Stats

<table>
<thead>
<tr>
<th></th>
<th>Result of gold standard test</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease present</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test Positive</td>
<td>True positive A</td>
<td>A+B</td>
</tr>
<tr>
<td>Test negative</td>
<td>False negative C</td>
<td>C+D</td>
</tr>
<tr>
<td><strong>Disease absent</strong></td>
<td>False positive B</td>
<td>A+B</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>A+C</td>
<td>B+D</td>
</tr>
</tbody>
</table>

**Sensitivity** = \( a/(a+c) \)

- Number of true positives divided by number of all people with the disease
- False negative ratio is equal to 1 - sensitivity
- High sensitivity is desirable for a screening test

**Specificity** = \( d/(b+d) \)

- Number of true negatives divided by number of all people without the disease
- False positive ratio is equal to 1-specificity
- High specificity is desirable for a confirmatory test

**Positive predictive value** = \( a/(a+b) \)

- Number of true positives divided by number of people who tested positive for the disease
  - The probability of having a condition, given a positive test.
  - The higher the prevalence of a disease, the higher the PPV.

**Negative predictive value** = \( d/(c+d) \)

- Number of true negatives divided by number of people who tested negative for the disease
  - The probability of not having the condition, giving a negative test.

Pre-test probability (prevalence) = \( (a + c)/(a + b + c + d) \)

Pre-test odds = prevalence/(1 - prevalence)

Likelihood ratio for a positive test result = sensitivity / (1 - specificity)

Likelihood ratio for a negative test result = (1 - sensitivity) / specificity

Post-test odds = pre-test odds x likelihood ratio

Accuracy = \( (a+d)/(a+b+c+d) \)

Post-test probability = post-test odds / (post-test odds + 1)

---

Biostatistics

**Prevalence** – total number of cases in a population at a given time
Prevalence ≥ incidence x disease duration
Prevalence > incidence for chronic diseases
Prevalence ≥ incidence for acute disease

**Incidence** – number of new cases in a population per unit time

**Reliability** – reproducibility (dependability) of a test
**Validity** – whether the test truly measures what it purports to measure. Appropriateness of a test.

---

**Study design**

**Case-Control Study**
Observational study
Pick a disease, follow the risk factors
Sample chosen based on presence (cases) or absence (controls) of disease.
Information collected about risk factors.
Often retrospective
--calculate odds ratio, cannot calculate true relative risk or measure incidence

**Cohort Study**
Observational study – calculate relative risk, incidence
Pick the risk factors, follow the disease
Sample chosen based on presence of absence of risk factors. Subjects followed over time for development of disease
EX – Framingham heart study (large prospective cohort study)
--time consuming, expensive, good for common diseases

**Clinical trial**
Experimental study
Compares therapeutic benefit of 2 or more treatments
compares two equal groups in which one variable is manipulated and its effect is measured.
Highest-quality when randomized and double-blinded

**Bias**
Selection – subjects chose group
Recall – knowledge of presence of disorder alters recall by subjects
Sampling – subjects are not representative therefore the results are not generalizable

**Ways to reduce bias**
1. blind studies (single vs double)
2. placebo responses
3. crossover studies (each subject acts as own control)
4. randomization
**Type 1 error** ($\alpha$)

Stating that there is an effect of difference when there really is not (to mistakenly accept the experimental hypothesis and reject the null hypothesis. $\alpha$ is a preset level of significance, usually $p<.05$. 

$P =$ probability of making a type I error
If $P<.05$, then there is a less than 5% chance that the data will show something that is not really there. 

$\alpha$ - you “saw” a difference that did not exist – for example, convicting an innocent man.

**Type II error** ($\beta$)

Stating that there is not an effect or difference when there really is (to fail to reject the null hypothesis when in fact the null hypothesis is false. $\beta$ is the probability of making a type II error.

$\beta =$ you did not “see” a difference that does exist – for example, setting a guilty man free

1-$\beta$ is “power” of study, or probability that study will see a difference if it is there.

*Type 1 kills everyone
Type 2 makes professors blue (because they can’t publish results)*

**Power**

Probability of rejecting null hypothesis when it is in fact false. It depends on:

1. total number of end points experienced by population
2. difference in compliance between treatment groups (differences in the mean values between groups).

If you increase sample size, you increase power. There is power in numbers.

