beta-lactam ring, but is heavily modified.

"Generations" of Cephalosporins

First Generation: (Cefazolin, Cephalexin, Cephradine, Cefadroxil) Good gram positive coverage, poor gram negative

Second Generation: (Cefoxitin, Cefuroxime) improved gram negative coveage, but still not active against *Pseudomonas.*

Third Generation: (Ceftriaxone) improved gram negative, but weak against staphylococcal species.

Fourth Generation: (cefepime) excellent gram negative coverage, regains gram positive function.

Resistance

Inactivation by Beta-lactamases or cephalosporinases, can be *constitutive* or *inducible*.

Side Effect Profile

- Similar to that of Beta-lactams. Has some degree of cross-reactivity with penicillins, estimated 5-10%
- Can also cause some GI distress.

Vancomycin

- Also inhibits cell wall synthesis, but does so with a different mechanism from PCNs
- Binds a peptidoglycan precursor permanently, and may also affect RNA synthesis
- Used for treating gram positive infections, particularly MRSA
- Oral preparation with NO systemic absorption, useful against C. Diff.

Resistance

Modified target via amino acid substitution. Most common in enterococcal species. Becoming much more widespread.

Adverse Effects

- Possible nephrotoxicity, ototoxicity
- Redman syndrome

Fluoroquinolones

- Ciprofloxacin, Levofloxacin, Gatifloxacin, Moxifloxacin, Norfloxacin, Lomefloxacin,
- Directly inhibit bacterial DNA synthesis (inhibit DNA gyrase and topoisomerase IV)
- Covers Gram negative bacteria, some Gram positives, mycobacteria (some coverage may select for resistant TB), atypicals

Resistance

Mutation in chromosomal gene alters target mechanism (encoded subunits of gyrase and topoisomerase) and regulates expression of cytoplasmic membrane efflux pumps or proteins that constitute OM diffusion channels

Adverse Effects

- GI (diarrhea, nausea.vomiting), rash, QT prolongation
- tendon rupture in elderly patients
- FQs implicated in the selection for severe C. Diff/PMC in North America

Aminoglycosides

- Includes drugs such as Gentamicin, Amikacin, Streptomycin
- Function by binding the 30S Ribsomal subunit, preventing bacterial protein synthesis.
- Can also disrupt cell membranes, killing bacteria.
- Very broad spectrum, with gram positive, gram negative, and cell-wall deficient mechanisms of action, has a very narrow TI requiring careful drug level monitoring

Resistance
Plasmid mediated enzymes that phosphorylate the AG, inactivating it.

Adverse effects
- severe nephrotoxicity (QD Dosing),
- ototoxicity

Tetracyclines
- Actively binds the 30S subunit of ribosomes, inhibiting binding of aminoacyl-tRNA.
- Wide range of efficacy, are primarily bacteriostatic.

Resistance
Efflux pumps are present which remove the drug from the inside of the cell.

Adverse Effects
- GI Distress and CDAD/PMC
- Photosensitivtiy
- Hepatotoxicity with higher doses, Nephrotoxicity as well
- Tooth discoloration, as it binds to forming bone

Macrolides
- Includes Erythromycin, Clarithromycin and Azithromycin
- Binds 50S subunit of Ribosome, causing inhibition of protein synthesis.
- Broad spectrum of activity against gram positive, gram negative, as well as cell-wall deficient organisms (mycobacterial, mycoplasma, Chlamydia), can be bactericidal or static depending on concentration.
- Can also affect intracellular organisms as well.

Resistance
Via altered ribosomal RNA target.

Adverse Effects
- Most commonly associated with GI distress, including N/V, diarrhea (improved with taking the medication with food.
- Can also cause a cholestatic hepatitis.
- Ototoxicity

Trimethoprim & Sulfamethoxazole
- Available as a fixed combination pill, with a ratio of 1:5
- Both affect bacterial folic acid synthesis at different points.
- Widespead activity, effective against many gram positive and gram negative organisms as well as PCP, Listeria, brucellosis, and toxoplasmosis.

Resistance
Unclear mechanism, is increasing

Adverse Effects
- Hypersensitivity- rash, ranging from mild to severe

- Hematologic effects include potential marrow supression

Metronidazole

- Initially used only for parasitic infections, including *Trichomonas*, *Entamoeba,* and *Giardia*.
- Is processed inside the parasite, with reduction of a nitro group creating DNA binding activity.- also effective against *C. Difficile*, where it can be used PO or IV with equal efficacy.

Resistance

In vitro only, no known clinical significance.

Adverse Effects

- Anorexia, Diarrhea, GI upset
- neurotoxicity and neuropathies can be seen in longer dosing regimens
- Also causes a disulfram like reaction

Rifamycins: Rifampin

- Inhibits bacterial DNA-dependent RNA polymerase
- Covers Gram positives Strep and Staph, not Enterococcus, some Gram negatives (N. gonorrheae, N. meningitis, M. catarrhalis, H. influenza, not E. coli, Klebs, Enterobacter, Salmonella, Shigella, does not cover any anaerobes

Resistance

Missense mutation in rpoB gene

Adverse Effects

- Hepatitis, Orange discoloration of urine

Fever

- Temperature > 37.5C (axillary or oral) is definied as fever; Temperature > 38.3C usually indicates and infectious etiology [T>38 (neutropenic pts)]
- Fever of unknown origin (FUO): T>38.3 for >3 weeks and after 1 week of inpatient diagnostic workup/3 outpatient visits

Etiologies

- Infection (bacterial, viral, fungal, parasitic)
- Connective Tissue Disease
- Malignancy (leukemia, lymphoma, renal cell carcinoma, metastatic disease)
- Miscellaneous: (DVT/PE, Medications, Drug withdrawal, hyperthyroidism)

History

- Travel, sick contacts, tuberculosis history/contacts, IDS risk factors, pets, occupation, medications, trauma, environmental contacts
- Localizing features: HA, vomiting, diarrhea, cough, hemoptysis, skin rash, joint/bone pains, confusion, sore throat

Physical Exam

Rash, lymphadenopathy, murmurs, hepatosplenomegaly, joint exam, pelvic exam (women with abdominal pain)

Laboratory

- FBP with differential; peripheral smear
- Blood Cultures (3sets sequentially for endocarditis)
- BUN/Cr
- Urinalysis, urine culture
- Rapid Test
- MPS
- Sputum cultures with AFB (pts with cough)
- Fungal Cultures (IDS/immunocompromised pts)
- Stool studies (diarrhea)
- LFTs
- ESR
- ANA/RF
- Fluid analysis (pleural, peritoneal, csf)
- Bone marrow biopsy

Imaging

- CXR
- Echocardiogram (new murmurs)
- Abdominal ultrasound (Abdominal pain)
- Joint xrays
- Arthrocentesis (joint effusions)

Treatment

- Antipyretic
- Cooling blankets for T>39
- Empiric antibiotics for hemodynamically unstable patients in whom infection is the primary concern and in neutropenic/asplenic patients.

HIV/AIDS

AIDS is defined as HIV infection with a CD4 count <200 OR HIV infection with an WHO clinical stage IV opportunistic infection/malignancy regardless of the CD4 count.

Epidemiology

Approximately 40 million people with HIV worldwide. Most with HIV-1—more virulent and widespread. HIV-2 found primarily in West Africa. HIV transmitted through unprotected intercourse (heterosexual and homosexual), from mother to fetus (before, during or after birth (via breast milk), infected blood products, or injections/treatments with unsterile needles/syringes. In Africa heterosexual intercourse is the major mode of transmission for adults.

WHO Clinical Stages

The presence of these opportunistic diseases, infections and malignancies parallels the decline in the patient's CD4 count.

Diagnostic studies

- Rapid preliminary test, 99% sensitive and specific – all are rapid ELISA tests and test for antibodies against HIV; SD Bioline and Determine are used as first line test for HIV in TZ(not useful in children < 18 months and will miss infection in the acute seroconversion period)
- Lab ELISA – used if rapid test negative and concern for HIV is still high
- Western blot – tests for HIV proteins, not currently available. Most specific
- PCR (viral load) – test for presence of HIV virus; qualitative or quantitative
- CD4 count – normal is >800; determines degree of immunosupression

Progression of HIV

At the time of infection the CD4 count drops drastically and the viral load is very high. Then the immune system starts to fight the virus and the viral load decreases to some "set point" and the CD4 increases.The set points determines how fast it will progress. Higher viral load set points means more CD4 destruction. After 5-10 years the CD4 count starts to decline. At this point the patient starts to develop the opportunistic diseases, infections and malignancies listed in the WHO Clinical Stages.

Initial approach to HIV+ asymptomatic patient:

- History: ask about fever, anorexia, weight loss, night sweats, lymphadenopathy, pruritis or rashes, cough, dysphagia/odynophagia, diarrhea, headaches, visual symptoms, seizures
- Physical Exam: temporal wasting, fever, lymphadenopathy; rashes or vesicles (examine the perianal and genitals); oral findings (thrush, hairy leukoplakia), signs of lung consolidation or crepitations; hepatosplenomegaly; peripheral neuropathies or focal neural deficits, cognitive impairment
- Labs: check CD4 and viral load, also consider CBC, creat, LFTs, PPD, CXR; other diagnostic tests as history requires

Work-up of Common Symptoms and OIs in HIV/AIDS

Acute retroviral illness: Occurs in some patients 10-30 days post-exposure. Can be asymptomatic or have glandular fever symptoms (malaise, fever, sore throat, myalgia, anorexia, arthralgia, headache, diarrhea, lymphadenopathy, rash involving the trunk and arms). Symptoms last 3-21 days. Treatment generally supportive. This stage often missed. Some patients with very high viral loads

have severe immunosuppression and present with opportunistic infections which can be life threatening.

Fever: Fever in HIV+ patient can have a variety of causes, some very serious and lethal. History and physical are important in narrowing the differential and if you suspect a life-threatening etiology empiric treatment should be started before lab result are obtained. Diagnostic studies for fever should be guided by CD4 count and history but at minimum the following should be done: **Blood smear for malaria, blood and urine cultures, CXR, UA, FBP, AFB**

Cough and Dyspnea: Persistent cough and/or dyspnea may be caused by bacterial or viral PNA, PCP, pulmonary TB, cardiac failure, bronchitis/asthma, malignancy (pulmonary KS); initial workup should include the following with consideration of further diagnostic tests based on the results. **CXR, sputum for AFB x 3, sputum culture, EKG, CT chest/bronchoscopy**

Dysphagia/Odynophagia: Pain and difficulty swallowing may be 2/2 oropharyngeal or esophageal candidasis, CMV or HSV infection. PE may reveal white curd-like lesions in the oral cavity (thrush) or ulcerations. If the diagnosis is not clear, consider (if available): **Barium swallow, OGD**

Diarrhea: Chronic diarrhea in HIV/AIDS patients can have many etiologies. Bacterial etiologies include bacterial infection with salmonella, shigella, campylobacter, yersinia, and c diff. Protozoal causes incluse giardia, amoebiasis, cryptosporidium and isospora, microsporidium, cyclospora. Other etiologies to consider include CMV, MAC, and AIDS enteropathy. Diagnostic studies should begin with: **stool culture and analysis, colonoscopy with culture and biopsy if available**

Persistent Generalized Lymphadenopathy: LAD may be caused by HIV itself, TB, KS, lymphoma. Investigations should include: **LN aspiration with AFB stain and biopsy, CXR, FBP with differential, ESR**

Skin rashes, sores and pruritis: HIV+ patients are prone to numerous dermatologic conditions. Etiologies include seborrheic dermatitis, HSV or VZV (vesicular rash, may follow a dermatone or be disseminated), cutaneous candidiasis, dermatophyte infections (proximal subungual onychomycosis, virtually pathognomonic for HIV), Kaposi's sarcoma (red-purple nonblanching nodular lesions), molluscum contagiosum (2-5 mm pearly papules with central umbilication) or HPV infection (warts). A diagnosis can often be made based on the physical exam however you can also consider: **skin scraping and microscopic examination (for fungal elements), culture of any discharge**

Altered Mental Status/Severe Headache: Neurological complaints or findings in an HIV+ patient should be taken very seriously as they can have devastating complications however often have treatable etiologies. Meningitis in HIV/AIDS patients can be fungal (Cryptococcus), bacterial, or viral (HSV, CMV). Neurosyphillis can also present with meningitis as well as cranial nerve palsies and dementia. Space-occupying lesions caused by toxoplasmosis, CNS lymphoma, PML, or abscesses may present as headache, focal neuro deficits or AMS. Again, if you have a high index of suspicion for a certain diagnosis do not wait for the lab results to return before starting empiric treatment. **CT scan if available, LP (if able to r/o herniation) including India ink stain for cryptococcal meningitis, serum cryptococcal antigen, RPR, blood cx**

HIV Treatment and OI Prophylaxis

HAART

Types of Antiretrovirals:

- Nucleoside reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Protease inhibitors (PIs)

Initiation

- Before initiating therapy, check a FBP, creatinine, LFTs and CD4 count.
- Initiation of HAART should be considered in the following patients:
    - Those with CD4 count of <200/mm3
    - WHO stage IV
    - WHO stage 3 and CD4 < 350
- As of 2012, the HIV guidelines are being changed and will recommend initiation of ART for all persons with CD4 <350 or WHO clinical stage III or IV

Regimens

HAART regimens usually will consist of an NNRTI + 2 NRTIs *or* a PI + 2 NRTI. The following are recommended ARV combination regimens in Tanzania for ART naïve patients (based on National Guidelines for the Clinical Mgt of HIV/AIDS)

First-line regimens include (exact regimen depends on individual cases)

1. Tenofovir + Emtricitabine (FTC) + Efavirenz (EFV) or Nevirapine (NVP)
2. Zidovudine (AZT) + Lamivudine (3TC) + Efavirenz (EFV) or Nevirapine (NVP).

Efavirenz is preferred for patients on anti-TB. Nevirapine is preferred for pregnant women in the first trimester or women who might become pregnant.

*stavudine (d4t) has been removed from the first line regimens due to severe peripheral neuropathy but is still being used in some parts of Tanzania as Triomune (d4t+3TC+NVP)

Monitoring

- Pt's should be seen 2 weeks after initiation of HAART to check for adverse effects and to have the LFTs and CBC checked.
- CD4 count and viral load should be checked every 6 months.
- Treatment failure (WHO criteria):
    - *Clinical* - Occurs of new or recurrent stage 4 disease after 6-12 months of ART.
    - *Immunological* - Fall of CD4 to pre therapy baseline (or below) or 50% fall from the on treatment peak or persistent CD4 <100 after 6-12 months of ART.
    - *Virologically*-Plasma HIV RNA >5000 copies/ml after 3 months of ART. Virological monitoring is the most accurate to identify early failure but is not readily available in our settings.

Prophylaxis against OIs

- PCP Prophylaxis: Cotrimoxazole should be started in patients with a CD4 < 350 or any WHO Clinical Stage II-IV or unknown CD4 or those with TB or a histor of TB across all CD4 counts.Dosing is 960mg once a day per oral every day.
- TB: All HIV+ patients with a positive PPD who are not on HAART and have no signs of active TB are eligible for TB preventative therapy. You must rule out active TB before starting preventative therapy to avoid drug resistance. Treatment consists of INH 5mg/kd QD + vitamin B6 x 9 months.

Treatment of Specific OI/Complications

- Candidiasis: Treat pharyngeal candidiasis with fluconazole 200mg po qd x 2 weeks. Oral candidiasis can be treated with nystatin oral suspension.
- Pneumocystis pneumonia (PCP): Treat with co-trimoxazole 100-120 mg/kg/day IV/PO in 2-4 divided doses for a total of 21 days. At BMC, we typically give cotrimoxazole 1920mg PO TDS x 3/52 for all adults. Consider adding steroids if hypoxia is present (prednisone 40mg po bid x 5 days followed by 40mg po qd x 5 days followed by 20mg po qd x 11 days)
- Cryptococcal meningitis: Ideal treatment is with treat with IV Amphotericin B 0.7mg/kg/day x 2 plus Flucytosine 50mg/kg/day x 14 days, however, in our setting, this is often not available. In this case reat with fluconazole IV1.2g/day x 2 weeks followed by 400mg po od x 8 weeks. After treatment patients should then be maintained on fluconazole 200mg OD untill CD4 count is >200 or for 6 months.
- HSV: mild/moderate cases can be txd with Acyclovir 400mg po tid x 7 days. More severe cases or recurrent HSV infections should be txd with Acyclovir 800mg five times a day for 5 days.
- VZV: Treat with Acyclovir 800mg 5 times a day for 7 days unless suspect disseminated VZV or ophthalmic nerve involvement in which case treatment should be started with IV acyclovir, 1mg/kg q8h x 7 days
- Toxoplasma encephalitis: Ideal treatment is with a combination of Pyrimethamine and Sulfadiazine but this is often not available in our setting. At Bugando, we treat with cotrimoxazole 1920mg PO BD x 6/52. Life long prophylaxis is recommended.

Tuberculosis (Pulmonary and Extra-pulmonary)

Definition

Tuberculosis is a systemic disease caused by Mycobacterium tuberculosis. The most frequent clinical presentation is pulmonary disease. Extrapulmonary disease may present as lymphatic involvement, genitourinary disease, osteomyelitis, miliary dissemination, meningitis, peritonitis, or pericarditis. Most cases are a result of reactivation of prior infection. Patient has highest risk are those with HIV, diabetes, chronic renal insufficiency, malignancy.

Epidemiology

- Thought to cause ¼ of preventable adult deaths in developing countries
- Causes 2-3 million deaths worldwide per year
- Risk factors (environment): close quarters, low light, crowded, low ventilation
- Risk factors (host): T-cell deficiency, steroid use, malnutrition

Microbiology

- Mycobacteria are slender, curved, aerobic bacilli whose cell wall components make them acid-fast on Ziehl-Neelson staining. Mycobacterium tuberculosis multiplies slowly so that up to 6 weeks are required for culture. Disease due to M. tuberculosis tends to progress slowly, and responds slowly to treatment.
- Cell wall with high lipid content that stains red ("acid-fast")
- Replication time=15-20 hours (compared with <1hour for other bacteria), so visible growth of colonies in culture takes 4-12 weeks

Transmission

M. tuberculosis is acquired by inhalation of microscopic droplets produced by individuals with active pulmonary TB during coughing, sneezing, or speaking. Overcrowded, close proximity contact and poorly ventilated conditions increase the risk of transmission.

Disease Pathogenesis

***TB infection*:** aerosolized droplets containing M. tuberculosis enter alveoli and initiate a non-specific response. The bacilli are ingested by macrophages and transported to regional lymph nodes. The may either be contained there or spread via the lymphatics or bloodstream to other organs. With the development of cell-mediated immunity, cytokines secreted by lymphocytes recruit and active macrophages, which organize into the granulomas characteristic of TB. Granulomas heal in the immunocompetant. Patients with granulomas are susceptible to reactivation at another point in time.

***Active TB disease*:** on average, about 5-10% of adults infected with M. tuberculosis ultimately develop active TB, usually occurring within 1-2 years after infection. HIV is an important risk factor for developing active TB, as is recent infection, diabetes, poverty. These patients may develop systemic disease directly from primary infection.