Power $= 1-\beta$

**Relative Risk**

<table>
<thead>
<tr>
<th>Disease present</th>
<th>Disease absent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure Positive</strong></td>
<td>True positive</td>
</tr>
<tr>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td><strong>Exposure negative</strong></td>
<td>False negative</td>
</tr>
<tr>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>

**Odds ratio** – approximates the relative risk if the prevalence of the disease is not too high.

--used for case control, retrospective studies

OR $= \frac{ad}{bc}$

**Relative risk** – disease risk in exposed group/disease in unexposed group

--used for cohort studies

RR $= \frac{[a/a+b]}{[c/c+d]}$

**Atributable risk** $= \frac{[a/a+b]}{[c/c+d]}$
--if the 95% confidence interval for OR or RR includes 1, the study is inconclusive

Screening accuracy

**Precision** – consistency and reproducibility of a test (reliability); absence of random variation in a test
(think about darts – all the darts are grouped together at 8 o’clock – this is precision)

**Accuracy** - trueness of test measurements
(think about darts – the darts are equally distant from the center, but not necessarily very close)

Getting Sued
If a patient sues you for professional liability, she must prove:
--you owed her duty of care
--you breached that duty
--your breach of duty (negligence) caused her injury
--she suffered damages as a result of that injury

**Duty of care**
--usually begins when you offer services and patient accepts services
--can not refuse to establish relationship in following circumstances:
  --you are a resident
  --patient seen in emergency room
  --may not transfer or refuse to treat patients with emergency medical conditions
--special sitations when relationship established
  --telephone contact
  --email contact
  --if member is managed care patient or if appt is for life threatening condition

**Breach of duty**
--an “act of commission” – you did something you should not have done
--“an act of omission” – you failed to do something you should have done
--provided treatment that did not meet the standard of care

**Causation**
--patient must prove that your negligence caused directly caused her injury

**Damages**
--patient must prove she suffered physical, financial or emotional injury

**Patient refusal of treatment**
Whenever a patient refuses a medical treatment, surgical procedure, or diagnostic test, the physician should document the informed refusal in the patient's medical record and include the following information:
  - The patient's refusal to consent to a medical treatment, surgical procedure, or diagnostic test
• Documentation that the need for the treatment, procedure, or test has been explained
• The reasons stated by the patient for such refusal
• A statement that the consequences of the refusal, including possible jeopardy to health or life, have been described to the patient

**Screening and Health Maintenance (breast, colon, cervical ca)**

1. **Colorectal Cancer (CRC)**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Risk Factors</th>
<th>Screening Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>Age &gt; 50, no GI sxs</td>
<td>a. FOBT q yr + flex sig q 5 yrs OR b. FOBT q yr + colonoscopy q 10 yrs</td>
</tr>
<tr>
<td>Moderate</td>
<td>a. One or multiple polyps, personal h/o CRC b. Fam h/o CRC/adenomatous polyps in 1st deg rel</td>
<td>a. colonoscopy q 3 yr, if nl → q5yr b. colonoscopy at age 40 or 10 yr before youngest family case, if nl → q3-5 yr</td>
</tr>
<tr>
<td>High</td>
<td>a. Fam h/o of FAP b. Fam h/o HNPCC</td>
<td>a. genetic testing at age 10, colectomy if + or if polyposis OR colonoscopy q 1-2 yr at puberty b. genetic testing at age 21; if + colonoscopy q 2 yr until age 40 → then q1yr</td>
</tr>
</tbody>
</table>

* for colorectal ca, colonoscopy = flex sig + barium enema but is more $$$

* Key points from Prolog
  • Hormone therapy with estrogen + progestin decreased risk of CRC in women by 20% in WHI study
  • 10% of CRC cases are attributable to family history CRC in 1st degree relative; 70% are sporadic

2. **Breast Cancer and Breast Diseases**

• Monthly self exams, physician exams q 3 yrs until 40, then yearly after that
• Mammogram q 1-2 yrs for age > 40; q 1 yr age > 50

• Key points from Prolog questions

<table>
<thead>
<tr>
<th>BRCA1/BRCA2 mutations</th>
<th>• Hereditary cancers = 5-7% all breast ca • 80% hereditary breast ca have BRCA1/2 gene mutations • Key risk factors in non-Ashkenazi ancestry: fam h/o BRCA1/BRCA2, personal or 1st degree relative h/o breast or ovarian ca • Key risk factors if Ashkenazi ancestry: one or more fam members with breast ca .50 yo; 1st or 2nd deg relative with breast ca at any age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Ca prophylaxis</td>
<td>• Tamoxifen (SERM) can be effective in preventing ER + breast CA; but can incr risk of endometrial polyps/neoplasia</td>
</tr>
</tbody>
</table>

**Evaluating Breast Masses**

• Differential dx of breast mass: benign tumors/cysts (fibroadenoma, fibrocystic changes, fat necrosis), ductal/lobular hyperplasia, carcinoma in situ, invasive cancer
• Breast mass → needle aspiration (cystic v solid, cells for cytology), ultrasound, MRI
• Clear fluid → low chance of malignancy
• Bloody fluid, mass recurrence, solid masses → surgical bx

3. **Cervical Cancer**

• Risk factors: multiple sexual partners, smoking, immunocomprised state
• Pap smears within 3 yrs of sexual activity or at age 21
• In U.S, rate of cervical ca plateaus at age 65 → American Cancer Society recommends discontinuing screening for low risk women at age 70
• Management of abnormal pap smears and colposcopy findings → see yellow book p171-172 or go to http://www.asccp.org/pdfs/consensus/algorithms_cyto_07.pdf
Primary Prevention and Counseling

1. Smoking and Smoking Cessation
   - Health risks: cardiovascular disease, COPD, malignancies, PUD, osteoporosis, peripheral vascular disease
   - Risks during pregnancy: spontaneous abortion, fetal demise, neonatal death, SIDS, low birth weight
   - USPHS “5 As” for smoking intervention (ask, advise, assess willingness to quit, assist with quitting, arrange follow up)
   - 5 stages of smoking cessation: precontemplation, contemplation, preparation, maintenance, relapse
   - Techniques: nicotine patch, nicotine gum, bupropion, behavioral modification

2. Alcohol and Drug Screening (Prolog Primary Care Case 128)
   - Screening tools: CAGE, TWEAK, AUDIT, T-ACE
   - TWEAK, AUDIT, T-ACE validated for use in women; TWEAK is most reliable and specifically use for pregnant women
   - CAGE questions are less effective in identifying drinking problems among women

Immunizations

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendations and contraindications</th>
</tr>
</thead>
</table>
| Influenza (given q 1 yr) | ● Adults > 50  
                           ● Adults < 50 with chronic medical problems  
                           ● Health care workers  
                           ● Pregnant women (Oct-May)  
                           Contraindications:  
                           ● H/o severe anaphylaxis to eggs  
                           ● *mild illness and breastfeeding are not contraindications |
| Pneumococcal             | ● Adults > 65  
                           ● Sickle cell disease, asplenia  
                           ● Chronic disease or immunocompromised  
                           ● Women with high risk pregnancies |
| Tetanus/diphtheria (booster q 10 y) | ● Primary series for everyone  
                                  ● Wound management  
                                  ● Travel to high risk areas |
| Hep B                    | ● Primary series as infant and high risk groups, health care workers |
| Hep A                    | ● Travel to endemic areas, chronic lover disease, HCV  
                                  ● Contraindications: Safety during pregnancy undetermined |
| MMR (live vaccine)       | ● Primary series as infant  
                           ● Adults born after 1957 with no immunity proof  
                           ● Women of reproductive age without immunity proof  
                           ● Health care workers  
                           Contraindications: Pregnancy, Immunocompromised |
| Varicella                | ● Primary series as infants  
                           ● Adults with no h/o chickenpox  
                           ● Close contacts of immunocompromised  
                           Contraindications: Pregnancy, Immunocompromised |
| Polio                    | ● Primary series as infants  
                           Unvaccinated adults traveling to endemic areae |
Contraception – see yellow book section p 94-102

Medical/Spontaneous Abortions – yellow book p 92

Dysfuntional/Abnormal Uterine Bleeding (Johns Hopkins Manual p424-425)
- Dx of exclusion, must r/o all else
- Common cause is anovulation/olig-ovulation; PCOS and morbid obesity may also contribute to DUB (Obesity: peripheral conversion of androstendione to estrone in adipocytes)
- Prolonge anovulation → unopposed estrogen state → risk of endometrial hyperplasia

<table>
<thead>
<tr>
<th>Managing AUB</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical</td>
<td>Surgical</td>
</tr>
<tr>
<td>- Hormones (progestins, combined estrogen/progestins, androgenic steroids, GnRH agonists)</td>
<td>Short Term:</td>
</tr>
<tr>
<td>- NSAIDs</td>
<td>- D+C</td>
</tr>
<tr>
<td>- Antifibrinolytics</td>
<td>- Endometrial Ablation</td>
</tr>
<tr>
<td></td>
<td>- Hysterectomy</td>
</tr>
</tbody>
</table>

Vaginitis
- Pruritis, discharge, odor, dysuria
- Physiologic pH of vagina = 4.0 → prevents overgrowth of vaginal flora
- Dx: clinical si/sx, wet prep

<table>
<thead>
<tr>
<th>BV</th>
<th>Trich</th>
<th>Candida</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>&gt; 4.5</td>
<td>5-7</td>
</tr>
<tr>
<td>Discharge/</td>
<td>Thin, white, adherent, +whiff test</td>
<td>Thin, frothy, white/gray/yellow, copious discharge. Erythematous cervix</td>
</tr>
<tr>
<td>exam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wet prep</td>
<td>Clue cells</td>
<td>Trichomonads, WBCs</td>
</tr>
<tr>
<td>Tx</td>
<td>Flagyl (recommended in pregnancy) v clinda</td>
<td>Flagyl Tx sexual partners</td>
</tr>
<tr>
<td>F/u</td>
<td>1 mo TOC in high risk pregnant pt</td>
<td>Not necessary if asymptomatic</td>
</tr>
</tbody>
</table>