Reactivation TB: Immune reaction (delayed-type hypersensitivity) leads to tissue destruction at site of replication→cavitating caseated lesions (large numbers of multiplying bacilli encircled by rim of giant cells and granulomas). Most often forms in apex of lung (most highly oxygenated). Cavitations

grow into airways, allowing bacilli now to be aerosolized in droplets and to be spread to outside world. Reactivation patients are the main cause of the spread of TB

Symptoms and signs

- Pulmonary TB: persistent cough, mucopurulent sputum, hemoptysis (only 10%)
- Systemic symptoms: fever, night sweats, weight loss, malaise
- Extrapulmonary TB: nonspecific aside from unilateral cervical lymphadenitis

Clinical Features: Pulmonary TB and Extra-pulmonary TB

***Primary TB*:** symptomatic primary TB is mainly a disease of children and the immunosuppressed. Signs of fever, malaise, cough, particularly in setting of recent TB exposure. A positive smear or culture is uncommon. CXR may show enlarged hilar or paratracheal lymph nodes with or without lung consolidation in lower lung zones.

***Reactivation TB**:* one or more non-specific systemic symptoms are usually present including weight loss, anorexia, fever, night sweats, or malaise.

In HIV negative adults, pulmonary TB is the most common presentation. It is also the most important type of TB epidemiologically since it accounts for the most transmission. TB may affect any organ in the body resulting in organ specific signs and symptoms. Extrapulmonary TB is more common in children and HIV positive patients.

Pulmonary TB: involves the lung parenchyma. History of cough is present in most cases. A cough of long durations > 2 weeks is indication for sputum smear for AFB. Cough may be productive or nonproductive, hemoptysis, chest pain, shortness of breath all possible symptoms. A patient may present looking ill and wasted with fever and tachycardia or look well. Chest exam may reveal localized crackles or pleural effusion. Sputum smear is usually positive in HIV negative patients but often negative in HIV positive patients. Complications include bronchiectasis and lung fibrosis.

***TB lymphadenitis*:** The second most common manifestation of TB. Usually unilateral and involves cervical lymph nodes. Nodes may initially be rubbery and nontender, become fluctuant and can sometimes progress to chronic draining abscesses.

***Pleural TB*:** an effusion can be detected on physical examination and confirmed by xray or diagnostic aspiration. TB is the most common cause of perstistent effusion in Africa in the absence of some other obvious cause. TB effusions are exudates and stained smear shows lymphocytes, but not usually acid fast positive. Pleural biopsy can confirm the diagnosis.

***Bone TB*:** most commonly affects the spine (Pott's disease). Vertebral collapse may ultimately produce a characteristic angular deformity and gibbus. Spinal TB responds well to anti TB treatment alone without surgery.

***Miliary TB*:** most commonly affects HIV patients. History of fever, weight loss and malaise. Physical findings often non specific, can find hepatomegaly, splenomegaly, tachypnea. Chest xray will show tiny nodular opacities. Sputum smear is usually negative. Diagnosis is by clinical suspicion.

****TB meningitis*:** is commonly seen in children or HIV patients. Clinical presentation includes headache, irritability, vomiting, lethargy, or unexplained neurological decline. History is less acute

than bacterial meningitis, meningismus may be mild at first. Cranial nerve palsies can occur as well as seizures. Diagnosis rests on CSF examination with lymphocytosis, raised protein and decreased glucose.

***Abdominal TB*:** gastrointestinal TB may present as partial bowel obstruction with a history of fever. It can occur at any site in the GI tract, common in terminal ileum. *Peritoneal TB* may also be suspected on basis of exudative ascites without another cause. **Adrenal TB* occurs when the adrenal glands are infected and eventually destroyed. This is the most common cause of adrenal insufficiency in our settings and should be treated with steroid replacement.

****Pericardial TB*:** often first suspected on the basis of globular enlargement of the cardiac silhouette on chest xray in patients with cariorespiratory symptoms. Seen more often in HIV positive patients. A pericardial rub or clinical features of cardiac tamponade (elevated JVP, pulsus parodoxus, hypotension) may be present. If untreated, patients can also develop constrictive pericarditis. Constrictive pericarditis risk can be reduced by adding steroids for the first 6-12 weeks of anti TB treatment.

***Genitourinary TB*:** can involve any part of the male or female genitourinary tract. Presentation is subacute and diagnosis requires TB culture or biopsies. Renal TB presents with pain on urination, hematuria, flank pain or mass. The urine contains pus cells but the culture is negative for common bacteria. Genital tract TB in women presents with infertility, pelvic pain, mass or bleeding. Epididymal swelling is most common presentation of genital TB in men.

****Larngeal TB:*** TB infection at the level of the larynx causes airway obstruction. Treatment is intubation, steroids (to decrease the swelling), and anti-TB.

*** = severe forms of EPTB for which steroids should be given**

Tuberculosis Diagnosis and Treatment

Diagnosis

***Sputum smears**:* 3 sputum samples should be examined whenever a cough has been present >2 weeks. Patients should submit 3 specimens within 24 hours: 1 sputum at first presentation (spot), the 2nd the next morning (morning) and the 3rd during following day (spot). 80% of cases will be detected with the first sputum, 15% with the second and 5% with the third.

- looking for acid fast bacilli via Ziehl-Neelsen staining: specific, but not sensitive, particularly if disease has not cavitated
- diagnosis of sputum negative TB: if 3 samples are negative and your suspicion is high, reassess the patient and repeat sputum exam after 1-2 weeks, following a trial of antibiotics and obtained chest xray. Consider alternative diagnoses such as: pneumonia, asthma, chronic bronchitis, bronchiectasis, lung cancer or abscess, non TB complications of HIV

Chest xray: There is no CXR appearance typical for PTB! A normal chest xray makes pulmonary TB less likely but chest xrays cannot distinguish reliably between TB and other diseases. Cavitations are fairly specific for TB, but are often absent particularly in HIV

Tuberculin skin testing (TST): Indicates exposure to TB but not necessarily active disease. Generally not used in adult patients at BMC.

***Culture of M.Tb*:** takes 4-12 weeks; more modern methods with liquid media or BacTec are more rapid and can provide results in <2 weeks.

ESR: nonspecific and should not be used as a routine diagnostic tool

Categories

- Category I – New smear positive PTB or new patients with severe forms of EPTB
- Category II – Relapse, treatment failure, or sputum smear positive after default
- Category III – New sputum smear negative PTB or less severe forms of EPTB
- Category IV – Chronic cases
    - *Severe forms EPTB* – meningitis, military, pericarditis, bilateral or large effusions, spinal, intestinal, GU tract
    - *Relapse* – smear positive after cure
    - *Treatment Failure* – a patient who remains smear positive after 5 months of therapy
    - *Default* – a patient who stopped therapy for > 2 months

Treatment:

Aims of treatment: to cure the patient, to prevent transmission in the patient's family and community, and to prevent development of resistant bacilli

Principles of anti TB therapy

- use at least 2 drugs to which the organism is presumed to be sensitive
- administer treatment for 6-9 months (for pulmonary and extrapulmonary TB)
- ensure the patient completes the full course of therapy

Anti-TB

- Izoniazide (H) – very potent; Major side effect liver toxicity. Peripheral neuropathy more common in diabetics, malnourished, alcoholics, HIV (in these patients give pyridoxine (vitamin B6) 25-100 mg OD)
- Rifampin (R) – very potent; high rate of drug interactions (induces CYP450 and lowers levels of NVP, OCPs, warfarin and anticonvulsants), can also cause hepatitis, red urine and N/V
- Pyrazinamide (Z) - may cause arthralgias, hepatitis
- Ethambutol (E) – less potent and main role is prevention of resistance to other drugs; may cause optic neuritis
- Streptomycin (S) – injectable; can cause ototoxicity/vertigo, local numbness at injection site, renal toxicity; contraindicated in pregnancy

Steroids

- Consider adding steroids if TB meningitis, TB pericarditis (to prevent restrictive pericarditis), pleural TB with large effusion, IRIS
- rare indications: TB laryngitis, massive lymphadenopathy with airway obstruction, renal TB, adrenal TB

Treatment Regimens

- Category I/III regimen: 2 RHZE/4 RH
    - in adults, fixed drug combinations (FDCs) are used
    - 4FDC RHZE contains R150mg/H75mg/Z400mg/E275mg
        - for adults > 50kg: 4 tabs OD x 2 months
        - for adults 31-50kg: 3 tabs OD x 2 months
    - 2FDC RH for daily use contains R150mg/H75mg
        - same as above
- Category III: 2SRHZE/1RHZE/5RH_3E_3
- Category IV: no treatment currently available

Drug resistance

About 5% of TB in Tanzania is resistant to INH. Resistance to both INH and rifampin (so called MDR TB – Multi Drug Resistant TB) occurs in 1%. Extended Drug Resistant (XDR TB) which is resistant to INH, rifampin and streptomycin is increasingly being reported in some parts of the world but has not been reported in TZ.

TB Preventative Measures

- Early diagnosis and treatment*
- DOT to assure that medications are taken*
- Isolation of sputum positive patients in the first 2 weeks of treatment (when possible)
- BCG immunization in infants
- Screening families and close contacts of smear positive patients to detect other cases of TB.
- INH prophylaxis in select populations (like HIV+)
- also help in reducing development and spread of MDR-TB

HIV and Tuberculosis

TB incidence has increased up to 6 fold in areas affected by HIV. TB is the most common cause of death in patients with HIV and the mortality of TB in the setting of HIV is much higher than TB in the absence of HIV. The main mechanism involved is suppression of cell-mediated immunity by HIV which impairs the immune response to TB and leads to increased rates of reactivation of latent TB. Primary TB is also possible. The HIV epidemic has also decreased the average age of TB patients.

Differences in TB among HIV positive patients

Presentation: extra pulmonary TB is more common in this population (50% vs 10% in the general population) so symptoms/signs are often nonspecific

Diagnosis The diagnosis of TB in HIV+ patients is difficult due to 3 main reasons:

1. CXR findings are often non-specific - HIV positive patients are less likely to produce upper lobe disease or cavities. More commonly have hilar adenopathy, effusions, miliary disease or opacities in lower/middle lobes.
2. Sputum for AFB is often negative, particularly if CD4 < 350
3. The possibility of other opportunistic infections (such as PCP) which can present with many of the same features of TB.

Treatment*:* same drug regimen in HIV patients and non HIV patients

- recurrence rates and re-infection is higher in HIV patients
- mortality during and after treatment is also higher in HIV patients
- rifampin lowers serum levels of most protease inhibitors and nevirapine; for this reason, patients on NVP should be switched to EFV if starting anti-TB
- if TB and HIV are diagnosed at he same time, anti-TB should be started immediately and ART should be started after 2 weeks (if CD4<50) or 2 months (if CD4>50) to prevent IRIS.

Malaria

Introduction

Human malaria is caused by 4 species of Plasmodia: P. falciparum, P. vivax, P. ovale and P. malariae. The majority of malaria infection in Africa is caused by P. falciparum while P. vivax infection is more commonly seen in Central America, the Middle East and India. P. falciparum can be associated with severe morbidity and symptoms can progress to coma or death very rapidly. The risk of severe disease is highest among nonimmune individuals, asplenic individuals, children less than 5 and pregnant women.

Tramsmission

Malaria transmission is predominantly via the bite of a female Anopheles sp. mosquito however other mechanisms exist including: congenitally acquired disease, blood transfusion, sharing of contaminated needles and organ transplantation. “Autochthonous” malaria can result if a mosquito feeds on a malaria-infected individual and transmits the infection by biting someone else.

Life Cycle

Sporozoites are transmitted from the salivary glands of the infected mosquito and travel in the host’s bloodstream to the liver where they invade the hepatocytes and multiply asexually to form the Pre-erthyrocytic schizonts which contain thousands of merozoites. When these mature(6-16 days) they rupture into the blood stream releasing the merozoites. These invade the red blood cells and begin to multiple asexually to form erthyrocytic schizonts over a 48-72 hours.Finally, new daughter merozoites are released from the red blood cells which then infect new red cells. With P. vivax and ovale infections, some parasites may lay dormant in the liver(formation of hypnozoites) and can cause late relapse after reactivating after many months; this does not occur with P. falciparum or malariae.Some of the merozoites that enter the RBC do not develop into schizonts but develop into gametocytes. These may persist for many weeks and differentiate into male and female gametocytes. The female mosquito will then ingest these and the cycle will restart.

Pathogenesis

Malaria is a multi system disease and not all aspect of its pathogenesis are completely understood. As the most death occur due to falciparium the below section will focus on its the pathogenesis.

Exponential parasite growth and red cell destruction

Red cells of any age can be invaded by the parasite. Falciparium has a short erthyrocytic cycle of 48 hours causing large destruction of red cells and a rapid increase in the merozoites. In addition there is also death of non infected cells and bone marrow suppression and hypoglycemia due to high parasite burden Combined these factors lead to severe anemia leading to hypoxia and metabolic acidosis

Sequestration of infected red cells

This is a characteristic feature of *P. Falciparum* . There is accumulation of mature parasites in capillary and post capillary venules in many tissues of the body including the brain, muscles and kidneys. There parasitic cells adhere to one another, to non-parasitized cells and to capillary endothelial through cytoadherence receptors. This leads to tissue hypoxia which contributes to the metabolic acidosis.

Cytokine activation

There is a significant increase in a number of pro inflammatory cytokine factors in particular TNF.There is is a clear relationship between their concentration and the severity of illness seen.The mechanism of damage are likely to include direct effects on cellular metabolism and stimulation of the release of other toxins.It is also thought the cytokine factors release act to up regulate the cytoadherence of cells contributing to the sequestration process and its consequences.

Immunity

Immune responses occur following infection with malaria and individuals living in endemic areas may develop partial immunity to disease following repeated infections. This does not prevent repeat infection, however the severity of symptoms is typically limited. This partial protection wanes quickly after leaving an endemic area. The main at risk groups are children under the age of 5 and pregnant women Particularly primigravidas and those with HIV.Natural immunity is found in those with sickle cell trait and G6PD deficiency.

Clinical Manifestations

Symptoms of malarial infections develop only with the erythrocytic stage thus patients may remain asymptomatic after being bitten by an infected mosquito anywhere from 1-4 weeks. Signs and symptoms are varied but typically include fever, chills, sweats, headache, myalgias, fatigue, nausea, vomiting, abdominal pain, diarrhea and cough. Febrile paroxysms often are daily and irregular early in infection however will typically become coordinated with the release of merozoites from the infected cells and then can typically occur every other day. Anemia, thrombocytopenia, splenomegaly, hepatomegaly and jaundice can develop and splenic rupture can occasionally occur. Cerebral malaria can present as an impaired state of consciousness and/or seizures and can result in coma and death. It is universally fatal if untreated and even with treatment has a 20% mortality rate with most of the death happening in the first 24 hours. Up to 10% of patients who survive will have persistent neurologic abnormalities. Risk factors for cerebral malaria include age (children and older patients), pregnancy, poor nutritional status, HIV infection, transmission intensity and h/o splenectomy. Other complications of P. faliciparum infection include renal failure, pulmonary edema/ARDS, hypoglycemia, anemia and bleeding and gastroenteritis.

Diagnosis

- Light microscopy of a Giemsa-stained thick and thin blood smear. First smear is postive in 95% of the cases. Because of the cyclical nature of the parasitemia, smears should be taken every 6-12 hours for 48 hours .The thick smear is more sensitive in diagnosis malaria and the thin smear allows examination of the morphology of the parasite (for species identification) and quantification of the percent of parasitized red cells.
- Rapid diagnostic test -Detects parasite specific antigens or enzymes , some can differentiate species.
- Other lab abnormalities that can be seen with malaria include evidence of anemia, hemolysis, thrombocytopenia, hyperbilirubinemia, abnormal renal function, mildly elevated transaminases, elevated LDH, and sometimes evidence of DIC.
- WHO criteria for severe malaria (1 or more of the following)

Clinical features	Laboratory findings
Prostration	Hypoglycemia < 2.2
Abnormal spontaneous bleeding	Metabolic acidosis (HCO3 < 15)
multiple convulsions	severe anaemia < 5
Pulmonary edema	Hyperparasitemia >5%
respiratory distress	serum lactate >2
impaired consciousness	renal impairment Cr > 265
Shock	Heamoglobinuria

Treatment

Treatment of malaria involves supportive measures as well as specific anti-malarial drugs. Patients with P. falciparum malaria should have their treatment commenced without delay and generally should be admitted to the hospital so that they can be observed for any evidence of complications. Severe malaria should be managed in the ICU where close monitoring, fluid resuscitation and electrolyte balance can be achieved. Thick and thin smears should be examined routinely to monitor the efficacy of therapy until the parasitemia is below 1%. Follow-up smears at 3, 7 and 28 days should be obtained to rule out recurrence or incomplete clearance of parasitemia.

Uncomplicated/non severe malaria

- First line -ACT bases therapy- 3/7 (In TZ, ACT = ALu (Artemether/Lumefantrine)
- Pregnancy - 1st trimester quinine, 2nd and 3rd ACT (although Quinine given in all 3 trimesters according to current TZ guidelines)

Complicated/severe malaria

- IV Artesunate or
- IV Quinine
- With both cases there should be follow up oral ACT for 7/7

Meningitis

This is a clinical syndrome that results from the inflammation of the meninges which can be caused by a wide range of organisms- Bacterial, viral, years helminths and rarely in some cases due to non infected causes such as SLE, sarcoid and Behcets. **In Africa acute bacterial meningitis is the most important form of acute meningitis but chronic meningitis is also common.**

Acute Bacterial Meningitis

Definition

Bacterial infection of the subarachnoid space

Microbiology

S. pneumoniae is the most common cause in adults followed by *N. meningitidis* and *H. influenza*. *Listeria* can be seen in the elderly, alcoholics, or patients with immunosuppression or malignancy. GNR and *staph* infections are rarer, they are usually a nosocomial or post-procedural infection (ie: after neurosurgery) but again must be kept in mind when dealing with an immunocompromised patient.

Clinical Manifestations

- fever
- headache, stiff neck and photosensitivity
- altered mental status
- seizures
- Focal neurology - localising signs - often CN V1palsy
- 2 out of 4 of these symptoms will be present in 95% of patients presenting with meningitis however keep in mind that the elderly and immunocompromised (ie: HIV+) may have an atypical presentation with lethargy and confusion as their primary symptoms and no fever
- Also bear in mind that those present comatose often have a poor prognosis.
- Crytococcal meningitis tends to produced a profound headache.

Physical Exam

- nuchal rigidity, kernig's and brudzinski's sign
- focal neuro findings
- fundoscopic findings (papilledema, absent venous pulsastions)
- rash: maculoapular, petechial or purpuric (may be associated with *N. Meningitidis*)

Diagnostic Studies

- blood cultures
- LP with gram stain and culture; consider a head CT to r/o mass effect before performing an LP if there is a presence of high-risk features (age >60, immunocompromised, h/o CNS disease, new onset seizures, altered mental status or focal neurological findings). However it should be noted that in pts with mass effect herniation may occur even without LP and may not occur even with LP. Also do India Ink staining to assess for crytococcus meningitis
- Serum Crytococcal antigen

CSF Findings in Meningitis

Condition	Appearance	Pressure	WBC/mm3 (Predom Type)	Glucose	Protein
Normal	Clear	9-18	0-5 (lymphs)	50-75	15-40

Bacterial	Cloudy	18-30	100-10,000 (polys)	<45	100-1000
TB	Cloudy	18-30	<500 (lymphs)	<45	100-200
Fungal	Cloudy	18-30	<300 (lymphs)	<45	40-300
Aseptic	Clear	9-18	<300 (polys -> lymphs)	50-100	50-100

Treatment of Meningitis

- For normal adults, empiric treatment consists of ceftriaxone 2g IV q12h +/- ampicilliln 2g IV q4h for *Listeria (if high risk for Listeria as with elderly or HIV+ve)*.
- If the patient is HIV positive or you have any suspicion that they are HIV + you may have to broaden your empiric coverage dramatically. Continue ceftriaxone to cover for bacterial meningitis but also consider ampicillin to cover for listeria, fluconazole to cover for cyrpto, acyclovir to cover for HSV or VZV, anti-TB meds to cover for TB meningitis (see TB lecture for details). You may also want to consider treatment for cerebral malaria, toxo, neurosyphillis.