Working up Myocardial Infarct
- EKG: early peaked T waves, ST elevation, Q waves, ST depression, T wave inversion; Q wave vs. non Q wave (distinguished by cardiac enzymes and EKG findings)
- Cardiac enzymes: CK-MB, Troponin I and T → q8h x 3
- Treatment: aspirin, beta-blockers, ACE-I, statin, oxygen, nitrates, morphine, heparin, revascularization (tPa vs PTCA), cardiac rehab
### Skin Disorders – Inflammatory, Infectious, and Miscellaneous

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rosacea</strong></td>
<td>Chronic reddening of face&lt;br&gt;Women 30 – 50 yo&lt;br&gt;Erythema, telangiectasia, papules, pustules&lt;br&gt;Tx with topical flagyl, systemic abx</td>
</tr>
<tr>
<td><strong>Seborrheic Dermatitis</strong></td>
<td>Chronic, idiopathic inflammatory skin dz&lt;br&gt;Common in skin folds, scalp, ears, nose&lt;br&gt;Tx with sunlight, ketoconazole, topical steroids</td>
</tr>
<tr>
<td><strong>Warts</strong></td>
<td>HPV 6 and 11 assoc w/condyloma acuminatum&lt;br&gt;Tx: freeze w/liquid nitrogen, surgical excision, laser therapy, podophyllin</td>
</tr>
<tr>
<td><strong>Herpes Zoster</strong></td>
<td>Reactivation of VZV (dormant in DRG)&lt;br&gt;&gt; 50 yo, mostly immunocompromised state&lt;br&gt;Dermatomal&lt;br&gt;Tx: symptomatic relief, antivirals +/- steroids</td>
</tr>
<tr>
<td><strong>Scabies</strong></td>
<td>Signs: pruritis, burrows, plaques, papules (hands/wrists)&lt;br&gt;Tx with Permethrin cream. Lindane contraindicated in pregnant/lactating women</td>
</tr>
<tr>
<td><strong>Psoriasis</strong></td>
<td>Abnormal prolif of skin cells; silvery scales&lt;br&gt;Chronic flares and remissions&lt;br&gt;Tx with steroids, MTX, infliximab, cyclosporine, systemic retinoids, phototherapy</td>
</tr>
</tbody>
</table>

### Skin Disorders – Precancerous and Cancerous

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Actinic Keratosis</strong></td>
<td>Rough, scaly lesions from sun exposure&lt;br&gt;Bx to r/o SCC&lt;br&gt;Tx with surgery, freezing, topical 5FU</td>
</tr>
<tr>
<td><strong>Basal Cell Carcinoma</strong></td>
<td>Most common skin cancer; sun exposure&lt;br&gt;3 Ps – pink, pearly papules&lt;br&gt;locally destructive, mets rare</td>
</tr>
<tr>
<td><strong>Squamous Cell Carcinoma</strong></td>
<td>sun exposure, higher chance of mets&lt;br&gt;crusting ulcerating nodule&lt;br&gt;good prognosis, bad if node involvement</td>
</tr>
<tr>
<td><strong>Melanoma</strong></td>
<td>sun exposure, most aggressive, highest mortality&lt;br&gt;ABCDE’s&lt;br&gt;Depth of invasion most important prognostic factor&lt;br&gt;Mets to nodes, lung, liver, brain, bone, GI tract</td>
</tr>
</tbody>
</table>
Preventative Health

<table>
<thead>
<tr>
<th>Intervention</th>
<th>High Risk Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriuria testing</td>
<td>DM</td>
</tr>
<tr>
<td>Bone Density</td>
<td>65 yo or younger if hi risk</td>
</tr>
<tr>
<td>Colorectal Cancer Screening</td>
<td>&gt;50yo (any mode)</td>
</tr>
<tr>
<td>Fasting Glucose Testing</td>
<td>BMI &gt;25, FH, GDM, PCO, HTN…</td>
</tr>
<tr>
<td>Hgb assessment</td>
<td>Excessive blood flow, ethnic risk</td>
</tr>
<tr>
<td>HCV testing</td>
<td>IVDU, dialysis, chronic elev LFTs</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>FH, DM, tob use, HTN</td>
</tr>
<tr>
<td>Mammography</td>
<td>Q1-2 yr &gt; 40yo, +/- CBE, SBE</td>
</tr>
<tr>
<td>STD testing</td>
<td>CT: all &lt;25 yo &amp; other hi risk</td>
</tr>
<tr>
<td></td>
<td>GC: all adolescents &amp; hi risk</td>
</tr>
<tr>
<td></td>
<td>HIV: all hi risk, inv cervical CA</td>
</tr>
<tr>
<td>Skin exam</td>
<td>Exposure, FHx, preCA lesions</td>
</tr>
<tr>
<td>TSH</td>
<td>Autoimmune dz, FHx of thyroid</td>
</tr>
<tr>
<td>TB test</td>
<td>HIV, alcoholic, IVDU, institutions</td>
</tr>
</tbody>
</table>