Aseptic Meningitis

Definition

Negative bacterial microbiologic data, CSF with pleocytosis with – blood and CSF cultures.

Etiologies

- Viral: enterovirus, HIV, HSV, VZV, mumps, viral encephalitis, adenovirus, polio, CMV, EBV
- Tuberculosis
- Parameningeal focus of infection (ie: brain abscess, epidural abscess)
- Fungal, spirochetal, rickettsial
- Partially treated bacterial meningitis
- Medications: bactrim, nsaids, pcn, INH
- Systemic illness: SLE, sarcoid, Bechet's, Sjogrens, RA
- Neoplasms: intracranial tumors, lymphomatous or carcinomatous meningitis

Empiric Treatment

- no abx if suspect viral etiology (unless you suspect HSV/VZV); otherwise start empiric antibiotics and wait for the CSF culture data
- anti-TB meds if suspect TB meningitis

Chronic Meningitis

Definition: Meningitis with symptoms lasting > 7 days. More common in Africa.

Etiologies: Usually aseptic. Usually due to TB or crypotococcal meningitis but can be due to partially treated bacterial meningitis or any of the other causes of aseptic meningitis listed above.

Treatment: Evaluate for cryptococcal meningitis. If no crypto, strongly consider empiric anti-TB + steroids.

Sexually Transmitted Infections

Treatment of STIs reduces transmission of HIV. WHO has developed syndromic approach to empirical treatment based on commonly seen signs and symptoms.

Males

Urethral discharge: Confirm presence of discharge, evaluate gram stained specimen under microscope. Major pathogens causing urethral discharge: Neisseria gonorrhoeae (Gram negative intracellular diplococci) and Chlamydia trachomatis (obligate intracellular bacterium). Treatment: Ciprofloxacin 500mg PO STAT or Ceftriaxone 125mg IM STAT (Gonorrhea) PLUS Doxycycline 100mg PO BD x 7 days or Azithromycin 1 gram PO STAT (Chlamydia)

Penile ulcers: Confirm presence. Treatment: Benzathine penicillin G 2.4 million IU IM STAT (2 injections into separate sites) or Procaine penicillin G 1.2 million IU IM OD x 10 days (syphilis) PLUS Ciprofloxacin 500mg PO BD x 3 days (chancroid- H. ducreyi gram negative rods)

Females

Vaginal discharge: Distinguish between vaginitis and cervicitis.

Cervicitis: Caused by Neisseria gonorrhea and Chlamydia trachomatis (cervical discharge). Treatment: Ciprofloxacin 500mg PO STAT or Ceftriaxone 125mg IM STAT (Gonorrhea) PLUS Doxycycline 100mg PO BD x 7 days or Azithromycin 1 gram PO STAT (Chlamydia)

Vaginitis: Caused by Trichomonas vaginalis, Candida albicans and Gardnerella. Treatment: Metronidazole 500mg PO BD x 7 days or 2grams PO STAT (Trich and BV) PLUS Fluconzaole 150mg PO STAT or Clotrimazole 200mg intravaginally OD x 3 days

Lower abdominal pain

- Evaluate for Pelvic Inflammatory Disease (PID)
- ** ALWAYS CHECK PREGNANCY TEST on women with lower abdominal pain**
- WHO criteria for treatment:
    - Lower abdominal pain (without missed period, recent delivery/abortion, rebound tenderness, guarding, vaginal bleeding)
    - Temperature > 38.0oc
    - Cervical Motion Tenderness
    - Vaginal discharge
- PID caused by Neisseria Gonorrheae, Chlamydia trachomatis, anaerobic bacteria

Treatment (inpatient): Ceftriaxone 250mg IM OD PLUS Doxycycline 100mg PO/IV BD PLUS Metronidazole 500mg PO/IV BD for at least 3 days after patient improved and then Doxycycline 100mg PO BD for 14 days.

Respiratory

Systematic Method for Reading Chest X-Rays

Indications

Any patient with severe or persistent shortness of breath, cough, hemoptysis, chest pain, chest trauma, evidence of tuberculosis or malignancy by history or pulmonary findings on physical examination.

Types of X-Rays

- Posterior-Anterior (PA) – best for most patients
- Anterior-Posterior (AP) – for patients who can't get out of bed (as in the ICU)
- Lateral – useful when combined with PA film to determine 3 dimensional positions of pathology
- Lateral Decubitus – an PA film performed with the patient lying on side; useful in determining size and flow of pleural effusions

Sysematic Method for Reading Chest X-rays

Always follow the same method (so that you don't miss anything).

Method: 123 ABCDE

1. *Identify the patient***:** make sure this is the correct patient and correct date

2. *Quality of film***:** films look very different depending on their quality

- Rotation: Identify the medial ends of the clavicles and select one of the vertebral spinous processes that falls between them. The medial ends of the clavicles should be equal distances from the spinous process.
- Penetration: Look for vertebral bodies visible through the heart shadows (too white = under penetrated, too dark = over penetrated)
- Inspiration: Should be able to see 7 anterior ribs, if > 7 consider hyperinflation, if < 7 consider if poor inspiratory effort for film

3. *External hardware:* Look for central lines, chest tubes, NG tubes (should be in stomach and below diaphragm), or endotracheal tubes (should be 2-4cm above the carina)

A*irway*: Identify the position of the trachea and carina and whether it is shifted to one side or another

B*ones and soft tissues***:** Evaluate external structures first that might get overlooked

- Bones- look for fractures, lytic bone lesions (cancer), dislocations
- Soft tissues- look for subcutaneous emphysema

C*ardiac shadow*

- Mediastinum- assess the size (if wide, consider aortic dissection), rule out pneumomediastinum (thin line of air around heart)
- Heart- assess the size (cardiomegaly- heart should be <1/2 total chest width, 2/3 of heart should be on L side)

- Heart borders- R border is RA, L border- From Diaphragm to to left hilum is LV. At the level of the Left hilum it is the left appendage . Above this is is the Pulomanry artery and aorta.
- Hila- main pulmonary arteries and bronchi compose hilum (lymphadenopathy, tumors, large PA can cause hilum to look bulky). Note left hilum is approxiamelty 2.5cm higher than the right.

D*iaphragms and pleura*: look at borders before the lungs

- Diaphragms – shaped like domes, flat suggests emphysema, R should be higher than L (elevated L could mean phrenic nerve paralysis), air below diaphragm suggests pneumoperitoneum
- Costophrenic angles – should be clear and sharp (if blunted, pleural effusion)
- Pleura- thickened pleura (suggests prior TB)

E*verything else*: ***Finally*** look at lung parenchyma

- Parenchyma- evaluate for alveolar process vs. interstitial process (air bronchograms present in alveolar filling), lobar infiltrate (bacterial) vs. diffuse infiltrate (viral, PCP)
- PTX- if no lung markings, consider PTX (tension PTX will have mediastinal shift)
- Nodules- consider cavitary lesions, tumors
- Vasculature- large vessels suggest vascular congestion

Pleural Effusion & Pneumothorax

Pleural Effusion

Anatomy

Pleura is the serous membrane that covers the lung parenchyma, the mediastinum, the diaphragm, and the rib cage. There are two types of pleura:

- Visceral pleura: covers the lung parenchyma including the fissures
- Parietal pleura: lines the inside of the thoracic cavity

A film of pleural fluid is normally present between the parietal and the visceral pleura which acts as a lubricant allowing smooth movement of the lung during respiration.

Physiology

Where does the fluid come from? It enters the pleural space from several different souces:

- Pleural capillaries
- Interstitial spaces of the lung
- Intrathoracic lymphatics/blood vessels: disruption of the thoracic duct, injury to the blood vessels, etc.
- Peritoneal cavity: requires there to be free fluid in the abdomen and openings in the diaphragm

How does the fluid move? Balance of hydrostatic and oncotic pressures.

How is the fluid absorbed again? Reabsorbed normally by pleural lymphatics

What are the effects of the pleural effusion?

- Effects on diaphragm: Diaphragm cannot be depressed
- Effects on lung: Lung volume is decreased unless the thoracic cavity is made larger to accommodate the lung + the extra fluid.
- Effects on heart: Compromise cardiac function

What are the CXR findings of pleural effusion?

1. For free flowing fluid, peural fluid accumulates in the depend part of the thoracic cavity. When patient is upright, fluid accumulates posteriorly and can look like a generalized ***homogenous opacification***.
2. There is ***costophrenic angle blunting***.
3. There can be a ***meniscus sign*** at the upper border of the fluid.

You need at least 200cc of fluid to be present for the lateral costophrenic angle to be blunted on a CXR. Ultrasound is more sensitive than CXR for detecting pleural effusion.

What is a loculated Effusion? When there are adhesions between the visceral and the parietal pleura and the pleural fluid becomes encapsulated. Occurs with conditions that cause pleual fluid. Caused yby pleural inflammation. Diagnosed with ultrasound.

What is the significance of an air fluid level? Suggests bronchopleural fistula, pneumothorax, rupture of the esophagus into pleural space, gas forming organisms

Symptoms
Shortness of breath, pleuritic pain, dry non-productive cough

Signs
- Abnormal chest excursion with inspiration
- Decreased tactile fremitus
- Percussion note is dull or flat
- Decreased breath sounds
- At the superior border of the fluid, there may be bronchial breath sounds-may be secondary to increased conductance of breath sounds through a partially collapsed lung
- Pleural rub
- Tracheal deviation (if effusion large)

Differential diagnosis
- CHF – cardiomegaly, JVD, LE edema
- Collagen/Vascular – joint disease, rashes (lupus, rheumatoid arthritis)
- Malignancy – lymphadenopathy, masses

Diagnosis
- Systemic factors (increased hydrostatic pressure, decreased oncotic pressure) -> transudate
- Local factors (increased pleural surface permeability) -> exudates
- Light's criteria: EXUDATE if ANY of the following 3 are found
    - Total protein effusion / total protein serum > 0.5
    - LDH effusion / LDH serum > 0.6
    - LDH effusion > 2/3 upper limit of normal of LDH serum

In resource limited settings where LDH is often not available: total protein effusion > 2.5 gm/L is often used to indicate an exudate effusion

Transudative effusions	Exudative effusions
Congestive heart failure Pericarditis Cirrhosis Nephrotic syndrome	Infection (bacterial, fungal, mycobacterial) Malignancy Pulmonary embolism Collagen Vascular Dz (RA, SLE) GI disease (pancreatitis, esoph rupture) Hemothorax (Hct eff/Hct blood > 50%)

Etiology	**Appear**	**WBC diff**	**RBC**	**pH**	**Gluc**	**Comments**
CHF	Clear, straw	<1000	<5000	normal	normal	Bilateral, cardiomegaly
Parapneumonic	turbid	5-40,000,	<5000	Normal/low	normal	

		neutrophils				
Empyema	pus	25-100,000, neutrophils	<5000	<7.2	low	Needs drainage!
TB	serosang	5-10,000, lymphocytes	<10,000	Normal	Normal or low	+AFB
Malignancy	Bloody	1-100,000, lymphocytes	<100,000	Normal	Normal	+cytology
PE	Sometimes bloody	1-50,000, neutrophils	<100,000	Normal	Normal	
Hemothorax	Bloody	1-50,000	>100,000	Normal	Normal	Hct ratio
Esophageal rupture	Turbid	5-50,000	<10,000	Very low	Low	High amylase

Pneumothorax

Definition
Accumulation of air or gas in the pleural space

Etiology
- Frequently caused by trauma. can also be iatrogenic from a procedure like thoracentesis or lung biopsy
- Primary spontaneous pneumothorax occurs in patients without an apparent underlying disease. Chest pain on the affected side with dyspnea is the typical presenting complaint. This often occurs at rest and is rarely life threatening. It occurs more freuqnently in med than women, and especially in young men (20-40 years old)
- Secondary spontaneous pneumothorax occurs in associationwith underlying lung disease. Although it most commonly occurs secondary to COPD, many other conditions are associated such as tuberculosis, PCP, malignancy, fibrosis.

Clinical features and diagnosis
- The major symptoms are chest pain and dyspnea.
- Physical exam reveals hyperresonance and decreased breath sounds over the involved side. If the pneumothorax is large enough to impair right heart filling/function, then there will JVD and a pulsus paradoxus and you may also find deviation of the trachea to the contralateral side.
- Chest x-ray shows an absence of lung markings beyond the distinctly white line of the visceral pleura. If the patient is upright, air rises to the apex. When the patient is supine, air rises to the anterior chest. May see a deep sulcus sign: anterior costophrenic angle is sharply delineated. On a lateral decubitus film, place the suspected side up (whereas it should be down for fluid). 5 ml of air is detectable.

Therapy
- A small pneumothorax of less than 15 % in a hemodynamically stable patient may be managed with observation as they can often resolve themselves.
- If the pneumothorax is larger than 15%, it is managaed by direct aspiration or tube thoracostomy.

- Tension pneumothorax occurs when there is a build up of positive pressure in the pleural space. Because of a ball-valve mechanism, air enters the pleural space but cannot leave. Patients who are intubated on mechanical ventilation are at particularly high risk.
- Spontanous pneumothorax has a tendency to recur. After 2 or 3 occurrences, consider pleurodesis--abrasion of the pleural surfaces which results in adherence of the visceral and parietal pleura, preventing re-accumulation of air in the pleural space.

Dyspnea and Respiratory Distress

Shortness of breath or dysnpea is the sensation of difficulty the breathing. Acute respiratory distress is a more severe form of dyspnea

History

Want to always get a detailed history from the patient. When did the shortness of breath start, how long does it last, any exacerbating or alleviating factors. Ask about associated symptoms of chest pain, wheezing, nausea, vomiting, fevers, cough, lower extremity swelling. Ask about orthopnea and paroxysmal noctual dyspnea (PND). Are they getting IV fluids, any recent medications?

Physical examination

- General: evaluate mental status, are they altered? In respiratory distress with tachypnea, increased work of breathing and using accessory muscles of respiration, nasal flaring?
- Get vital signs
- Pulmonary exam: look for decreased breath sounds, rales, wheezes, tracheal deviation, poor air movement
- Cardiac Exam: listen for murmurs, gallops
- Extremities: look for lower limb swelling, bilateral or unilateral, cyanosis? Clubbing?

Causes of respiratory distress

Cardiac*:* left heart failure (due to ischemic heart disease, anemia, cardiomyopathy, myocarditis, pericarditis), pericarditis, valvular heart disease

Pulmonary: asthma, COPD, pleural effusions, aspiration, pneumothorax, pulmonary embolism, Tuberculosis or any pulmonary parenchymal disease such as pneumonia, pulmonary hypertension

Diseases of the chest: wall and muscles, spine, diaphragm, or pleura

Miscellaneous: thyrotoxicosis, acidosis, gross ascites, sepsis, ARDS

Evaluation and Treatment

- immediately sit the patient up and apply oxygen (in COPD patients, give oxygen but watch closely for hypercapnea, decrease oxygen it patient becomes sleepy)
- obtain a full set of vital signs
- obtain chest xray and EKG
- obtain full blood panel, creatinine
- if you suspect pulmonary edema -> give lasix 40 mg
- if wheezing -> give nebulizer treatments
- if febrile or you suspect pneumonia -> start antibiotics: Amoxicillin is a good first choice. However, if the patient has severe pneumonia, or can't tolerate PO, then give Ceftriaxone. If you suspect aspiration, add Metronidazole for coverage of anaerobic bacteria

Asthma

Definition: a syndrome of intermittent reversible airway obstruction.

Pathophysiology: A medium airway disease with 3 major contributors: 1) mucosal inflammation with increased TH2 lymphocytes, eosinophils, mast cells and mucus production, 2) bronchial hyper-reactivity to allergens/irritants, and 3) smooth muscle contraction. Chronic, poorly controlled asthma leads to airway remodeling with hyperplasia of smooth muscle and mucosal glands as well as submucosal fibrosis and eventually produces irreversible obstruction.

Epidemiology: Prevalence in US and Europe: 5-10%. Prevalence in SSA: 3-5%. Prevalence in SSA is increasing, especially in higher socio-economic classes and cities. Prevalence is higher in pre-pubertal children (especially boys). Over 40yo, prevalence is higher in females. Family history is present in 30% of cases.

Subtypes

1. Childhood Asthma – most cases present between 1-10 years of age and 50% resolve by the end of puberty.
2. Atopic Asthma – a genetic predisposition associated with eczema or seasonal allergic rhinitis.
3. Adult Onset Asthma – starts after puberty. Likely to persist for life.
4. Occupational Asthma – associated with occupational exposure. Common exposures include flour dust, animal allergens, platinum salts, kerosene, and ammonia. Often symptoms only improve during long vacations (> 2 weeks). Avoidance is essential but symptoms may not resolve for 2-3 years.
5. Exercise-induced Asthma – symptoms only present with exercise. Pretreatment with beta-agonist is recommended. Dx: PFR drops by 20% with exercise.
6. Cough Predominant Asthma – cough is predominant or only symptom.
7. Aspirin-sensitive Asthma – Asthma symptoms and nasal congestion worsen one hour after aspirin ingestion. Often associated with nasal polyps. Treatment is avoidance of all NSAIDs

Symptoms: Asthma should be considered in any patient with chronic, intermittent cough, dyspnea, chest tighness or wheeze. The cough is typically paroxysmal, productive of scan sputum and worse at night. The dyspnea is often described as chest or throat tightness with air hunger. All symptoms of asthma are generally worse at night because of the diurnal variation of smooth airway contraction in the airways.

Signs: During acute asthma exacerbations, observation often reveals tachypnea with increased work of breathing (grunting, nasal flaring, and/or subcostal/supraclavicular retractions). Patients often appear anxious. Palpation and percussion are usually normal although the chest can be hyperresonant. On ascultation, diffuse expiratory wheezes with an increased expiratory time are often heard. In very severe asthma, there may be poor air movement and no detectable wheeze. Atelectasis often causes decreased breath sounds in the bases. Barrel chest may be present in chronic asthma. Physical examination often normal between episodes.

Differential Diagnosis (for wheezing) – asthma, atypical pneumonia (if fever), PCP (if HIV positive), pulmonary edema (if history/exam consistent with CCF), COPD (if smoker, obstruction not

reversible), PE (if risk factors for DVT), tuberculosis (if symptoms are chronic and fever, night sweats or wt loss), or helminth infection with migration of larvae through the lungs (like strongyloidiasis).

Investigations:

- Oxygen saturation – <93% indicates hypoxia.
- Peak flow rate (PFR) – ideally should be compared to patient's personal best measured at time when patient is asymptomatic. If personal best is not known PFR should be compared to predicted PFR by age and weight. If > 80% obstruction is minimal, if 50-80% obstruction is moderate, if < 50% obstruction is severe. In asthma, PFR should improve by 15% after dose of beta agonist.
- CXR – typically will show hyperexpansion with flattening of the diaphragms and clear lungs. Streaky atelectasis often also present.
- CBC
- HIV test
- Sputum for culture and sensitivity – if fever and sputum.
- Sputum for AFB x 3 – if productive cough > 2wk with fever, night sweats or wt loss.