**Otitis Media**

- **Otitis media w/ effusion**: no abx, TM may be discolored, opacified, decr mobility, air/fluid behind it
- **Acute otitis media**: bacterial infx, distinct fullness/bulging/red TM, severe pain; observation for 48-72 hrs vs Rx for amoxicillin or macrolide if pcn allergy (if given initially shortens duration by 1day), Auralgan for topical pain relief

**Resp Tract Infxn**

- **Acute Bronchitis**: only indication for abx is Pertussis or underlying lung dz
- **Influenza**: rapid antigen test (<1h), Rx for neuraminidase inhibitors shorten sx by 1day (not amantidine/rimantidine b/c resistance to Influenza A)

**Asthma**

- airway obstruction, bronchoconstriction, inflammation (IgE)
- triggers: allergen, envmt, exercise, emotional, infxn, drugs (ASA, sulfites, Bblockers)

*Chronic tx*: track sx with Peak Flow, spirometry FEV1/FVC to document degree of obstruction; inhaled Bagonist PRN, inhaled steroids/long-acting B2, mast cell stabilizer (cromolyn -good for atopic pt), leukotriene-inhibitor (singulair)

*Acute tx*: assess severity, 02, albuterol/ipatropium nebs, systemic steroids (oral as good as IV), MagSO4 2g IV conisider admission if no improvement over 6hrs or
PEFV <40% predicted; **send home w/ 3-10 d course of oral steroids and inhaled steroid rx

Good charts from up to date:

### Classifying asthma severity and initiating treatment in youths greater than or equal to 12 years of age and adults

<table>
<thead>
<tr>
<th>Components of severity</th>
<th>Classification of asthma severity (≥12 years of age)</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
<td>Mild</td>
</tr>
<tr>
<td>Impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁/FVC:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-19 yr 85 percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-39 yr 80 percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-59 yr 75 percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-80 yr 70 percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
<td>3-4x/month</td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily</td>
</tr>
<tr>
<td>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</td>
<td>≤2 days/week</td>
<td>&gt;2 days/week but not daily, and not more than 1x on any day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV₁ between exacerbations</td>
<td>FEV₁ ≥80 percent predicted</td>
</tr>
<tr>
<td></td>
<td>FEV₁ &gt;80 percent predicted</td>
<td>FEV₁/FVC normal</td>
</tr>
<tr>
<td>Risk</td>
<td>Exacerbations requiring oral systemic corticosteroids</td>
<td>0-1/year (see footnote)</td>
</tr>
</tbody>
</table>

Consider severity and interval since last exacerbation
Frequency and severity may fluctuate over time for patients in any severity category

Relative annual risk of exacerbations may be related to FEV$_1$

Recommnended step for initiating treatment

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4 or 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stepwise approach for managing asthma in youths greater than or equal to 12 years of age and adults</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Step 1**

- **Preferred:** Low-dose ICS
- **Alternative:** Cromolyn, LTRA, Nedocromil, or Theophylline

**Step 2**

- **Preferred:** Medium-dose ICS + LABA
- **Alternative:** Low-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 3**

- **Preferred:** High-dose ICS + LABA
- **Alternative:** Medium-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 4**

- **Preferred:** High-dose ICS + LABA + oral corticosteroid
- **Consider Omalizumab for patients who have allergies**

**Step 5**

- **Preferred:** High-dose ICS + LABA + oral corticosteroid
- **Consider Omalizumab for patients who have allergies**

**Step 6**

- **Preferred:** High-dose ICS + LABA + oral corticosteroid
- **Consider Omalizumab for patients who have allergies**

Each step: patient education, environmental control, and management of comorbidities.

Steps 2-4: consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see footnotes).

Quick-relief medication for all patients

- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
**Allergies**
- Allergic rhinitis - seasonal allergens: March-May (tree pollen), June-July (grass), Aug-Oct (ragweed); also mold spores mites etc
- Symptomatic relief: antihistamine (loratadine, cetirizine have less side effect, don’t cross blood-brain barrier), nasal steroids, nasal cromolyn, eye drop antihistamine (olopatadapentine)
- Immunotherapy/hyposensitization (shots): varies in efficacy, less popular now

**HTN**
- Stage 1: systolic 140-159 or diastolic 90-99
- Stage 2: systolic ≥160 or diastolic ≥100
- Malignant HTN - retinal hemorrhages/exudate/papilledema, DBP >120
- Essential (1mary): risk fx- black, salt/etoh use, dyslipidemia, obesity, stress
  - Indicated w/u: CBC, U/A, BMP, lipids, EKG