Treatment

Inpatient - All patients with severe or life-threatening asthma should be admitted to the hospital. In severe asthma patients will be unable to speak in full sentences, RR>25, HR>105, PFR<50% predicted. In life-threatening asthma patients will have silent chest, cyanosis, bradycardia, hypotension, feeble respiratory effort or confusions and these patients should be admitted to the ICU. The following should be given immediately:

- Oxygen (4-10L/min)
- Salbutamol 2 puffs every hour (or 5mg via nebulizer or spacer, if available)
- Prednisolone 60mg PO OD x 5/7 or
- If unable to take PO, hydrocortisone 200mg IV Q6H
- No sedatives!
- If pt still has symptoms of severe asthma:
    - Amophylline 250mg IV over 20 minutes then 1g over 24 hours.
    - Consider Magnesium 2gm IV stat.
    - Consider intubation but only if all other treatment has failed.

Outpatient – The goal of outpatient management is to prevent exacerbations and airway remodeling. In all patients with asthma. In all patients, identify trigger(s) and teach patient to avoid the trigger! Common triggers include allergens, viral infections, exercise, cold, emotion, smoke. Encourage smoking cessation or abstinence as smoking worsens all forms of asthma. Encourage exercise. The following medications should be used:

- Salbutamol 2 puffs (100ug each) as needed for symptoms
- Pt must be educated on how to correctly use inhaler!
- Inhaled corticosteroid, increase dose until patient has symptoms < 2x/wk ("step up"). Start at 200mcg/day for children and 400mcg/day for adults and increase to maximum of 800mcg/day. Most asthma can be controlled with inhaled corticosteroids alone if used correctly.

- If still having symptoms >2x/wk at maximum dose of inhaled corticosteroid, add salmeterol or theophylline BD
- If still having symptoms > 2x/wk, add low dose oral steroids
- Once patient's symptoms have been well controlled for 6 months, reduce medications to minimum necessary for symptoms < 2x/wk ("step down")

Chronic Obstructive Pulmonary Disease (COPD)

Definition

- summarized from GOLD definition below
- A syndrome of Irreversible, persistent, progressive airflow obstruction.

Subtypes

There are many subtypes of COPD including:

Chronic bronchitis – chronic productive cough for three months in each of two consecutive years in a patient in whom other causes of chronic cough have been excluded. More common in smokers, those exposed to indoor cooking with biofuels and in the elderly.

Emphysema – abnormal or permanent enlargement of the airspaces that are distal to the terminal bronchioles. This is accompanied by destruction of the airspace walls, without obvious fibrosis. More common in smokers, those exposed to indoor cooking with biofuels and in the elderly.

Bronchiectasis – dilation of large and medium size airways with pooling of secretions usually due to recurrent pulmonary infections (usually in childhood). Bronchiectasis is much more common in Africa tha in the US/Europe due to higher incidence of pulmonary infections. It can be caused by any pulmonary infections but is particularly common after TB and measles pneumonitis. Bronchiectasis usually presents with chronic cough productive of copious sputum and/or hemoptysis.

Chronic Asthma – Irreversible airway obstruction due to untreated asthma which has progressed to permament airway fibrosis.

Symptoms – COPD should be considered in any patient with chronic respiratory complaints such as dyspnea on exertion, cough, or acute exacerbations of respiratory complaints such as wheezing, cough, or dyspnea. Often the cough will be associated with sputum production that is whitish in color, mucoid in quality and is worse in the morning. During acute exacerbations the mucus will often turn purulent and the patient may have a fever. Some patients will have a history of hemoptysis. Many patients will have a history of smoking or exposure to smoke from indoor cooking with biofuels.

Signs: Early on, exam can be normal. Mild disease will sometimes have prolonged expiration and wheezes on forced exhalation. With disease progression, signs of hyperinflation will be present: decreased breath sounds, wheezes, crackles a the lung bases, and distant heart sounds. Anteriorposterior diameter of the chest may be increased. The patient may lean forward on their arms and support their weight on their arms (tripod-ing). Accessory respiratory muscle use (neck and shoulder), pursed lip breathing, paradoxical retractions of the lower interspaces during inspiration, cyanosis, signs of right heart failure (cor pulmonale) including enlarged tender liver, neck vein distention especially during expiration.

Differential Diagnosis: asthma, atypical pneumonia (if fever), PCP (if HIV positive), pulmonary edema (if history/exam consistent with CCF), PE (if risk factors for DVT), tuberculosis (if symptoms are chronic and fever, night sweats or wt loss), central airway obstruction (cancer,

lymphadenopathy), or helminth infection with migration of larvae through the lungs (like strongyloidiasis).

Diagnosis: Check pulmonary function tests (PFT's). FEV1/FVC ratio less than 0.70 indicates obstruction. Once obstruction identified and there is no other explanation for obstruction, classify the severity according to the GOLD criteria:

- GOLD 1 - Mild - FEV1 > 80% predicted
- GOLD 2 - Moderate – FEV1 50-80% predicted
- GOLD 3 - Severe – FEV1 30-50% predicted
- GOLD 4 - Very Severe – FEV1 < 30% predicted

Investigations

- Oxygen saturation with pulse oximetry – <93% indicates hypoxia.
- Arterial blood gas (in severe exacerbations) - look for hypoxemia and hypercapnea
- CXR – only 50% sensitive for diagnosis of chronic disease, but needed to rule out other diseases. Chronic findings include flattened diaphragm, increased radiolucency of the lung, bullae. In acute exacerbation want to rule out pneumonia, acute heart failure, and pneumothorax
- CBC
- HIV test
- Sputum for culture and sensitivity – if fever and sputum.
- Sputum for AFB x 3 – if productive cough > 2wk with fever, night sweats or wt loss.

Treatment

Acute exacerbation

- increase in symptoms including one of the three cardinal symptoms (cough, sputum production, and dyspnea)
- Patients should be admitted to the hospital if they have high risk comorbidities (pneumonia, cardiac arrhythmia, heart failure, diabetes mellitus, renal failure, liver failure), inadequate improvement of symptoms with initial therapies in casualty, marked increase in dyspnea, inability to eat/sleep due to symptoms, worsening hypoxemia or hypercapnea
- In a severe exacerbation patients will be unable to speak in full sentences, RR>25, HR>105, silent chest, cyanosis, bradycardia, hypotension, feeble respiratory effort or confusions and these patients should be admitted to the ICU.
- The following should be given immediately:
    - Oxygen (4-10L/min) **to target saturation of 90-94%** (Pa02 of 60-70 mmHg)
    - Salbutamol 2 puffs every hour (or 5mg via nebulizer or spacer, if available)
    - Ipratropium 2 puffs 4 hourly
    - Prednisolone 60mg PO OD x 10-14 days, then taper
    - If unable to take PO, hydrocortisone 200mg IV Q6H
    - Antibiotics – if patient has 2 out of 3 cardinal symptoms or needs hospitalization: ceftriaxone 1gm IV bd 7/7, azithromycin 500mg IV OD x 5/7 (or ciprofloxacin 500mg PO BD x 5/7)
    - No sedatives!

- If pt still has symptoms of severe COPD: consider intubation but only if all other treatment has failed.

Stable Chronic Disease (Outpatient)

- Mild COPD
    - Salbutamol 2 puffs (100ug each) as needed for symptoms
    - Pt must be educated on how to correctly use inhaler!
- Moderate COPD
    - Add one or more a long-acting bronchodilator
- Severe COPD
    - Add an inhaled glucocorticoid if needed for better control
- Very Severe COPD
    - Consider long term oxygen therapy
    - If still having frequent symptoms can add theophylline BD
    - Rarely if frequent symptoms despite maximum therapy can add low dose oral steroids

Hemoptysis and Pneumonia

Hemoptysis

Definition

- hemoptysis is the expectoration of blood > 100-600 ml over 24 hours
- Be careful to distinguish hemoptysis from hematemesis or blood from gums, throat or nose
- *Massive hemoptysis* is a medical emergency. Massive hemoptysis can be fatal, with deaths occuring by exsanguination or asphyxiation from flooding of the alveoli with blood and intractable hypoxemia.
- ***Top 3 causes of massive hemoptysis in Africa: TB, bronchiectasis and carcinoma***
- Always remember the 3 principles of management 1) maintain airway patency and oxygenation 2) localize the source of bleeding 3) control hemorrhage

Vascular Anatomy

The pulmonary circulation: carries deoxygenated blood from the right ventricle across the pulmonary capillary bed and returns oxygenated blood via the pulmonary veins. This is a low pressure circuit with normal pressures of 15-20/5-10 mmHg. Blood originating from the pulmonary parenchyma can be from an infection such as pneumonia, lung abscess or TB or from diffuse process such as Goodpasture's syndrome.

The bronchial circulation: is the nutritional source for the structural elements of the lung. Bronchial arteries branch from the aorta and are at systemic pressure. They can bleed profusely when airways are diseased, as seen with bronchiectasis or with endobronchial tumors.

History

- ask about tobacco history, prior lung, cardiac or renal disease
- ask about any prior episodes of hemoptysis
- productive cough, infection, skin rash, travel history
- ask about chest pain and shortness of breath
- any bleeding disorders

Physical Exam

- examine skin: look for signs of Kaposi's sarcoma, vasculitis
- look for splinter hemorrhages as sign of endocarditis
- listen for cardiac bruits or murmurs (large AVM)
- listen for cardiac sounds such as loud P2, TR as signs of pulmonary hypertension
- look for clubbing (nonspecific sign)
- examine legs for signs of DVT

Etiology

- **Acute:** pneumonia, bronchitis, pulmonary embolism
- **Chronic:** tuberculosis, lung cancer, bronchiectasis

Airways disease

- Bronchiectasis: is due to destruction of the cartilaginous support of the bronchial wall by infection or bronchial dilatation owing to parenchymal retraction from alveolar fibrosis. This

causes bronchial artery hypertrophy and augmentation of anastomoses with the pulmonary artery bed

- Carcinoma: 7-10% of patients with bronchogenic carcinoma present with blood streaked sputum; massive hemoptysis is rare. Vast majority of primary lung cancers associated with hemoptysis are squamous in origin. In metastatic lung disease, the lesion is usually endobronchial.
- Foreign body and Airway Trauma

Parenchymal Disease

- Bacterial Pneumonia
- Tuberculosis: may cause hemoptysis either in active disease (cavitary lesions, rupture of pulmonary artery aneurysms) or as late sequelae (rupture of aneurysms or secondary to bronchiectasis). Rupture of Rasmussen's aneurysm can occur with active disease or as a late finding. It occurs when there is rupture of ectatic portions of the pulmonary arteries traversing thick-walled cavities.
- Fungal Infection: (mycetomas) forms in patients with pre-existing cavitary disease, aspergilloma
- Lung abscess: causes hemoptysis, probably because of necrotizing effect of the primary infection on lung parenchyma and vasculature
- Autoimmune disorders: Wegener's, Goodpasture's, SLE pneumonitis
- Coagulopathy: especially in patients with thrombocytopenia
- Iatrogenic hemoptysis: from bronchoscopy or biopsy

Vascular

- Pulmonary Embolism
- Mitral Stenosis or Congenital heart disease: cause hemoptysis via pulmonary hypertension, which leads to varices in the submucosa of the bronchial walls

Miscellaneous

Catamenial hemoptysis results from ectopic uterine tissue in lung/pleural. Hemotysis occurs at same time as patients menstrual cycle

Management

- consider TB in anyone with chronic cough and hemoptysis
- *Maintain airway patency:* asphyxiation is the most frequent complication of massive hemoptysis. ---Obtain chest xray and oxygen saturation if available to assess the status of oxygenation and the amount of blood in the lung. Moniter patient in the ICU. If bleeding site is known, in massive hemoptysis, place the patient in the lateral decubitus position with the affected lung in the dependent position.
- Obtain IV access
- Obtain routine lab date: FBP, BUN/creatinine, PT/PTT and urinalysis
- *Localize the source of bleeding:* if there is any doubt, the source of the bleeding (pulmonary versus GI versus ENT) should be investigated. Take a thorough history and physical exam.
- in general, bronchoscopy is the diagnostic procedure to identify source of bleeding
- *Control the hemorrage:* correct coagulopathy, for severe hemoptysis give vitamin K 1 mg IV. Cross match blood if needed. Bronchoscopy can control hemorrhage through vasoconstrictive agents

Pneumonia

Definition = acute infection of lung parenchyma

Clinical manifestations

- Cough, fever, tachycardia, pleuritic chest pain, shortness of breath, sputum production
- CXR: infiltrate (can be different patterns i.e. lobar, interstitial, cavitary)

Microbiological Differential Diagnosis

1. Typical bacteria: Strep pneumoniae, H. influenzae, Staph aureus, Moraxella catarrhalis
2. Mycobacteria: Mycobacterium tuberculosis, atypical mycobacteria
3. Atypical bacteria: Legionella, Chlamydia pneumoniae, Mycoplasma pneumoniae,
4. Viral: influenza, RSV, HSV, CMV*
5. Fungal: PCP*, cryptococcal, histoplasmosis
6. occur only in immunocompromised patients such as HIV+ve patients

   Remember, TB is a type of pneumonia

Treatment

- In hospital Ceftriaxone 1 gram IV OD
- For atypical PNA (especially in HIV patients), add erythromycin or azithromycin
- If patient is hemodynamically unstable, add gentamycin for double gram negative bacterial coverage
- For suspected aspiration pneumonia (especially in stroke patients), add metronadizole 500 mg IV tds for anaerobic coverage
- For suspected PCP pneumonia, add Septrin 1920 mg 8 hourly x 21 days. If pt has PCP + hypoxia (“severe PCP), add prednisolone 40 mg bd x 5 days, then 40 mg daily x 5 days then 20 mg daily x 5 days then 10mg daily x 5 days
- For suspected TB pneumonia, add anti-TB

Pulmonary Embolism

Definition

Pulmonary embolism (PE) is an obstruction of the pulmonary artery or one of its branches by material that originated elsewhere in the body. One of the most common causes of a PE is a thrombus that has traveled to the lung. We will focus on today.

Subtypes

1. Massive – causes hypotension (systolic blood pressure < 90mm Hg or a drop in the systolic of >40mm Hg from baseline) for >15 minutes.
2. Submassive – All PE's not meeting the definition of massive.
3. Saddle PE – lodges at the bifurcation of the main pulmonary artery into the left and right.

Pathogenesis/Pathophysiology

Most thrombotic PE's come from DVT's. The majority of DVT's come from the lower extremities, although they can come from other deep veins. Once a thrombus travels to the lung, it causes hemodynamic changes (increased pulmonary vascular resistance → decreased cardiac output), inflammation, impaired gas exchange and sometimes infection. Untreated PE has a mortality rate of 30%.

Risk Factors

- Immobilization
- Surgery within the past three months
- Stroke
- Paresis
- Paralysis
- Central venous instrumentation in the past three months
- Malignancy
- Chronic heart disease
- Autoimmune disease
- History of venous thromboembolism
- Obesity
- Cigarette smoking

Clinical Presentation

Symptoms

- Dyspnea at rest or with exertion
- Pleuritic chest pain
- Cough
- Orthopnea
- Calf or thigh pain
- Calf or thigh swelling
- Wheezing
- Hemoptysis

Signs

- Tachypnea
- Rales
- Tachycardia
- Decreased breath sounds
- Fourth heart sound
- Accentuated pulmonic component of the second heart sound
- Jugular venous distention
- Signs of lower extremity DVT (edema, erythema, tenderness, palpable cord)

Differential Diagnosis

Other types of embolism other than thrombus (amniotic fluid embolism, fat embolism, etc.), pneumothorax, myocardial infarction, acute decompensated CCF, aortic dissection pneumonia, COPD exacerbation.

Diagnosis

Difficult to make based on history and physical alone

Investigations

- CT scan of the chest if available
- CXR
- Ultrasound of the lower extremities
- Full blood picture
- D-dimer
- ECG

Treatment

- Anticoagulation (treatment doses of heparin, transition to warfarin)
- Thrombolysis (rarely done)
- Inferior vena cava filter (if available)
- Embolectomy (rarely done)

Neurology

Stroke

Definition: A syndrome of focal or global neurologic deficit that develops suddenly and lasts more than 24 hours in a person with no history of recent head injury. If < 24 hours, it is called a transient ischemic attack (TIA). Strokes can be categorized as *ischemic* (embolic or thrombotic) or *hemorrhagic* (intracerebral or subarachnoid). Main risk factors for stroke in Africa are hypertension (#1), DM, hypercholesterolemia, smoking, atrial fibrillation, rheumatic heart disease, sickle cell anemia, and HIV.

Differential Diagnosis: space occupying lesion (neoplasm or infectious), trauma (subdural or epidural hematoma), toxins (including medications), hypo/hyperglycemia, electrolyte abnormalities (ex hypo/hypernatremia)

Ischemic Stroke

Epidemiology/Natural History: More common and accounts for 85% of all strokes. Usually occurs in elderly patients except in cases of sickle cell anemia or rheumatic heart disease. Mortality rate is low in the first week (10-20%) but many patients will die of complications in the first 1-2 months including: aspiration pneumonia, septic decubitus ulcers and DVT.

Etiologies

- Thrombotic – usually related to atherosclerosis
- Embolic – as with atrial fibrillation, rheumatic heart disease or endocarditis

Symptoms and Signs: The most common symptoms/signs of stroke are hemiparalysis, aphasia and coma. Signs and symptoms of ischemic strokes are variable depending on the artery and part of the brain that is affected. For example:

- Anterior Cerebral Artery - Hemiplegia (leg>arm); Confusion, urinary incontinence, primitive reflexes
- *Middle Cerebral Artery* (Most Common) - Hemiplegia (face/arm>leg); hemianesthesia; aphasia (if dominant hemisphere)
- Posterior Cerebral Artery - Thalamic syndromes with contralateral hemisensory disturbance
- Lacunar (involving internal capsule)- Pure hemiplegia

Physical Exam: Perform a close cardiovascular exam for rhythm, murmurs, carotid and subclavian bruits; look for signs of peripheral emboli such as Janeway lesions or splinter hemorrhage. Do a complete and thorough neurological exam.

Diagnostic Studies

- Most important: urgent noncontrast head CT if available (will help differentiate between ischemic vs hemorrhagic stroke)
- blood work should include at least a HIV Test, CBC, creatinine, lipids, glucose and electrolytes (to r/o electrolyte imbalance or hypoglycemia as cause of symptoms); PT/PTT if you are considering a hemorrhagic stroke as you may want to reverse coagulopathies
- Consider EKG
- Consider carotid dopplers if available
- Consider TTE if available (to look for vegetations or thrombus)

Treatment

- Consider thrombolysis (if available) if onset of symptoms is within 3 hours, there is a large deficit, and there is no evidence of hemorrhage or other contraindications to lysis
- We usually do not perform lysis in our setting.
- start ASA 150mg daily x 30 days (only if can r/o hemorrhagic stroke by CT)
- BP should not be lowered in the first 48 hours unless it is very severe (SBP >200) After 48 hours, lower blood pressure slowly
- start statin (simvastatin 20mg)
- start ranitidine or a PPI to prevent stress ulcers
- start subcutataneous heparin to prevent a DVT (if can rule out hemorrhagic bleed)
- change position every 4-6 hours to prevent decubitus ulcers
- keep the head of the bed elevated to prevent aspiration
- watch for signs of cerebral edema/elevated ICP (usually peaks at 3-4 days post stroke); if evidence of elevated ICP (like declining GCS or papilledema) start mannitol
- after 48 hours, start Physical Therapy! Physical therapy is very important in stroke management. It should be started early and continued for at least 2-3 months.

Hemorrhagic Stroke

Epidemiology: Less common (15%) but more severe. Usually occurs in elderly patients or middle aged patients with severe hypertension. Patients often present with coma, headache and/or vomiting. Otherwise, symptoms are similar to ischemic stroke (see above). Almost 50% mortality in the first week. More of these patients will be referred to hospitals like BMC due to the severity of their stroke.