2ndary HTN:
- **Cause**
  - Renal dz
  - OCP use
  - Pheochromocytoma
  - Hyperaldosteronism
  - Renal vascular dz
- **Suspect if**
  - Elev Cr, proteinuria, GFR < 60 ml/min
  - paryoxysmal, HA/sweating/palpitations
  - unexplained hypokalemia
  - Acute rise in bp, MaligHtn, unilat sm kidney, h/o diffuse atherosclerosis, unexplained heart failure

**Angiogram is definitive test; MR angiography, CT angiography, and duplex Doppler not sensitive enough to use if low risk**

- Cushing classic s/sx
- Thyroid classic s/sc
- OSA obesity, excessive daytime fatigue
- Coarctation lagging periph pulses, bruit over back

antihtn therapy: 40 % decr stroke, 25% decr MI, >50 % decr heart failure incidence
initial therapy: lifestyle modification, low dose **thiazide**
- ACE-I if: LV dysfxn, STEMI or ant infarct, DM, systolic dysfxn
- ACE-I and ARB if: heart failure, proteinuric chronic renal failure
- B-blocker if: h/o AMI, stable heart failure
  - **otherwise do not use for 1mary prevention b/c not as good at decr stroke rates!!!**

Other options, patient specific: Ca-channel blocker, alpha blocker

**GI disorders**
- Dyspepsia
- PUD
- GERD
- IBS
## Headache

<table>
<thead>
<tr>
<th>Category</th>
<th>Subtypes</th>
<th>History/Exam Findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>Classic (with aura), common (without aura), complicated (prominent neuro symptoms), basilar, hemiplegic, ophthalmoplegic</td>
<td>Unilateral, pulsating, nausea/vomiting, photophobia, phonophobia, scintillations/scotoma</td>
<td><strong>Acute:</strong> hydration, NSAIDS, triptans, antiemetics (metoclopramide, prochlorperazine) <strong>Preventative:</strong> eliminate triggers, TCAs, SSRIs, β-blockers, Ca-channel blockers, valproate</td>
</tr>
<tr>
<td>Cluster</td>
<td>Unilateral, periorbital, stabbing, conjunctival injection, lacrimation, rhinorrhea</td>
<td></td>
<td>100% O2, corticosteroids, ergotamines</td>
</tr>
<tr>
<td>Tension</td>
<td>Bilateral, “tight band”</td>
<td></td>
<td>NSAIDS, tylenol, muscle relaxants, relaxation techniques</td>
</tr>
<tr>
<td>Rebound</td>
<td>Daily analgesic use</td>
<td></td>
<td>Wean off of NSAIDs</td>
</tr>
<tr>
<td>Secondary</td>
<td>Sinusitis</td>
<td>Sinus tenderness, nasal congestion</td>
<td>Antibiotics</td>
</tr>
<tr>
<td></td>
<td>Meningitis</td>
<td>Fevers, nuchal rigidity (Kernig’s &amp; Brudzinski’s sign)</td>
<td>Antibiotics</td>
</tr>
<tr>
<td></td>
<td>Temporal arteritis</td>
<td>Temporal artery tenderness, visual changes, jaw claudication, elevated ESR</td>
<td>Steroids</td>
</tr>
<tr>
<td></td>
<td>Pseudotumor cerebri</td>
<td>Papilledema</td>
<td>Serial LPs</td>
</tr>
<tr>
<td></td>
<td>Subarachnoid bleed</td>
<td>Sudden onset of severe headache, nuchal rigidity</td>
<td>Urgent neurosurg c/s</td>
</tr>
<tr>
<td></td>
<td>Intracranial mass</td>
<td>Progressive headache, often worst in the am</td>
<td>Varies</td>
</tr>
</tbody>
</table>

**Red flag signs:** new headache, change in frequency or severity, fever, neurologic signs, papilledema → *consider imaging +/- LP in these cases*

## Depression

**Symptoms:**

SIG EM CAPS = Sleep (hypersomnia or insomnia), Interest (loss of), Guilt (feelings of), Energy (↓), Mood (depressed, sadness), Concentration (↓), Appetite (↑or↓), Psychomotor agitation or retardation, Suicidal ideation

**Diagnosis:**

Depressed mood or loss of interest/pleasure + 4 other symptoms, symptoms lasting ≥ 2 wks

**Treatment:**

Antidepressants: SSRIs, TCAs, Bupropion, MAOIs, Mirtazapine, Trazodone  
Psychotherapy: when combined with pharmacotherapy, more effective than either alone  
Other: ECT, mood stabilizers, antipsychotics
**Anxiety Disorders**

**Types:** Generalized anxiety disorder, Panic disorder, Phobias, Obsessive-compulsive disorder

**Treatment:**
Pharmacotherapy: benzodiazepines (careful with respect to tolerance/dependence), Buspar, SSRI
Psychotherapy: CBT especially helpful

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**Premenstrual Syndrome/ Premenstrual Dysphoric Disorder**

**Diagnosis:**
Symptoms occur repetitively in the luteal phase of the menstrual cycle or during the first few days of menses (patients symptom-free during the follicular phase)
Symptoms interfere with daily activities
PMS - Physical symptoms (bloating, breast tenderness, headaches, etc)
PMDD – Physical symptoms + at least one affective symptom (anger, irritability, etc)

**Treatment:**
Certain antidepressants: SSRIs, venlafaxine, clomipramine, nefazodone (can dose daily or just during the luteal phase)
Second-line therapies: alprazolam, GnRH agonists, danazol
Possible efficacy (being studied/evidence still lacking): OCPs, spironolactone, exercise, relaxation techniques, agnus castus fruit extract, calcium, magnesium, vitamin B6

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**Low Back Pain**

**Disc disease:** pain typically worse with sitting/flexion, often associated radiculopathy, +straight leg test. Responds to extension exercises, NSAIDs, steroids. Surgery as a last-resort if motor weakness develops or if symptoms persist >6 months.

**Facet joint inflammation/pain:** pain typically worse with prolonged standing, exacerbated by extension maneuvers. Responds to chiropractic maneuvers, NSAIDS.

**Muscle strain:** least common type of back pain, usually sudden onset, associated with trauma/activity. Responds to NSAIDs, muscle relaxants, heat, stretching

**Other:** Cauda equine syndrome (bowel/bladder incontinence, saddle anesthesia -> requires emergent imaging/mgmt), Osteomyelitis, Spinal stenosis (LBP classically improves with sitting/stooping forward), Neoplastic disease, Compression fracture
Diabetes

Types:
Type 1 diabetes (beta-cell destruction leads to absolute insulin deficiency)
Type 2 diabetes (progressive insulin secretory defect on the background of insulin resistance)
Other specific types of diabetes due to other causes, e.g., genetic defects in beta-cell function,
genetic defects in insulin action, diseases of the exocrine pancreas, and drug or chemical induced
Gestational diabetes mellitus

Screening:
Individuals >45 and individuals <45 with risk factors (obesity, family history, etc)
If negative screen, repeat every 3 years
If impaired fasting glucose, consider oral glucose tolerance test or repeat screen yearly

Diagnosis:
Fasting plasma glucose is the preferred diagnostic test (100-125 = impaired glucose tolerance, >125 = diabetes), should be repeated to confirm diagnosis
Random plasma glucose >200 also diagnostic
Oral glucose tolerance test not recommended for routine clinical use except in postpartum
evaluation of patients with GDM

Treatment (Type II):
Diet and exercise (can often avoid pharmacotherapy with these modifications alone)
Control risk factors for macrovascular disease
  BP check at each visit, treat to <130/80
  Smoking cessation counseling at each visit
  Annual screening for hyperlipidemia (goal LDL <100)
Glycemic control
  Actually little evidence that tight glycemic control (in outpatient setting) linked to better
  outcomes, however ADA recommends home glucose monitoring and checking HgA1C
every 3-6 months (goal <7%)
Pharmacotherapy
  Metformin should be 1st-line therapy in all Type II diabetics. If this does not achieve
  adequate glycemic control, can add second oral hypoglycemic or go directly to insulin
  Aspirin 81 mg daily for all diabetic patients
Screen for disease complications
  Retinopathy: Ophto exam after diagnosis, then yearly
  Nephropathy: Send urine for microalbumin yearly, start ACE or ARB of screen positive
  Neuropathy: Comprehensive (monofilament) foot exam yearly, brief foot check at each
  visit, routine foot care
  PVD: Check pulses at each visit, consider baseline ABIs
  CAD: Baseline EKG if patient is >35 or with known heart disease, ADA guidelines no
  longer recommend screening "high risk" diabetic patients with cardiac stress testing -
candidates for screening with stress testing are patients with a history of peripheral or
  carotid arterial disease and those over age 35 who have a sedentary lifestyle and are
  planning to begin a vigorous exercise program
Osteoporosis

Pathogenesis:
- uncoupling of bone resorption and formation
- communication between osteoblasts and osteoclasts occurs and is thought to be mediated by cytokines (interleukin-1, tumor growth factor) and skeletal growth factors
- estrogen receptors present on osteoblasts; with the onset of estrogen deficiency, osteoclastic bone resorption increases
- in the elderly, a decrease in the formation of active vitamin D leads to a decrease in intestinal absorption of calcium

Prevention: Calcium (1200 mg per day) & Vitamin D (800 IU per day) supplementation, weight-bearing exercise, smoking cessation, low-dose bisphosphonates, raloxifene

Screening: Recommendations vary but most sources suggest DEXA scans of the hip and spine for all women >65 and all postmenopausal women <65 with risk factors for fracture (previous fragility fracture, risk of falls, steroid use, smoking, family history of fracture.) Suggestions of when to repeat screening also vary, but 3-5 years seems to be a commonly cited interval