Etiologies

- Intracerebral (ICH): usually associated with HTN, sometimes coagulopathy
- Subarachnoid Hemorrhage (SAH): RARE; ruptured aneurysm, trauma

Clinical Manifestations

- ICH: sudden impairment in level of consciousness, vomiting, +/- headache, may see progressive focal neurologic deficit depending on site of bleeding
- SAH: severe headache, nausea and vomiting, often described as ‘thunderclap’, can see nuchal rigidity (blood is a meningeal irritant), impairment in level of consciousness

Physical Exam/Diagnostic Studies

- similar to exam/workup for ischemic stroke
- consider an LP to check for xanthochromia if you are suspicious for SAH

Treatment

- reverse any coagulopathies
- BP control with goal of SBP 140-160 to prevent further bleeding
- ranitidine to prevent stress ulcers
- consider nimodipine (a CCB) and phenytoin if suspect SAH as they decreases the risk of vasospasm and seizure in these patients
- change positions, raise head of bed and start physical therapy as in ischemic stroke

Altered Mental Status

Definition

A broad term used to describe a change in the patient's mental status.

Subtypes

- Delerium: alteration of both level of arousal and thought content (comprehension, coherence, reasoning) that is acute in onset and fluctuates (waxes and wanes), frequently induced by physiologic derangement (infection, stroke, metabolic disorder, drugs, toxins, etc.) and exacerbated by environmental factors (catheters, unfamiliar setting, etc.)
- Pychosis: psychiatric disease accompanied by visual or auditory hallucinations
- Dementia: slowly progressive degenerative process affecting primarily memory and impairs performance of activities of daily living, much more common in the elderly, sometimes impairing other mental faculties

Distinguishing features

Feature	*Dementia*	*Delirium*
Onset	Insidious	Acute
Course	Stable in short term	Fluctuating
Consciousness	Clear until late disease	Impaired
Orientation	Decrease	Fluctuating
Attention	Normal until late disease	Distractible, hypo- or hyperalert
Hallucintations/delusions	±paranoid delusions	±visual hallucinations, paranoid delusions
Thinking	Impoverished, vague, perseverative	Disorganized, incoherent
Sleep-wake cycle	Often fragmented	Always disrupted
Response to questions	'Near misses'	Incoherent

Etiologies

The differential diagnosis for causes of altered mental status and acute confusional state are very broad. **In order to remember the differential diagnosis of acute confusional state it is useful to think of 6 categories**, but **is** often multifactorial**!**

1. **Vital Sign Abnormalities:** temperature, blood pressure, pulse rate, oxygenation
2. **Toxic/metabolic:** toxins, alcohol, illegal/prescription/herbal drugs, imbalanced blood sugar, imbalanced electrolytes (Na, K, Ca), uremia/AKI/CKD, hepatic encephalopathy or failure, acidosis/alkalosis
3. **Infectious:** malaria, meningitis from TB/fungus/virus/bacteria, encephalitis, bacteremia/sepsis, HIV, local infection that has become systemic
4. **Structural** (trauma, hemorrhage, stroke, infectious or malignant space occupying lesion, hydrocephalus, Alzheimer's, degenerative chronic diseases such as Parkinson's, multiple sclerosis, Lewy-body dementia)
5. **Seizures**
6. **Psychiatric:** Diagnosis of exclusion (psychosis, schizophrenia, conversion disorder etc.)

History (Symptoms)

- Very important/helpful for distinguishing the diagnosis or cause of the recent changes

- Usually gathered from a family member or friend
- Focus on the onset, duration, tempo, and progression of symptoms
- Assess medications the patient takes and any changes (changed dose, cessation, new meds)
- Ask about family and social history, diet, alcohol, tobacco,

Exam (Signs)

- Will vary depending on the cause. But you should look for any of the following:
- Vital signs: fever, high/low heart rate, blood pressure, or breathing rate
- Neurological exam (focal neurological deficits, rigidity, tremor, ataxia, clouded or decreased consciousness, change in alertness, agitation, attention span, impaired memory, meningismus, trauma, papillary changes, decreased mini-mental status exam)

Investigations

For all patients:

- Full blood picture (FBP)
- Random blood glucose (RBG)
- Sodium/Potassium/Calcium/Creatinine
- Rapid test for HIV
- Malaria parasite smear
- Lumbar puncture (unless contraindicated)
- Head CT scan if available without contrast

For some patients (based H&P and availability

- Erythrocyte sedimentation rate (ESR)
- RPR/VDRL test for syphilis
- Thyroid stimulating hormone (TSH)
- Urinalysis (UA) and urine culture
- Blood culture
- Chest x-ray
- Cervical spine imaging
- Electroencephalogram (EEG)
- Echocardiogram

Treatment

- ABC's! (airway, breathing, circulation)
- Identify and treat any rapidly reversible causes
    - Hypoxia – give oxygen
    - Hypoglyemia – give dextrose
    - Narcotic overdose – give narcan
    - Dehydration – give intravenous fluids (IVF)
    - Poisoning – give antidote if available
    - Adrenal insufficiency – give steroids
    - CNS mass – give steroids
- If concerned about infectious etiologies, give antimicrobials
- Treat any other underlying causes if identified (hypothyroidism, vitamin deficiencies,)
- If delirious at night, turn on the lights to improve orientation and provide reassurance
- Treat persistent disturbed behavior (agitation, delusions, hallucinations) with chlorpromazine 25-50mg IM/PO 6 hourly, or haloperidol 1.5-3mg po tds.
- Avoid benzodiazepines
- Admit to the hospital if patient is not improving or needs continued monitoring.

Seizures

Definition

- ***Seizures*** are defined as excessive abnormal electrical activity of the brain leading to a clinical event
- ***Epilepsy*** is a condition where a person has recurrent seizures due to a chronic, underlying process
- ***Status epilepticus***: patient has recurrent seizures for > 15 minutes without regaining consciousness between each episode, can be fatal

Etiology

- Idiopathic
- Infections of the CNS: bacterial meningitis, fungal meningitis, herpes encephalitis
- Structural abnormalities: primary or metastatic CNS tumors, toxoplasmosis, AVM
- CNS inflammatory process: CNS lupus, CNS vasculitis
- Cerebral infarction: more common in embolic stroke
- Acute or preexisting brain injury: trauma, hemorrhage (subarachnoid hemorrhage, subdural hematomas)
- Nonstructural precipitants include: electrolyte abnormalities (hyponatremia, hypocalcemia, hypoglycemia), uremia, liver failure, hypoxia, fever (mostly in children), medication (alcohol withdrawal, illicit drugs, cyclosporine)

History

- Ask about: biting of tongue, urinary or fecal incontinence, aura, postictal confusion
- Ask about: Prior history of head trauma, stroke, tumor, vascular malformation
- Evaluate for: Sleep deprivation, systemic disease, electrolyte derangements, acute infection, drugs that lower seizure threshold, alcohol use

Types of seizures

Partial/Focal*:* involves discrete areas of the cerebral cortex, affects one part of the body (can secondarily generalize

Simple Partial: Clinical presentation: no altered consciousness, present with motor, sensory or psychic symptoms. Post-ictal state can include Todd's paralysis (transient hemiparesis)

Complex Partial: Clinical presentation: present with transient altered consciousness, unable to respond to verbal or visual commands. Impaired recollection or awareness of ictal phase. Will also have automatisms (lip smacking, chewing, foot shuffling, hand fumbling)

Generalized: both cerebral hemispheres simultaneously are involved

Absence (petit-mal): sudden, brief stare (10 seconds), lapse of consciousness without loss of postural control, usually in children, ages 4-8 years old. Child can present like he/she is "daydreaming" or has a decline in school, will also have mild automatisms, no post-ictal state

**Tonic/clonic (grand mal)*: tonic phase with contraction of muscles (causing expiratory moan, cyanosis, pooling of secretions, tongue biting) → clonic phase with intermittent relaxing and tensing of muscles. The most common type of seizure.

Atonic: sudden loss of postural tone lasting 1-2 seconds, no postictal confusion. Can be dangerous since patient just drops, can have trauma

Myoclonic: sudden, brief muscle contraction in metabolic disorders, degenerative CNS disease, anoxic brain injury

Evaluation (especially for first time seizure)

- consider syncope, migraine, TIA or psychogenic seizures (often convulsion disorder response to stress) in your differential
- perform a full neurological exam
- obtain electrolyes including sodium, calcium, potassium and BUN/creatinine.
- obtain random blood glucose
- obtain FBP
- obtain a CT scan of head if possible
- if patient has history of HIV → perform lumbar puncture after looking for papilledema
- if patient has meningeal signs (nuchal rigidity, fevers) → perform lumbar puncture

Treatment

- lower patient to the ground or a flat surface, onto their side to decrease risk of aspiration
- protect head to prevent head trauma
- start oxygen therapy by facemask
- make sure there is nothing in the mouth, suction the mouth if there are any contents
- give diazepam 10 mg IV immediately if actively seizing
- status epilepticus: if patient continues to seize, can give another dose of diazepam → if seizing continues, give phenytoin → if seizing continues, give Phenobarbital, consider intubation
- remember that when giving phenytoin to control seizures, you have to give a loading dose of 1 gram then 300 mg OD after that
- once resolved, consider the following **chronic medications** for at least 12 months (and often lifetime). Remember to counsel not to bath/swim alone drive any vehicle.

Seizure type	*1st line drug*	*2nd line drug*
Partial	Carbamezepime or Valproate	Phenytoin
Tonic-clonic (grand mal)	Phenytoin	Phenobarbital

At Bugando, diazepam, phenytoin, phenobarbital and carbamazepime are primarily available. The WHO still recommends phenobarbital for use in Africa for most types of seizures as it is inexpensive and widely available.

Headache

Causes of Headache: There is a very broad differential for headache but you can narrow it down with a good history and physical exam. The important thing to do is remember and consider conditions that are life-threatening and/or treatable. Your differential should include:

- Infectious etiologies: Malaria, meningitis, encephalitis, brain abscess, malaria, typhoid fever, arboviral infection, sinusitis
- Hypertension
- Vascular etiologies: Stroke, subarachnoid hemorrhage (SAH), subdural hematoma etc.
- Brain tumor
- Giant cell arteritis (GCA): generally seen in pts >50 yrs old; may have constitutional symptoms such as low-grade fevers, fatigue, weight loss; also may have tender temporal arteries and scalp, jaw claudication

If you are convinced that there isn't a secondary cause for the patient's headache, consider a primary headache syndrome. The primary headache syndromes are much more common than the life-threatening causes:

- Migraine: unilateral or bilateral, retro-orbital, throbbing or pulsitile, lasts 4-72 hours, often accompanied by nausea, vomiting, photophobia, can be preceded by a visual aura.
- Cluster headache: periodic, paroxysmal, brief, sharp, orbital HA that may wake the pt up from sleep, +/- lacrimation, rhinorrhea, conjunctival injection or unilateral Horner's syndrome
- *Tension headache: band-like pain associated often with muscle contraction in neck and lower head. This is the most common cause of headache

Clinical Evaluation

History

- Quality, severity, location, duration, time of onset, precipitants/relieving factors
- Associated symptoms (visual changes, nausea, vomiting, photophobia)
- Focal neurological symptoms
- Head or neck trauma, constitutional symptoms
- Medications, substance abuse

Exam

- Vital signs
- General and neurological exam, optic/fundoscopic exam

Labs and studies

Only done if indicated by the history and physical. For example, CBC, Lumbar Puncture, malaria smear, blood and CSF cultures, CT head if you if any o the warning signs below; check an ESR if considering giant-cell arteritis.

Warning Signs that would make you want to do more investigations including possibly CT scan of the Brain:

- worst headache ever
- pain wakes pt up from sleep
- vomiting
- fever
- abnl neurological exam

Treatment

- Treatment should be based on the underlying condition.

Endocrine

Diabetes Mellitus

Definition

Diabetes Mellitus is a syndrome causes by the lack or diminished effectiveness of endogenous insulin. Type 2 DM is caused by insulin resistance in combination with relative insulin deficiency.

Clinical Manifestations

- polyuria
- polydipsia
- polyphagia with unexplained weight loss
- can also be asymptomatic

Diagnosis

- Fasting glucose > 7.0mmol/l or random glucose >11.1mmol/l
- diagnosis requires 1 abnormal glucose value if symptomatic or 2 separate abnormal measurements if pt is asymptomatic

Complication of Diabetes Mellitus

Acute Complications (uncontrolled hyperglycemia, DKA, HHS)

Chronic Complications (can be microvascular, macrovascular or avascular)

Microvascular

- Retinopathy
    - non-proliferative: 'dot and blot' and retinal hemorrhages, cotton wool/protein exudates
    - proliferative: neovascularization, vitreous hemorrhage, retinal detachment, blindness
    - both treated with photocoagulation
- Nephropathy
    - microalbuminuria -> proteinuria +/- nephrotic syndrome -> eventual renal failure
    - difffuse glomerular basement membrane thickening
    - treatment: strict BP control, ACE-I, low protein diet
- Neuropathy
    - symmetric peripheral neuropathy: symmetric distal sensory loss, paresthesias, +/- motor loss
    - autonomic neuropathy: gastroparesis, neurogenic bladder, impotence, orthstatic hypotension
    - mononeuropathy: sudden onset of peripheral or CN deficit (footdrop, CN III>VI>IV)

Macrovascular

- Stroke, Myocardial Infarction or Peripheral Arterial Disease
- Accelerated atherosclerosis incoronary, cerebral and peripheral arterial beds (ie: diabetics are at a higher risk for MI, CVA, and foot ulcers)

Avascular (Infections)

- Diabetic foot*, candidiasis, mucormycosis, necrotizing external otitis
- Dermatologic

- Necrobiosis lipodica diabeticorum, lipodystrophy, acanthosis nigricans

Treatment and Management

Glucose Control

Oral Agents

- metformin: decreases hepatic gluconeogenesis and increases insulin sensitivity; side effects include N/V and diarrhea, rarely can cause lactic acidosis; contraindicated in liver or renal failure
- sulfonylureas: increases insulin secretion at B-cell; side effects include weight gain and hypoglycemia
- thiazolidinediones: increases insulin sensitivity at adipose and muscles; can cause weight gain, hepatotoxicity, fluid retention and CHF; contraindicated in liver disease and heart failure; monitor LFTs

Insulin therapy

- consider starting if mono oral therapy not adequate and definitely start if combo oral therapy not enough. Start with a short-acting/long-acting mix of insulin at .5 units/kg/day, 2/3 in morning and 1/3 in evening, titrate up as necessary. Should be given 20 min before breakfast and evening meal

Risk Factor Control

- encourage weight reduction, diet, exercise
- should be on daily ASA unless contraindicated (eg: h/o GI bleed)
- start ACE-I if + microalbuminuria
- strict BP control: goal <130/80, start ACE-I as first line as nephro-protective
- lipid control: goal LDL <100, TG <150, HDL >40; there is a benefit of statins in all diabetics even w/o overt CAD

Diabetic Follow-Up

Clinic check list: every 6 months check

- Treatment compliance and glucose control
- BP
- Injection sites
- Feet: pulses, numbness, sores, nail care
- Eyes: acuity, cataracts, retinopathy
- Urine dipstick for albumin
- +/- serum creat
- Regularly screen for TB as risk is high

Acute Complications of Diabetes Mellitus in Adults

Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS)

Definitions

HHS: extreme hyperglycemia w/o ketoacidosis, but with hyperosmolar state and altered mental status in type 2 diabetics. Usually hyperglycemia → osmotic diuresis → dehydration → more hyperglycemia.

DKA: a triad of hyperglycemia, anion gap metabolic acidosis, and ketonemia. Occurs mostly in type 1 Diabetics. Hyperglycemia develops from decreased glucose uptake into the cells, increased gluconeogenesis. Ketosis develops because of inability to use glucose → mobilization and oxidation of fatty acids and increased ketogenic state of the liver with decreased ketone clearance.

Precipitating events (VERY similar for both)

HHS: Inadequate insulin intake (under treated OR noncompliant), **DEHYDRATION**, infection (pneumonia, UTI, sepsis), acute illness (myocardial infarction, stroke, acute pancreatitis, acute renal failure, mesenteric ischemia, cholecystitis, etc), mediations (steroids)

DKA: Inadequate insulin intake (under treated OR noncompliant OR newly diagnosed diabetes [20-25%]), infection (pneumonia, UTI, sepsis), acute illness (myocardial infarction, stroke, acute pancreatitis, acute renal failure mesenteric ischemia, cholecystitis, etc), medications, steroids

Clinical Presentation

HHS: Usually insidious (subacute) presentation of polyuria, polydipsia, and weight loss a few days before hospital admission. Present with dehydration and altered mental status. Usually sugar > 600 but even > 1000!

DKA: Usually acute presentation over 24 hours. Present with h/o polyuria, polydipsia, nausea, vomiting, abdominal pain, hyperventilation (2/2 metabolic acidosis) called Kussmaul's respirations (with odor of acetone), eventually altered mental status, somnolence as academia progresses. Usually sugar >500 but < 800

Physical Exam

HHS: Signs of volume depletion (low skin turgor, hypotensive, tachycardic, dry mucous membranes), altered mental status

DKA: Signs of volume depletion (low skin turgor, hypotensive, tachycardic, dry mucous membranes), +/- altered mental status, Kussmaul's respirations (deep and fast) to compensate for metabolic acidosis, fruity odor of breat from acetone

Laboratory investigations

Hyperglycemia and hyperosmolality are the two primary laboratory findings in patients with DKA or HHS; patients with **DKA also have a high anion gap metabolic acidosis** (Na – [Cl +HCO3])Most patients: acute increase BUN and creatinine (reduction in glomerular filtration rate induced by hypovolemia).

All pts: Electrolytes (correct sodium for glucose = Measured sodium + 0.016 * (Serum glucose - 100), anion gap, urine ketones, serum ketones if urine ketones +, CBC, urinalysis, ABG (if available)

Treatment: Fluid + Insulin Infusion + Frequent reassessment

DKA: rule out possible precipitants, AGGRESSIVE hydration with normal saline, frequently requires 3-6 liters, insulin bolus of 10 units followed by 0.1 units/gk/hr insulin infusion until ketones negative, RBG every 2 hours, when glucose < 14…add dextrose to the IVF and continue insulin drip to metabolize ketones, change to SC insulin when ketones are negative. Give potassium as needed.

HHS: rule out possible precipitants, AGGRESSIVE hydration with normal saline, frequently requires 6-10 liters, insulin bolus of 10 units followed by 0.1 units/gk/hr insulin infusion until ketones negative, RBG every 2 hours, when glucose < 14…add dextrose to the IVF and continue insulin drip to metabolize ketones, change to SC insulin when ketones are negative. Give potassium as needed.

Thyroid Disease

Introduction

Thyroid disease is common and can mimic many other diseases so it should be considered in the differential diagnosis of many conditions. Hypothyroidism and hyperthyroidism are often (but not always) associated with enlargement of the thyroid gland (ie goiter) that can be either nodular or diffuse. Nodular and diffuse goiter can also occur without hypothyroidism or hyperthyroidism.

Hypothyroidism

Physical Manifestations

- Early Sx: weakness, fatigue, arthralgias, myalgias, headache, depression, cold intolerance, weight gain, constipation, menorrhagia, dry skin, coarse hair, brittle nails, delayed DTRS, diastolic HTN
- Late Sx: slow speech, hoarseness, loss of outer third of eyebrows, myxedema (non-pitting thickened skin), periorbital puffiness, bradycardia, pleural/pericardial/peritoneal effusions
- **Myxedema coma** (rare): hypothermia, hyporeflexia, bradycardia, hypotension, AMS (50% mortality)

Etiologies

Primary (increased TSH, decreased T4)

- Goitrous (enlarged thyroid):
    - Hashimoto's thyroiditis: common in women 20-60yo and due to automimmune destruction of the thyroid; associated with other autoimmune disorders
    - Iodine deficiency – common in rural areas but becoming less common with iodine supplementation of salt and other foods
    - Post-viral thyroiditis (De Quervains): less common, 6 weeks after a viral prodrome; tender goiter; labs may reveal hypo- hyper or euthyroid. Self-limiting but may require treatment. May also see elevated ESR and fever.
- Non Goitrous: surgical, s/p radioactive iodine/radiation, drugs like amiodarone

Secondary (decreased TSH, decreased T4) Hypothalamic or pituitary failure – very rare

Diagnostic Tests

- TSH, FT4
- anti-thyroid peroxidase and anti-thyroglobulin antibodies if available (Hashimoto's)

Treatment

- Thyroid replacement with levothyroxine, start with 50-150mcg OD (1.5ug/kg/day), recheck TSH q6weeks and titrate until TSH <5; use a lower starting dose (.5ug/kg/day) if pt at risk for ischemic heart disease as levothyroxine can cause ischemia
- If due to iodine deficiency, give Schiller's iodine (1:30 dilute Lugol's iodine) 2 drops OD x 6mo

Hyperthyroidism

Clinical Manifestations

- Restlessness, insomnia, heat intolerance, sweating, moist warm skin, fine hair, tachycardia, palpitations, AF, weight loss, increased freq of bowel movements, menstrual irregularities, hyperreflexia, osteoporosis, lid lag
- **Thyroid Storm**: (seen with stress or surgery) delirium, fever, tachycardia, systolic hypertension (wide pulse pressure and low MAP), diarrhea (20-50% mortality)

Etiologies

Primary (decreased TSH, increased T4)

- Goitrous (enlarged thyroid):
    - Toxic multi-nodular goiter – common; thyroid has multiple nodules
    - Graves disease – common in women 20-40yo, Genetic predisposition leads to antibodies to TSH receptors
        - Unique Sx: diffuse, nontender goiter, proptosis (check sclera visibility above pupil), diploplia, pretibial myxedema
        - Dx: thyroid stimulating antibodies
    - Thyroiditis (see above)
    - Toxic Adenomas: nodule producing T3/T4
- Non Goitrous: iodine-induced, struma ovarii (T3/T4 producing ovarion tumor)

***Secondary (increased TSH, increased T4)* -** TSH-secreting pituitary tumor

Diagnostic Tests

- Increased FT4/FT3; Decreased TSH (except for tumors)
- Thyroid ultrasound – to assess for nodules
- Radioactive iodine uptake scan
    - Homogenous uptake—Graves
    - Hetergeneous increase—multinodular goiter
    - Single “hot nodule” —toxic adenoma
    - No uptake—thyroiditis, iodine load, struma ovarii

Treatment

- Start with B-Blockers (Propranolol): control tachycardia and decrease T4->T3 conversion
- Graves/Thyroiditis: anti-thyroid medications or radiation
    - PTU/methimazole/carbimazole (inhibit T3/T4 synthesis)
    - Radioactive iodine
- Nodular Hyperthyroidism: often treated with surgery but can also be treated with antithyroid medications or radiation

Thyroid Nodules

- The most common cause of thyroid nodules in our setting is **multi-nodular goiter** which is benign and common in areas of recently treated iodine deficiency.

- **Thyroid adenomas** are also common.
- **Thyroid carcinoma** is a rare but deadly cause of thyroid nodules. Features associated with thyroid carcinoma include
    - Age <20 or >70
    - h/o neck radiation therapy
    - large size
    - worrisome U/S findings (hypoechoic, solid, irregular borders, microcalcifications, central blood flow)
    - cervical LAN
- FNA should be performed for
    - Nodules >10mm with irregular borders, microcalcifications, or chaotic intranodular vascular spots
    - Nodule of any size in a patient with h/o neck radiation therapy or a family history of MEN2 or medullary thyroid cancer

Sick Euthyroid Syndrome

Abnormal TFTs due to non-thyroidal disease. Seen in severe illness. TSH decreased or normal, T3/T4 decreased or normal. Does not require treatment but needs to be followed up

Hematology & Oncology

Anemia

Anemia is a disorder of the red blood cell. Anemia is present when there is a decreased level of hemoglobin in the blood below the reference level for the age, sex and pregnancy state of the individual.

Symptoms

Depends on acuteness and severity of anemia. Symptoms can occur when anemia is chronic, however most patients are asymptomatic. Symptoms which relate to the underlying cause include non-specific complaints such as fatigue, headache, faintness, dyspnea, palpitations, intermittent claudication, tinnitus.

Physical Exam Findings

- General: pallor of mucus membranes, signs of hyperdynamic circulation (tachycardia, bounding pulse, cardiomegaly, and systolic flow murmur), heart failure, orthostatic hypotension
- Specific: koilonychia (ridging and spoon shape nails in iron deficiency anemia), jaundice (hemolytic anemia), bone deformities (thalassemia), leg ulcers (sickle cell disease), splenomegaly, petechaie/purpura (bleeding disorder), glossitis (iron, folate, vitamin B12 deficiencies), neurologic abnormalities (vitamin B12 deficiency)

Classification of Etiologies

Decreased production	Increased destruction or loss
Nutritional deficiencies -iron deficiency* -vitamin B12 deficiency -folate deficiency* *Bone marrow suppression* -Infections: HIV*, tuberculosis*, malaria, schistosomiasis*, hookworm*, hepatitis -Drugs: Isoniazid, chloramphenicol, alcohol, zidovudine, 5-FU, hydroxyurea -Chronic disease*: renal and liver disease, rheumatologic diseases, hypothyroidism *Hemoglobinopathies* -Thalassemias	*Blood loss* -acute or chronic GI bleeding* -menstrual bleeding* -trauma *Hemolysis* -Malaria -G6PD deficiency* -Microangiopathic hemolytic anemia: TTP, HUS, DIC, eclampsia, HELLP -Hereditary spherocytosis -Autoimmune hemolytic anemia -Sickle cell disease* -Paroxysmal nocturnal hemoglobinuria -Hypersplenism

***** these are some of the most common contributor to anemia among adults in Africa

Of note, most anemia among adults in Africa is multifactorial (ie due to multiple factors above and not to one factor alone), and each factor must be treated in order for the patient to improve.

Laboratory Findings

Red cell values: vary according to age, sex, pregnancy state

- normal hemoglobin in men 13-18 g/dl normal MCV 76-96
- normal hemoglobin in women 11.5 -16.5 normal MCV 76-96
- in adults, severe anemia is defined by a hemoglobin of < 7 g/dL.

Leukocyte and platelet counts: distinguish isolated anemia from pancytopenia. If pancytopenia, bone marrow aspiration/biopsy should be considered as the problem is usually in the bone marrow.

Reticulocyte count: Increases with the severity of the anemia, as in chronic hemolysis. A lower reticulocyte index in the face of anemia suggests: impaired bone marrow function, deficiency of iron, vitamin b12 or folate; lack of erythropoietin (renal failure); ineffective erythropoiesis

Peripheral Blood Blood smear: very useful in pointing towards specific types of anemia. See below for findings.

Classification of anemia by size

Microcytic anemia

Iron deficiency anemia: most common worldwide. Clinically: brittle nails, atrophy of papillae of tongue, brittle hair. Etiology: poor diet, chronic blood loss (schistosomiasis, worms, GI loss from esophageal varices, peptic ulcer). Diagnosis: MCV < 80, blood smear shows hypochromic red cells, pencil shaped (poikilocytosis), target cells. Treatment: iron replacement ferrous sulfate 200 mg tds

Anemia of chronic disease: associated with chronic inflammatory or malignant disease. Etiologies: infectious (TB, lung abscess, pneumonia, endocaritis) or non-infectious (rheumatoid arthritis, lupus), malignancy. Clinical features: normocytic anemia, reduced serum iron and TIBC, normal or raised ferritin. Treatment is treat underlying cause.

Thalassemia: heterogeneous group of genetic disorders which result from a reduced rate of synthesis of alpha (4 chains) or beta chains (2 chains) of hemoglobin. Changes in normal ratio results in each of the disorders. Thalassemia minor: often asymptomatic. Beta thalassemia major: autosomal recessive, presents with hepatosplenomegaly, bone expansion, infections. Diagnosis; severe hypochromic microcytic anemia with raised reticulocyte count, target cells

Normocytic Anemia

Anemia of chronic disease: see above

Hypothyroidism: treatment is thyroid replacement

Acute blood loss: can be normocytic before iron stores are reduced

Pure red cell aplasia: destructive antibodies or lymphocytes leading to ineffective erythropoiesis. Associated with thymoma and parvovirus. Diagnosis: lack of erythroid precursors on bone marrow biopsy. Treatment: supportive care

Macrocytic Anemia:

Vitamin B12 deficiency: Etiologies include malnutrition (alcoholics, vegetarians), pernicious anemia, decreased absorption (celiac sprue, Crohn's disease), increased competition (fish tapeworm, intestinal bacterial overgrowth). Clinical features neurologic changes (numbness, paresthesias, decreased vibratory and positional sense, ataxia). Smear shows hypersegmented neutrophils. Treatment: replacement of B12

Folate deficiency: Etiologies include malnutrition (alcoholics, elderly), decreased absorption (sprue), impaired metabolism (methotrexate, trimethoprim, antimalarials). Treatment: folate repletion

Hemolytic Anemia: See table for etiologies

- Due to red cell destruction and increased red cell turnover. Bone marrow is able to compensate 5 times the normal rate.
- Clinical features: jaundice, hepatosplenomegaly, dark urine.
- Labs: increased reticulocyte count, indirect hyperbilirubinemia, shistocytes on blood smear
- Treatment: treatment underlying cause of hemolysis

***Sickle cell disease: a severe hemolytic anemia caused by inheritance of a point-mutated gene. The mutation results in a Glu-Val amino acid substitution in position 6 of the Beta globin chain of the hemoglobin molecule and formation of HbS. When deoxygenated, the HbS molecules polymerize into long fibers and cause the red blood cells to sickle.

- Clinical features: severe anemia causes crises. Typically hemoglobin levels are 6-8 g/dl, reticulocytes 10-20%. Often get painful swelling of hands and feet. Shortness of breath, chest pain with infiltrate on chest xray is called acute chest syndrome
- Crises: painful vascular-occlusive crises precipitated by infection, dehydration, deoxygenation. Infarcts may occur in bone.
- Complications of sickle cell include renal failure, bone necrosis, infections (Salmonella osteomyelitis), splenomegaly. In Africa, average survival for sickle cell disease is < 13 years old.
- Laboratory findings: hemoglobin levels of 6-8 g/l, sickle cells on blood smear.
- Management: avoid precipitating factors. Give folic acid, improve hygiene. Give malaria prophylaxis. In sickle cell crisis: give IV fluids with normal saline, give antibiotics for signs of infections. Obtain urine dipstick, chest xray and FBP. Give oxygen and transfuse blood for severe anemia.

Approach to Anemia

- Obtain a thorough history: menstrual history, bleeding tendencies, hematuria, rectal bleeding, melena. Consider colonoscopy/endoscopy, urinalysis/ urine cytology for hematuria, pelvic ultrasound for fibroids.
- Check FBP, MCV, peripheral blood smear
- Determine underlying cause of anemia
- If hemodynamically unstable or very symptomatic, transfuse packed red blood cells
- Treat underlying cause of anemia
- Consider blood transfusion (BT) if hemoglobin < 7 g/dL and patient is symptomatic
- If the patient has signs of heart failure due to anemia, give Lasix 20mg IV stat with BT

Bleeding Disorders

Definition: Abnormal bleeding results from disorders of initiation of hemostasis and consolidation of hemostasis. Initiation of hemostasis involves the vascular endothelium and platelets. This manifests as purpura and hemorrhage from or into skin and mucous membranes.

Pathophysiology: All bleeding disorders are due to 1 of the following 3 things:

1. Thrombocytopenia - an abnormally low platelet count may result from defective production, increased destruction or splenic pooling. This is can present with splenomegaly and anemia.
2. Defective Platelet Function: Purpura from this cause can be seen in hemorrhagic fevers (lassa, dengue), alcoholism, hepatic cirrhosis, uremia, and leukemias. It can also result from ingestion of drugs such as NSAIDs. Rarely it is inherited as with VonWillebrand's Disease.
3. Clotting Factor Deficits: congenital or acquired (due to liver dyfunction, Vitamin K deficiency, DIC etc.)

Clinical presentation of bleeding disorders:

- *Platelet:* site: skin and mucous membranes, lesions: petechiae and ecchymoses, bleeding: after minor cuts and mild bleeding after surgery
- *Coagulation defects:* site: deep in soft tissue (muscle, joints), lesions: hemarthroses and hematomas, bleeding: unusual after minor cuts but can be severe after surgery

Types of Bleeding Disorders

Platelet Disorders

Thrombocytopenia and risk of bleeding:

- platelet count > 100,000: no risk of bleeding
- platelet count 50,000-100,000: risk with major trauma
- platelet count 20,000-50,000: risk with minor trauma
- platelet count < 20,000: risk of spontaneous bleeding

Etiologies:

- *Decreased Production of platelets:*
    - infections like typhoid, brucellosis
    - hypocellular bone marrow: seen in aplastic anemia, drugs (thiazides, antibiotics) and alcohol
    - cellular bone marrow: seen in leukemia
    - marrow replacement: seen in hematologic and solid tumors, granulomas (TB)
- *Increased Destruction of platelets:*
    - immune mediated:
        - Primary: immune thrombocytopenic purpura (ITP)
            - treatment: steroids, do not give platelets
            - Primary: onyalai. A profound acquired thrombocytopenia that affects young people in southern africa. Clinical features: hemorrhagic bullae on mucous membranes and epistaxis. Treatment: transfusions and possible splenectomy

        - Secondary: infection (HIV, malaria, dengue), lymphoproliferative disorders (lymphoma), drugs (heparin, quinine, sulfonamides), autoimmune disease
    - *non immune mediated:*
        - DIC (disseminated intravascular coagulation) is the widespread or uncontrolled deposition of fibrin in the circulation, followed by increased activation of fibrinolysis. Clinical features: hemorrhage, depleted platelets, decreased fibrogen and increased PT/PTT, microangiopathic hemolytic anemia with schistocytes on blood smear.
        - HUS/TTP: HUS (hemolytic uremic syndrome: microangiopathic hemolytic anemia + thrombocytopenia + renal failure) TTP (thrombotic thrombocytopenic purpura: microangiopathic hemolytic anemia + thrombocytopenia + alerted mental status + fever + renal failure)
        - Splenic sequestration
- Disorders of Platelet Function:

Coagulopathies:

These occur in 2 forms: congenital (hemophila A, hemophilia B, and von Willebrand' disease. 2nd form is acquired (malabsorption with Vit K Deficiency, liver disease, DIC)

Congenital coagulopathy (rare)

- Types: 1) hemophilia A = factor VIII deficiency 2) hemophilia B = factor IX deficiency
- Clinical features: bleeding into joints and muscles is common
- Diagnosis: by history, family history, increased PTT and factor VIII assay

Acquired coagulopathy

- Vitamin K deficiency or Malabsorption:
- etiology: malnutrition, decreased absorption, liver disease (decreased stores)
- diagnosis: prolonged PT which becomes normal with administration of vitamin K 10 mg IV
- Liver disease: bleeding cause is multifactorial including coagulation factor deficiency, liver no longer producing adequate amounts of fibrinogen, impairment in synthesis of vitamin K dependent factors
- bleeding with liver disease should be treated with cryoprecipitate, FFP

General evaluation for bleeding disorders:

Take a good history and physical exam asking about bleeding tendencies, where they bleed and when, family history, gum bleeding, heavy menstrual periods and excessive bleeding after cuts. Examine the skin and joints carefully looking for purpura, examine for splenomegaly

- obtain FBP, PT/PTT and look at blood smear
- obtain reticulocyte count
- treatment is based on underlying cause of bleeding disorder

Lymphadenopathy

Definition: lymph node enlargement

Signs/Symptoms

Patient may complain of swollen glands or mass. Systemic illness with enlarged lymph nodes can have a variety of constitutional symptoms such as weight loss, fevers, nightsweats, fatigue and malaise.

Physical Exam

The major lymph nodes to inspect and palpate include cervical nodes, axillary nodes (enlarged in breast cancer), epitrochlear nodes (enlarged in syphillus), and inguinal nodes. Always try to measure the size of the lymph node in centimeters. Take note if the enlarge lymph node is unilateral or bilateral, tender or nontender, whether it is mobile and whether it is erythematous. Lymph nodes from infection can be unilateral or bilateral and are usually mildly tender and mobile. Lymph node enlargement from malignancy can be nontender and fixed. Note whether lymphadenopathy is generalized or localized. Also ask the patient the duration of time the lymph nodes have been enlarged.

Etiology

Viral (most common cause of mild, transient lymphadenopathy lasting < 6 weeks):

- EBV, CMV, HSV, VSV, hepatitis, measles
- HIV: usually see generalized or local lymph node enlargement when patient is symptomatic from HIV itself. Enlarged lymph nodes can also be a sign of HIV related illness such as tuberculosis, histoplasmosis, CMV infection, Kaposi's sarcoma, lymphoma, dermatological conditions such as seborrhoeic dermatitis. Persistent generalized lymphadenopathy is common in HIV positive patients and is often due to HIV alone. This illness is defined as follow: 1) more than 3 separate lymph node groups affected 2) at least 2 nodes > 1.5 cm in diameter at each site, 3) duration > 1 month 4) no local or contiguous infection that might explain the lymphadenopathy is found 5) exclude treatable causes such as syphilis and tuberculosis

Bacterial (2nd most common):

- generalized lymphadenopathy (tuberculosis, atypical mycobacteria)
- TB adenitis (scrofula) is common in our setting and typically causes unilateral cervical lymphadenopthy with discharging sinuses in patients without HIV infection; in the setting of HIV infection, the lymphadenopathy is often diffuse and bilateral and may indicated disseminated disease
- localized lymphadenopathy = local adenitis (streptococci, staphylococci)
- tends to be severe and acute in onset

Neoplasm (3rd most common – to be discussed in another lecture):

- lymphoma, leukemia, metastatic carcinoma

Fungal and parasitic:

- Toxoplasmosis, histoplasmosis

Immunologic:

- drug hypersensitivity (phenytoin), serum sickness, collagen vascular disease

Evaluation

If the lymphadenopathy is mild and < 6 weeks, the patient should be seen again after 2-4 weeks but no immediate investigation is necessary. If the lymphadenopathy is severe (i.e. very large or painful or associated with B symptoms), the patient should have the following investigations.

The lymph node enlargement is usually a cause of another overlying illness. It is important to guide your evaluation based on the patient's history and physical exam and most likely diagnosis. To start, you can order a FBP (can check for blood disorders), chest xray (look for signs of tuberculosis) and a rapid test for HIV. You can also guide your bloodwork based on physical exam, such as, if patient complains of abdominal pain and distention -> order abdominal ultrasound and liver function tests also.

Lymph node biopsy is also another method of diagnosis if the cause is still in question, can be useful in cases of malignancy.