Dual-energy x-ray absorptiometry (DEXA):
- T-score: number of std deviations from the mean for normal young adults of the same sex
- Z-score: number of std deviations from the mean for persons of the same sex and age
- WHO defines osteoporosis as a T-score below –2.5 and osteopenia as a T-score between –1.0 and –2.5
- Z-score below –1.5 suggests a secondary cause of osteopenia (osteomalacia or a number of medical conditions)

Treatment: Bisphosphonates, SERMs, Calcitonin nasal spray
**Thyroid Disease**

**Hypothyroidism**

Clinical presentation: fatigue, lethargy, cold intolerance, constipation, bradycardia, hyperlipidemia, delayed DTRs, menorrhagia, dry skin, thinning hair, arthralgias/myalgias

Causes: Hashimoto’s thyroiditis (hypothyroid stage), subacute thyroiditis (hypothyroid stage), drugs (lithium, PTU, methimazole), infiltrative disease (amyloidosis, scleroderma), congenital, iatrogenic (post-ablation or thyroidectomy)

Diagnosis: Send TSH, and if elevated confirm with free T4

Treatment: Levothyroxine

**Hyperthyroidism**

Clinical presentation: fatigue, nervousness, heat intolerance, diarrhea, weight loss, tachycardia, atrial fibrillation, hypertension, resting tremor, irregular menses, sweating, osteoporosis, proptosis

Diagnosis:

![Flowchart diagram showing thyroid function tests and diagnoses]

- Decreased TSH → Send Free T4
- Increased Free T4 → Perform radioactive iodine uptake scan
- Normal Free T4 → Suggests Hashimoto’s or subacute thyroiditis in transition from hyper- to hypo-thyroid stage
- Decreased Free T4
  - Pituitary hypothyroidism
  - Hypothalamic hypothyroidism

- Increased Uptake
  - Subacute thyroiditis
  - Hashimoto’s thyroiditis
  - Exogenous T3/4 (synthroid)
  - Postpartum thyroiditis
- Decreased Uptake
  - Graves’ disease
  - Toxic adenoma
  - Multinodular goiter

Treatment: propranolol (symptomatic relief), propylthiouracil, methimazole, radioactive thyroid ablation (more severe cases), thyroidectomy (treats goiter, obstruction)
<table>
<thead>
<tr>
<th>Type</th>
<th>Pathophysiology</th>
<th>Clinical Pearls</th>
<th>Lab Studies</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>Autoimmune inflammatory process</td>
<td>Early morning stiffness, symmetric joint swelling, MCP/PIP involvement, characteristic joint deformities, subcutaneous nodules, systemic manifestations (fever, anemia, pleural effusion, etc)</td>
<td>Rheumatoid factor ESR X-Rays can show joint erosions</td>
<td>Disease-modifying antirheumatologic drugs (Methotrexate, azathioprine, hydroxychloroquine, etc), Glucocorticoids, Biologics (etanercept, infliximab, etc), NSAIDs</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>Degenerative arthritis, often secondary to acute trauma or wear-and-tear</td>
<td>Often affects older patients, overweight patients. Involves weight-bearing joints, improves with rest</td>
<td>X-Rays can show joint space narrowing, subchondral sclerosis, osteophytes</td>
<td>Weight-loss, Acetaminophen, NSAIDs, joint injections (corticosteroids, hyaluronic), topical therapies, glucosamine, surgery as last resort</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>Associated with HLA-B27</td>
<td>Usually affects spine and SI joints, reduced spinal mobility</td>
<td>Lumbar X-Ray shows “bamboo spine”, Pelvic x-Ray shows pseudowidening, erosions, sclerosis of SI joint</td>
<td>Similar to rheumatoid arthritis</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>S. aureus, Streptococcus, C. trachomatis, N. gonorrhoea</td>
<td>Hot, swollen, painful joint. Decreased ROM, Fevers</td>
<td>CBC, ESR, Joint fluid analysis/culture</td>
<td>Antibiotics NSAIDs</td>
</tr>
<tr>
<td>Gout</td>
<td>Uric acid crystals</td>
<td>Hot, swollen, painful joint, Usually monoarticular. Gout classically involves 1st MTP joint</td>
<td>Elevated uric acid, joint fluid shows negatively birefringent crystals, classic x-ray findings</td>
<td>NSAIDs (indomethacin) or steroids acutely (can also use colchicine but becoming less common), then allopurinol for maintenance</td>
</tr>
<tr>
<td>Pseudogout</td>
<td>Calcium pyrophosphate dehydrate crystals</td>
<td>Similar to gout</td>
<td>Joint fluid shows positively birefringent crystals</td>
<td>NSAIDs, steroids</td>
</tr>
</tbody>
</table>