***If a node is rapidly enlarging or there is nodal asymmetry and systemic complaints not otherwise explained-> the lymph node should be biopsied to exclude Kaposi's sarcoma, lymphoma, infiltrative tuberculosis or fungal disease

Treatment

Treatment is guided by underlying diagnosis that is causing lymphadenopathy.

Lymphoma and Leukemia

Lymphoma and leukemia are considered disorders of the white blood cells.

Pathophysiology

- Dysregulation of hematopoiesis, the development of all blood lineages
- This dysregulation is often related to specific chromosomal abnormalities.
    - Acute Promyelocytic leukemia is associated with a t(9;22)
    - CML is associated with the formation of bcr-abl, via t(15;17)

Types

Leukemias are divided into 2 main subgroups: Chronic and Acute

- **Chronic** leukemias most often are indolent, requiring longer periods of time to manifest themselves, often with increased mature forms of cells.
- **Acute** leukemias are often characterized by rapid replacement of marrow with blast cells, i.e. immature forms. They are often rapid in their course, displacing normal hematopoiesis resulting in severe anemia, thrombocytopenia, and leukopenia.

Lymphomas consist of malignant transformation of cells living in lymphoid tissues. Divided into two groups: Hodgkin's, and Non-Hodgkin's. Both usually involve malignant growth of the spleen and lymph nodes.

Lymphomas

Non-Hodgkin's Lymphoma (NHL) (non-Burkitts):

- *Epidemiology:* Most common lymphoma in Africa; 500x more common in HIV
- *Definition:* heterogeneous group of tumors of B or T cell origin. Low grade lymphomas indolent but incurable. High-grade more aggressive but curable. High-grade NHL more common in Asia and Africa, and strongly associated with malaria (as in Burkitt's lymphoma) and HIV infection.
- *Clinical Presentation:* NHL rare before 40 years except among HIV infected patients. Lymphadenopathy common but extra nodal spread occurs early. First presentation may be in the skin, gut, CNS, or lungs. Often symptomless, systemic symptoms similar to hodgkin's lymphoma. Marrow involvement may cause pancytopenia, infection is common
- *Diagnosis:* same as Hodgkin's, need aspirate to evaluate cells. Staging is less important in the low grade NHL since 70% have spread at presentation, but may be more important in high grade tumors. Consider lymph node biopsy, chest xray
- *Management:* Curable but depends on grade. Symptomless low grade tumors may go into remission without therapy. Chlorambucil or cyclophosphamide may control symptoms that occur. Splenectomy may help with severe splenomegaly. Surgery used for bulky disease. Optimum treatment for high grade tumors is 6 weeks of chemotherapy (doxorubicin, cyclophosphamide, vincristine, bleomycin, and prednisolone).

Burkitt's lymphoma

Definition*:* A lymphoblastic non-hodgekins lymphoma, which is the most common childhood cancer in tropical Africa. There is a peak incidence at 5-10 years, with a male predominance.

Epidemiological patterns:

- second most common lymphoma in Africa
- it is endemic in tropical Africa and in areas with high malaria, with a peak at 5-10 years
- it has intermediate incidence in north Africa, western Asia, and South America
- it occurs sporadically in the West
- Correlates with Epstein-Barr virus (EBV) before the age of 1 year, and with malaria.

Clinical Presentation
- often with tumors of the jaw, but may involve other bones and also solid organs, GI involvement
- Histology: "starry sky" (isolated histiocytes on a background of abnormal lymphocytes)

Diagnosis*:* aspirates of tumor show large blasts with deeply basophilic cytoplasm and numerousvacoules

Management
- Highly curable.
- single dose of cytotoxic drug (cyclophosphamide 30 mg/kg IV) produces short term remission in some patients but the optimum treatment is multiple drug chemotherapy for 6-12 week. The chemotherapy regimens used vary between sites.

Hodgkin's Lymphoma (HL):
- *Epidemiology:* Third most common lymphoma in Africa; peaks during late childhood (10-20yo) and middle age (around 50yo)
- *Definition:* A malignant proliferation of lymphoid cells that is characterized histologically by Reed-Sternberg cells. HL is not common. High incidences in childhood in north Africa and sub-saharan Africa. EBV exposure has been linked to etiology (EBV DNA has been found in some Reed-Sternberg cells).
- *Clinical features:* presents with very enlarged, painless lymph nodes, usually in neck or axilla which have been described as "rubbery" in character. 25% have general symptoms of malaise, fever, weight loss, nightsweats (B symptoms). Signs: lymphadenopathy, anemia, hepatosplenomegaly
- *Diagnosis:* lymph node biopsy, FBC, LFTs, uric acid, chest xray, bone marrow biopsy
- *Management:* Curable. Radiation for low stages + chemotherapy for higher stages

Leukemias

Acute Lymphoblastic Leukemia (ALL)
- *Epidemiology:* most common malignancy among young children (usually 2-5 years)
- *Definition:* neoplastic proliferation of lymphoblasts
- *Clinical features:* due to malignant infiltration, will see lymphadenopathy, hepatosplenomegaly, bone pain. Also will see anemia, hemorrhage or thrombosis, and infections following immune depression
- *Diagnosis:* by peripheral smear, will see blasts cells and with bone marrow biopsy. WBC is raised in many patients to an abnormally high level. Check uric acid levels.
- *Management:* Curable. supportive care (transfusions for anemia, allopurinol for hyperuricemia). Prevention of infection with antibiotics ant antimalarials. Chemotherapy consists of: vincristine,

prednisolone, daunorubicin, may need CNS methotrexate infusion. Maintenance chemo required for 2-3 years, may see relapse in blood, CNS and testes

Acute Myeloblastic Leukemia (AML)

- *Epidemiology:* more common in elderly patients
- *Definition:* neoplastic proliferation of blast cells derived from myeloid cells in bone marrow
- *Clinical features:* similar to ALL. In tropical Africa, patients may present with chloroma: a solid tumor arising from the orbit. Gum hypertrophy can be seen with some subtypes
- *Diagnosis:* peripheral smear looking for blasts, bone marrow biopsy
- *Management:* Poorer prognosis. supportive as in ALL. Chemotherapy requires special centers. Bone marrow transplant reserved for those who have sibling matched donor or those who relapse

Chronic Lymphocytic Leukemia (CLL)

- *Epidemiology:* generally only occurs in very elderly patients
- *Definition:* monoclonal proliferation of well-differentiated lymphocytes. 90% are B cell variants incuding: hairy cell leukemia
- *Clinical features:* slow onset with bleeding, weight loss, infection, anorexia. Hepatosplenomegaly and enlarged rubbery lymph nodes also seen on exam. Spleen is enormous in areas with malaria.
- *Diagnosis:* blood shows marked lymphocytosis, thrombocytopenia. Bone marrow biopsy
- *Managemetn:* Very slowly progressive so chemotherapy is not always needed, prednisolone helps.

Chronic Myeloid Leukemia (CML)

- *Definition:* uncontrolled proliferation of myeloid cells, 90% have Philadelphia chromosome (9,22) translocation, resulting in BCR/ABL gene fusions: better prognosis
- *Clinical features:* chronic presentation with weight loss, lethargy, sweats, fever, anemia, gout, abdominal pain, hepatosplenomegaly, generalized lymphadenopathy
- *Diagnosis:* white blood cells extremely elevated, reduced Hb
- Management: Hydroxyurea can be used to control proliferation during the chronic phase. Patients uniformly will enter a blast phase at some point during their course. Treatment usually includes imatinib (Gleevec) chemotherapy, but only allogeneic bone marrow transplant is curative.

Solid Tumors

Intro to Cancer

Cancer is a common condition worldwide; Lung cancer was the most common cancer worldwide, followed by stomach, liver, colon, and breast. These are the incidence of cancer East Africa:

Estimated Age-Standardized cancer rates in Eastern Africa by sex, circa 1990 per 100,000 population		
Cancer Type	**Estimated rate (Male)**	**Estimated Rate (female)**
All	186.5	180.7
Cervix		49.2
Breast		19.4
Ovary		7.8
Uterine		4.8
Prostate	27.4	
Liver	21.8	9.5
Esophageal	17.4	4.8
Oropharyngeal	16.9	10.4
Gastric	14.1	13.3
Bladder	8.0	4.5
Lymphoma	7.5	4.5
Colon	6.5	3.9
Lung	5.5	1.3
Melanoma	5.3	4.3

Most common cancer types, by sex	
Male	**Female**
Prostate	Cervical
Liver	Breast
Esophageal	Gastric
Oropharyngeal	Oropharyngeal
Gastric	Liver

Esophageal CA and hepatocellular carcinoma are considered to be particularly endemic to Africa. There are also significantly higher rates of bladder, lung, and laryngeal cancer. These differences are thought to be related to environmental differences, including exposures to infectious (*S. haemotobium*, HBV, HCV, HPV) and non-infectious sources.

Basic Cancer biology

Cancer is a result of gene mutation, either in:

1. oncogenes (genes that are typically involved in some component of the cell cycle, now altered)
2. tumor suppressor genes (genes that usually regulate cell cycle and apoptosis that may become mutates, removing the “brakes” from the cell cycle

3. Sometimes an accumulation of somatic mutations must occur before the cancer develops.

Basics on the management and evaluation of cancer patients

Cancer requires early intervention

- cancer should be suspected in any elderly patient with unexplained illness
- before treatment of a cancer patient, all patients should have a diagnosis of cancer based on tissue pathology.

Signs and symptoms common to many types of cancer

- *Pain:* due to direct effect of tumor (infiltration of nerves or compression) or metastatic spread to bone.
- *Weight loss:* due to involvement of GI track (obstruction, metastatic liver involvement) or to increased cell turnover and metabolic rate.
- *Tumor mass:*diagnose the type of cancer with fine needle aspiration.
- *Fever:* may be a feature of certain cancers, such as renal cell cancer or liquid tumors. Also consider superinfection.
- *Anemia: U*sually normocytic normochromic, due to malabsorption. You can also get hypochromic with bleeding. Also you can have marrow involvement related to the cancer

3 questions to ask during the initial evaluation of patients with cancer:

1. What is the histiologic diagnosis of the tumor
2. Do we know where it has spread
3. How is this cancer creating symptoms or affecting the well being of the patient.

The Bosl 4:

1. Its not cancer until its proven to be cancer
2. If it is cancer, it is curable until proven otherwise
3. If its not curable, its treatable until proven otherwise
4. If the cancer itself is not treatable, the patient always is.

Initial Evaluations:

- Diagnosis: Tissue is the Issue. You need a sample to diagnose the cancer.
- Staging: Helps to determine which treatment options have proven efficacy or might be of benefit for the patient. Helps to determine overall prognosis as well. Often requires imaging techniques
- Manage the patient: Even if we do not have therapy available for the cancer, we always have therapy available for the patient (Symptom management)

Overview of Treatment options:

Surgical resection:

- can be curative for early tumors
- can be used for palliation
- can be used with chemotherapy
    - -Adjuvant chemotherapy: surgery followed by chemotherapy to treat tumor
    - -Neoadjuvant chemotherapy: chemo shrink tumors, followed by surgery

Radiation therapy:

- can be used for either curative or palliative therapy.
- side effects include fibrosis, marrow disorders, lung disease etc

Chemotherapy-

- often works better against tumors that are dividing quickly and always in the cell cycle.
- often affects normally fast growing tissues as well
- may involve hormonal therapy such as SERMs in Breast CA or androgen antagonists in Prostate Ca

Management of Symptoms:

- assessing pain and treating it aggressively is of extreme import
- often involves a combination of long acting agents, short acting agents for breakthrough pain, and topical agents (lidocaine patches)

Common Cancers in Adults in Africa

Kaposi's Sarcoma (in HIV patients)

- Many people with HIV have cutaneous manifestations and KS is one of them.
- *Definition:* Tumor of the endothelial cells, caused by HHV-8, a sexually transmitted herpesvirus. Lesions of the skin and sometimes viscera. Two other forms are recognized: 1st is classic KS (in equatorial Africa), slowly progressive in adults, limited to one region, espeically the feet. 2nd is indolent skin tumor of elderly men.
- *Presentation:* multiple nodular, pigmented lesions. Black on black skin and purple on pale skin. Small, macular, erythamtous early on, difficult to see. May become inflamed or ulcerate. Can occur on all parts of the body. Face, soles and oral cavity are common sites. Visceral disease may occur without skin involvement—the only visible lesion may be within the oral cavity. Oral lesions are not raised, may result in bleeding or pain/dysphagia.
- Kaposi's sarcoma commonly involves lymph nodes, GI tract (stomach, duodenum, rectum), and lungs (cause dyspnea, cough, chest tightness, hemoptysis, bronchoconstriction)
- *Diagnosis:* can be made clinically in most cases; a punch biopy is otherwise needed
- *Treatment*: the clinical course of KS is slow, patients normally die from HIV related infections. Pulmonary KS can be rapidly fatal.
- The lesions may respond to chemotherapy, relapse is common. Cutaneous KS is usually treated with anti-retroviral therapy
- Initial therapy is usually based on one agent, such as doxorubicin, etoposide, vincristine, or bleomycin. Subsequent combination therapy is required for more complicated lesions.

Melanoma

- *Definition*: Proliferation of melanocytes due to damage from UV radiation
- *Presentation:* in Africans often presents on the soles or feet or palms, as pigmented skin is often protective. Can also presents on the mucosal surfaces or on the retina.
- *Diagnosis*: Is made by biopsy of the lesion with pathological diagnosis
- *Treatment*: wide surgical resection is the treatment of choice. Chemotherapy is of limited utility in metastatic disease.

Lung Cancer

- *Definition/Epidemiology:* Fairly common in southern Africa due to rates of smoking, mining, asbestos exposure. Increasing in frequency in northern
- *Presentation:* cough, change in cough, hemoptysis, weight loss, shortness of breath, hoarseness, asymptomatic
- Small cell cancer
    - responsible for paraneoplastic syndromes, produce ectopic hormones such as ACTH or ADH -> causing SIADH hyponatremia
    - can also secrete PTHrP, cause Eaton-Lambert Syndrome
    - centrally located
    - treated with chemotherapy, radiation. Surgery not recommended for advanced disease
- Non-Small Cell Lung Cancer (NSCLC)
    - Squamous Cell Cancer
        - Centrally located, associated with smoking
        - Can cause hypercalcemia as well
    - Large Cell Carcinoma
        - Peripheral location
    - Adenocarcinoma
        - Peripheral location, NOT ASSOCIATED WITH CANCER
        - treatment chemo, radiation
- *Staging:* requires a CT scan of the Chest, Abdomen, and Pelvis for evaluation of metastatic disease, most Lung CA is diagnosed with metastatic disease already present.
- Also requires a Head CT
- *Treatment*: early NSCLC can be treated with surgical resection +/- chemotherapy. Small cell is always presumed to be metastatic, and is treated with chemotherapy and radiation

Nasopharyngeal CA

- *Epidemiology:* Common in Northern and Eastern Africa; Almost always 2/2 EBV exposure.
- *Presentation*: expanding mass in the upper nasopharynx with subsequent neck swelling, cranial neuropathies, hoarseness, difficulty swallowing
- *Treatment:* Radiation therapy, 5 yr survival ~ 50%. Chemotherapy options usually include platinum agents.

Breast Cancer

- *Risk Factors/Epidemiology:* Risk factors include unopposed estrogen exposure (early menarche, late child-bearing, HRT), family history (BRCA1/2), radiation exposure. Relatively uncommon in Africa, which is thought to be most due to child-bearing age.
- *Presentation:* lump in the breast. Look for breast asymmetry, dimpling of breast, retraction of breast and palpate for mass. Also feel for axillary lymphadenopahy since the tumor can metastasize there first
- A younger women age < 30 with a breast mass should be monitered for 1 month to note any change in mass
- *Evaluation:* Mammography. Screening mammograms should begin at age 40 in settings where they are routinely available. Masses should undergo mammography -> Biopsy.
- Biopsy should include staining for ER/PR if available, as well as Her2/Neu.

- *Treatment:* Surgery (Modified radical mastectomy with axillary lymph node dissection, or lumpectomy if RT is available), if Stage II or more, use adjuvant chemotherapy. If ER/PR+, consider estrogen receptor blockers (Tamoxifen) and aromatase inhibitors (anastrozole); if Her2Neu positive, consider mAb trastuzumab.

Esophageal cancer

- *Epidemiology:* Very common in some parts of Africa, thought to be related to environmental exposures- Seen in Kenya, Ethiopa, and Zimbabwe, as well as Uganda. Thought to be realted to diet, EtOH, tea, and soil composition. Most often Sq Cell CA. Another type of esophageal CA is adenocarcinoma, which is more related to GERD, Barret's esophagus. *Presentation:* Present with dysphagia, odynophagia and weight loss
- *Treatment:* Surgical procedures, RT for palliation, chemotherapy is usually ineffective

Colon cancer

- *Epidemiology*: relatively uncommon in Africa, thought to be mostly due to dietary issues, but incidence may increase with urbanization.
- *Presentation:* can present with abnormal bowel movements or change in daily bowel movements, weight loss, lower GI bleed. Any elderly patient with iron deficiency anemia should have colon cancer on their differential.
- *Treatment:* surgery +/- chemotherapy

Hepatocellular carcinoma:

- *Epidemiology:* usually seen in patients with cirrhosis, Associated with HBV, HCV, *Aspergillus flavus* associated with food storage.
- *Presentation:* Can present with RUQ or ascites, recent weight loss. Often a mass is found on abdominal exam. Often found on US of the abdomen for other reasons.
- *Evaluation:* Can be diagnosed with elevated alpha feta protein level. Abdominal ultrasound may be able to see mass.
- *Treatment:* Prognosis grim; if very localized can try resection. Techniques also available include HAE (Hepatic artery embolization), HAI (Hepatic artery infusion), cryoablation.

Genitourinary malignancy

Renal cell cancer: can present with hematuria, fever, flank pain. Treatment is surgery

Bladder Cancer:

- *Epidemiology:* Squamous Cell Cancer of the bladder is associated with *Schistosoma Haematobium*, due to highly inflammatory response to eggs in bladder wall. Early treatment of this infection is key to therapy
- *Presentation*: Hematuria, often painless. Pts can also present with necroturia, or the passing of pieces of inflamed dead tissue. Evaluation usually requires urologic consult with cystoscopy.
- *Treatment*: Radical Cystectomy. Chemotherapeutic agents involving platinum are often used for adjuvant treatment in the setting of advanced disease.

Prostate Cancer:

- *Epidemiology*: Disease of old men. Screening involves PSA when available, levels greater than ~3ng/dl usually mandate bx; however not particularly sensitive, estimated 25% of prostate CA has nl PSA levels.

- *Presentation*: Classically an older male who presents with increasing urinary hesitancy, frequency, or ejaculatory problems. Later presentations often include obstruction, hydronephrosis, LE outlet obstruction, and bone pain. Exam usually involves a firm, often enlarged nodular prostate.
- *Evaluation:* Trans-urethral biopsy, CT pelvis, and Bone scan if available
- *Treatment:* Radical Prostatectomy is the treatment of choice. Also available are TURP, brachitherapy, RT, and systemic chemotherapies; Hormonal therapy is extremely important, involves Anti-androgens followed by an LHRH Agonist.

Cervical cancer

- *Epidemiology:* Related to HPV, E6 and E7 proteins bind to p53 and Rb. One of the most common cancers in Africa. Proceeds from CIN to to malignancy.
- *Presentation:* can present with vaginal bleeding, discharge or asymptomatic.
- *Evaluation:* PAP smears!!
- *Treatment:* ranges from colposcopy to surgery with radiation depending on severity of lesion.

Complications of Solid Tumors

Spinal Cord Compression

- presents with lower extremity weakness, deceased sensation, decreased rectal tone, saddle anesthesia (decreased sensation along buttocks), loss of bowel or bladder control
- need to start steroids IV immediately with suspicion of cord compression
- obtain spinal xrays
- delay in treatment will result in paraplegia

Pleural effusions

- often large unilateral effusions, exudative
- will reaccumulate

Miscellaneous

Dermatology Exam & Skin Disorders

Dermatology Exam

Skin

- Color: cyanosis, jaundice, changes in melanin
- Moisture: moist, dry, oily
- Temperature: cool, warm
- Texture: smooth, rough
- Mobility: decreased in edema
- Turgor: decreased in dehydration

Describing Lesions:

- Anatomic location
- Arrangement: linear, clustered, dermatomal
- Type: macule, papule, pustule, bulla, tumor
- Color: red, white, brown, blanching

Nails:

- Color: cyanosis, pallor
- Shape: clubbing

Hair:

- Quantity: thin, thick
- Distribution: patchy loss or total alopecia
- Texture: Fine vs coarse

Types of Skin Lesions:

Primary lesions

- Macule: Circumscribed, flat, nonpalpable spots <1cm (freckles, tattoos)
- Patch: same as a macule but >1cm in size
- Papule: palpable, elevated, solid mass, <1cm (wart, acne)
- Plaque: same as papule but >1cm and flat topped (psoriasis)
- Nodule: palpable, solid lesion >1cm and not flat-topped (lipoma)
- Wheal: relatively transient, superficial area of local skin edema
- Vesicle: circumscribed superficial elevation of skin filled with serous fluid, up to .5cm (chickenpox, genital herpes)
- Bulla: same as vesicle but >.5cm
- Pustule: vesicle filled with pus rather than serous fluid
- Wheal: itchy, transiently edematous area

Secondary lesions

- Erosion: loss of superficial epidermis leaving a moist area that does not bleed
- Ulcer: deeper loss of surface that may bleed and scar
- Fissure: a linear crack

- Crust: dried residue f serum, pus, or blood
- Scale: thin flake of exfoliated epidermis

Skin Disorders

Contact Dermatitis

This is an inflammatory reaction of the skin that may occur as a response to an external irritant. Pts most commonly present with pruitis and rash. Skin lesions are erythematous, weepy, crusted patches or plaques with sharp angles and straight borders. Treatment is with avoidance of the suspected agent and topical steroids

Scabies

Scabies are transmitted by close personal contact. Infection causes small itchy papules and linear burrows, particularly in the finger webs and flexor wrist surfaces. Other sites include elbows, axillae, genitalia, peri-umbilicus and breasts. Itching is worse at night. Macules and pustules can occur and scratching may result in secondary bacterial infections. Treatment should be given not only to the symptomatic patient but also to household members even if they are not symptomatic. Treatment consists of malathion .5%, permethrin 5% cream, or benzylbenzoate 25% cream. The medication should be applied to the whole body and left on for 24 hours before washing off. Malathion and permethrin are applied twice, 1 week apart, and benzylbenzoate is applied on 3 consecutive days.

Molluscum Contagiosum

A poxvirus infection that is most common in young children however is also one of the most common cutaneous findings in AIDS patients. PE reveals 2-5mm discrete, dome-shaped, shiny papules with central umbilication. In adults the lesions are often found in the perianal and perigenital areas. Lesions are asymptomatic unless inflamed or irritated. They will usually resolve spontaneously over months to years but can be treated with curettage, liquid nitrogen therapy, or application of trichloroacetic acid.

Leg/foot ulcers

Common causes of leg or foot ulcers include complications from diabetes (both from peripheral vascular disease as well as neuropathy leading to decreased sensation/increased trauma), peripheral vascular disease, sickle cell disease, tropical ulcers (ulcer 2/2 mixed bacterial infection following minor trauma), and chronic osteomyelitis. Leprosy should also be considered in any patient with a painless burn, injury or ulcer of a limb. Management consists of identifying and if possible eliminating the source of the ulcer, elevating the legs, protection against weight-bearing, and dressing the wounds with clean bandages. If you suspect an infective cause of the ulcer or an overlying cellulites you will want to start antibiotics.

Erythema multiforme (Stevens-Johnson syndrome)

Erythema multiforme is an immune-mediated disorder that is due to drugs (typically penicillin, sulfonamides, phenytoin), infections (especially herpes simplex and mycoplasma) or malignancy. The severe form of the disease is called Stevens-Johnson syndrome and manifests with varying degrees of sloughing of the epidermis and mucous membranes. SJS is a life-threatening disease. Typical lesions include pink-red to red-blue macules, papules, plaques, target lesions and bullae. Lesions may be found anywhere but typically are on the extremities, palms and soles. Treatment focuses on the discontinuation of suspected drugs and treating any underlying infections. Other therapeutic

maneuvers are directed to symptoms and may include hydration, antihistamines, analgesics and wet dressings. Care in a burn unit or ICU may be required. Systemic corticosteroids are often used but their efficacy is unproven.

Pemphigus vulgaris

A serious autoimmune disease of skin and mucous membranes. It is often fatal without appropriate immunosuppressive drugs. Onset is usually between ages 40-60. Erosions often start in the oral mucosa progressing from localized skin blisters to generalized bullae. Lesions are painful but not pruitic. PE will reveal flaccid vesicles and bullae containing serous fluid with a predilection for the scalp, face, axillae, groin and back. Oral erosions are common. Pressure on the bullae may cause lateral extension of blisters (Nikolsky's sign). Treatment is supportive and oral prednisone is given to control new bulla formation.

Leprosy

Leprosy is a chronic inflammatory disease caused by mycobacterium leprae infecting macrophages and peripheral Schwann cells. Most people are able to develop an effective immune response however about 5% of people infected are unable to clear M. leprae and will develop clinical leprosy. Patients typically present with skin lesions (most commonly macules or plaques), weakness or numbness due to peripheral nerve damage, or a burn/ulcer in an anaesthetic hand or foot. Ulceration and digit loss seen in leprosy is due to secondary damage in neuropathic hands and feet and is not an intrinsic disease feature. Treatment usually consists of 6-12 months of rifampicin + dapsone or clofazimine, +/- steroids for nerve damage.

Bone Disease

Osteoporosis

Definition

- reduction in bone density or presence of a fragility fracture
- (T-score of -2.5 or lower = osteoporosis, T-score of -1 to -2.5 = osteopenia)
- Bone density = amount of bone mineral per unit area
- T-score indicates number of standard deviations from peak bone mass

Epidemiology:

- Very prevalent in the elderly in Western countries.
- >10 million Americans with osteoporosis, >18 million with osteopenia)
- Much lower incidence in African countries due to various factors.

Why is osteoporosis a problem?

- Decreased bone density (mineral & matrix) leads to increased fractures, resulting in increased morbidity and mortality.
- *Have students guess which bones are most susceptible to fractures.*

Pathophysiology:

- Bone remodeling: Bones are dynamic organs that undergo constant remodeling to adapt to physical stress placed upon them. They also act as a calcium reserve to aid in the maintenance of serum calcium levels.
- Osteoclasts: cause resorption of bone and release calcium into blood
- Osteoblasts: formation and mineralization of new bone
- Balanced osteoblastic & osteoclastic activity results in maintenance of a stable bone mass/density.
- Most adults reach a peak bone density between 20-30 years of age. After this point, increased osteoclastic activity & reduced osteoblastic activity result in imbalanced bone remodeling and increased overall bone resorption relative to formation (normal = 1-2% per year).

Factors that affect peak bone mass:

- Gender
- Race
- Genetic factors
- Gonadal steroids
- Timing of puberty
- Calcium intake
- Exercise

Secondary causes of osteoporosis:

- **Hypogonadism (most notably early menopause)**
- Hyperthyroidism
- Hyperparathryoidism
- Hypercortisolism (endogenous or exogenous)
- **Vitamin D Deficiency**
- **Diabetes Mellitus**
- Malabsorption/malnutrition

- Chronic Kidney Disease
- Severe liver disease
- Malignancy
- Drugs:
- **Glucocorticoids**
- **Alcohol**
- **Cigarettes**
- Anticonvulsants
- Thyroxine
- Chemotherapy

Diagnosis:

- Dual energy x-ray absorptiometry (DEXA) of lumbar spine & femur is used as a screening device in Western Countries for patients > 65 yrs (or younger if risk factors present)
- Diagnosis can also be made by fragility fracture:
    - Vertebral compression fracture
    - Wrist or hip fracture

Prevention & Treatment:

- Calcium
- Vitamin D
- Bisphosphonates
- The estrogen controversy

Renal Osteodystrophy

Definition: Derangements in mineral & bone metabolism due to chronic kidney disease & secondary hyperparathyroidism.

Pathophysiology: Progressive decrease in glomerular filtration rate (GFR) causes inability to excrete phosphorous. Increased phosphate levels cause inhibition of calcitriol (active metabolite of vitamin D). Decreased vitamin D levels cause decreased absorption of calcium. Low serum levels of ionized calcium rapidly stimulate parathyroid hormone (PTH) secretion, which induces calcium resorption from bone & renal phosphorous excretion. Renal phosphorous excretion is limited by the reduced function of damaged kidneys which causes continuation of PTH stimulating cycle.

Clinical Manifestations:

- Bone pain
- Fractures
- Myopathy (proximal)
- Pruritis (likely multifactorial)
- Vascular & soft tissue calcification

Diagnosis:

- Bone biopsy is gold standard, but rarely done due to invasiveness.
- Radiographic signs: erosive defects, pseudocysts
- Laboratory evidence: high serum phosphorous, high serum PTH, low/normal calcium

Treatment:

- Not removed through dialysis because the vast majority of phosphorous is intracellular
- Phosphate binders - Calcium carbonate, calcium acetate, sevelamer hydrochloride
- Avoid calcium citrate due to high aluminum content
- Calcitriol (vitamin D)

Osteoarthritis

Definition: non-inflammatory arthritis characterized by deterioration of articular cartilage & reactive formation of new bone at articular surface

Clinical manifestations:

- joint pain, most commonly in knees, hips, spine, hands
- Bony enlargement of DIP joints = Heberden's nodes
- PIP joints = Bouchard's nodes
- Symptoms of deep ache, joint stiffness (worse with activity)

Labs: synovial fluid WBC < 2000 (mononuclear predominance), normal/slightly elevated ESR

Radiologic findings: narrowed joint spaces, osteophytes, subchondral sclerosis & bony cysts

Treatment: physical therapy, weight-loss, acetaminophen, NSAIDS, intra-articular steroid injections

Approach to Arthritis

Definition: Athritis vs. Athralgia

Athralgia is a subjective symptom of pain within a joint Just as neuralgia describes the symptom of nerve pain and myalgia describes the symptom of muscle pain, so arthralgia describes the symptom of joint pain. Arthritis is an objective finding of inflammation of the joint on exam. Physical exam findings that demonstrate arthritis include heat/warmth, redness, swelling/effusion, pain, and loss of function. Be careful to distinguish arthritis from inflammation of surrounding structures (burisitis, tendonitis, etc.). Arthritis is usually worse with movement of the affected joint. Arthritis is a commonly divided into the following categories based on presenting symptoms.

<table>
<tr><th>Acute</th><th colspan="4">Chronic</th></tr>
<tr><td rowspan="3">Infection
Trauma/hemathrosis
Crystal deposition
Reactive
Early Chronic</td><td colspan="3">Signs of Inflammation</td><td>No Signs of Inflammation</td></tr>
<tr><td>Monoarticular</td><td>Oligoarticular</td><td>Polyarticular</td><td rowspan="2">Osteoathritis</td></tr>
<tr><td>Indolent infection
Early oligoarticular
Early polyarticular</td><td>Indolent infection
Seronegative
Early polyarticular</td><td>RA
SLE
Scleroderma
Polymyositis dermatomyositis</td></tr>
</table>

RA: rheumatoid arthritis. SLE: systemic lupus erythematous.

Epidemiology

Osteoarthritis is the most common type of arthritis world wide, is more commonly found in older patients and is usually progressive in nature. Acute monoarticular pain is usually caused by crystal deposition (gout, calcium pyrophosphate deposition), but it is very important to rule out infectious causes of joint disease. If you treat infectious arthritis early in its course, you will prevent long term joint damage.

Clinical Manifestations Acute Joint Pain

Infection	Trauma	Crystal Deposition	Reactive
Fever	History of injury	Recurrent exacerbations	Preceding infectious illness
Red, hot swollen joint More commonly large joints Poly or monoarthritis Neisseria, Haemophilus, and streptococcus	Rapid swelling of knee	Monoarticular Red, hot, swollen joints Gout often affects 1st metatarsophalangeal joint	Swelling and pain (but no redness) Uveitis, urethritis, conjunctivitis,

Clinical Manifestations of Chronic Joint Pain

Rheumatoid arthritis	Osteoarthritis	Scleroderma, polymyositis, dermatomyositis, SLE
Age varies considerably Stiff after resting (morning stiffness)	Usually > 40 years old Stiff after effort (evening stiffness)	Vary according to disease
Metacarpohalangeal Proximal interphalangeal Heberden's nodes absent Joint soft, warm, tender Symmetric joint involvement	Disatal interphalangeal Carpometacarpal, knee, hip, spine Heberden's nodes frequently present Joint hard and bony Assymetric joint involvement	

Investigations

- Rapid test for IDS
- Erythrocyte sedimentation rate (ESR)
- Rheumatoid factor (RF) titers
- Evaluation of synovial fluid (cell count, differential, culture, gram stain, crystal analysis)
- Radiographic study of affected joints
- Brucella serology
- Full blood picture
- Blood culture
- Creatinine
- Urine dipstick

Arthrocentesis – Analysis of Joint Fluid

	Normal	Noninflammatory	Inflammatory	Septic
Appearance	clear	clear, yellow	Clear-opaque, yellow-white	Opaque
WBC/mm3	<200	<2000	>2000	>2000 but usually >100,000
Neutrophils	<25%	<25%	≥50%	≥75%
Culture	negative	negative	Negative	Positive
Glucose	≈serum	≈serum	25<glu<serum	glu <25
Conditions		OA, trauma	RA, crystal, CTD, seroneg	Infection

Treatment

Treat the underlying disease process.

Medical Ophthalmology

Visual Loss

History and Exam:

- ask about onset of loss, duration and progression of symptoms
- measure the visual acuity with and without a pinhole
- examine the cornea and pupil
- dilate the pupil and examine the optic disc and retina with an ophthalmoscope

Differential:

- Refractive errors include:
    - myopia: short sightedness causing poor distance vision; will correct with pinhole
    - hypermetropia: long-sightedness giving difficulty with near vision in young pts
    - astigmatism: die to a different refraction in 2 axes of the eye
    - aphakia: refractive error due to absence of the lens
    - pesbyopia: poor accomidation giving difficulty in reading, usually after age 40
- Cataracts: most common cause of bilateral blindness worldwide. Gradual and progressive decrease in visual acuity. Grey-white to white opacity in the pupil. Fundoscopic exam shows opacity of the red reflex with obscuration f the fundal detail. Pupil reaction to light is *normal* in an uncomplicated cataract. They are treated surgically under local anesthesia.
- Corneal Opacity: May follow a corneal ulcer, injury, or due to a specific eye disease such as vit A deficiency, trachoma, or leprosy. Appears as a white opacity on cornea usually obscuring the pupil. Treatment limited.If both eyes affected,maybe corneal transplant or optical iridectomy
- Glaucoma: Causes 10-20% of all blindness. Acute with a red painful eye OR chronic with gradual progressive nerve damage and vision loss. Early diagnosis difficult without proper equipment; late glaucoma seen on fundoscopic exam cupping of the optic disc and poor pupil reaction to light. Mgt: decrease intraocular pressure with life-long drops or filtration surgery. Tx does not restore sight but is given in effort to preserve remaining vision.

Red Eye

History and Exam

- ask about any known cause, particularly any injury
- measure visual acuity
- carefully examine the eyelids, conjunctiva, cornea, and pupil

Differential

if history of trauma, consider

- Corneal or conjunctival foreign bodies: if present, use local anesthetic drop to conjunctiva and remove gently with corner of thick paper. Use antibiotic ointment and eye pad for 1 day
- Corneal abrasions: Scratche to the cornea removes epithelial cells. Sudden severe pain and photophobia. Dx confirmed by applying florescein to stain. Treat with antibiotic ointment and eye pad until pain resolves and epithelium has healed

- Hyphaema: severe blunt injury causing bleeding in the eye. Level of blood (hyphaema) visible between cornea and iris. Usually resolves over days with rest. Avoid anticoagulants (ASA or NSAIDS). If painful give acetazolamide 250mg qds for 3-7 days to lower the IOP.

if no h/o trauma, consider

- Conjunctivitis: Infective (bacterial or viral) or allergic. For infective prescribe antibiotic ointment for 5-7 days. Chlamydial conjunctivitis (trachoma) will discussed below.
- Corneal ulcers: Spontaneous or from trauma. Sx: Usually severe pain and blurred vision. PE: redness around the eye and opacity on cornea which stains with florescein. In severe cases fluid level of pus inside the eye (hypopyon). Tx: based on cause. Treat herpes simplex with acyclovir ointment. Treat bacterial infection with intensive topical or sub-conjunctival antibiotics. Treat fungal infections with antifungals. Vit A deficiency is txd with vit A 200,000 iu x 3. Treat exposure ulcers (i.e. from leprosy causing eyelids to stay open) with antibiotics and by taping eye closed.
- Uveitis: Anterior = iritis. Posterior = choroiditis. Many causes: leprosy, onchocerciasis, toxo, TB, syphilis, etc. Sx: mild to severe pain, usually with blurred vision and photophobia. PE: dilated blood vessels around margin of cornea and irregular pupil margins. Mgt: dilate the pupil and use topical anti-inflamatory agents. Choroiditis Sx: painless visual loss (severe attack may cause discomfort). A white inflammatory lesion on retina. Mgt: treatment of the cause.
- Acute glaucoma: If the IOP increases suddenly over hours or days then the eye becomes red and very painful with severe loss of vision. Uncommon <50yo. Spontaneously or complication of old cataract. Cornea appears hazy and the pupil is semi-dilated and fixed to light. Tx: acetazolamide 500mg stat and then 250 qds. Surgical treatment is often also required.

Other Eye Conditions

- **Trachoma**: chronic conjunctivitis caused from repeated infection with Chlamydia trachomatis. Inflammation leads to conjunctival scarring. Eyelashes to turn in and cause corneal ulceration, scarring and blindness. PE: trichiasis (inturned eyelashes or previously removed eyelashes), corneal opacities, conjunctival inflammation and scarring. Tx: either azithromycin 20mg/kg po as a single dose or tetracycline 1% topical ointment bd x 6 weeks.
- **Vit A deficiency**: leads to xerophthalmia (dry eyes) thencorneal ulcerations and blindness. See nutritional deficiencies lecture.
- **Onchocerciasis**: Eye/skin infection with filarial worm Onchocerca valvulus. Causes keratitis, corneal scar, iritis, chorioretinitis, night blindness, optic neuritis and secondary optic atrophy.
- **HIV infection**: ocular manifestations include herpes zoster ophtalmicus (treat with oral acyclovir), squamous cell carcinoma of the conjunctiva (treat with surgical excision if possible), and CMV retinopathy (treat with gancyclovir or foscarnet). CMV retinopathy is the most common OI of the eye and the major cause of blindness. It is bilateral in 50% of cases. Appearance is one of red hemorrhages and yellow necrotic tissue. It is progressive and can destroy the whole retina, unfortunately treatment is expensive and has severe side effects.