Acne Vulgaris

Inflammatory skin condition assoc. with papules & pustules involving pilosebaceous units

Pathophysiology:
- 4 main factors – follicular hyperkeratinization with plugging of sebaceous ducts, increased sebum production, Propionibacterium acnes overgrowth within follicles, & inflammatory response
- Hormonal activation of pilosebaceous glands which may cause cyclic flares that coincide with menstruation

Clinical Manifestations:
- In areas with increased sebaceous glands (face, back, chest, upper arms)
- Stage I: Comedones: small, inflammatory bumps from clogged pores
  - Open comedones (blackheads): incomplete blockage
  - Closed comedones (whiteheads): complete blockage
- Stage II: Inflammatory: papules or pustules surrounded by inflammation
- Stage III: Nodular or cystic acne: heals with scarring

Differential Diagnosis:
- Differentiate from rosacea which has no comedones**
- Perioral dermatitis based on perioral and periorbital location
- CS-induced acne lacks comedones and pustules are in same stage of development

Diagnosis:
- Mild: comedones, small amounts of papules &/or pustules
- Moderate: comedones, larger amounts of papules &/or pustules
- Severe: nodular (>5mm) or cystic

Management:
- Mild: topical – azelaic acid, salicylic acid, benzoyl peroxide, retinoids, Tretinoin topical (Retin A) or topical antibiotics [Clindamycin or Erythromycin with Benzoyl peroxide]
- Moderate: above + oral antibiotics [Minocycline 50mg PO qd or Doxycycline 100 mg PO qd], spironolactone
- Severe (refractory nodular acne): oral Isotretinoin 0.5-1.0 mg/kg/d BID x15-20 weeks

Isotretinoin: affects all 4 pathophysiologic mechanisms of acne
- Adverse effects: dry skin and lips (MC), highly teratogenic, increased triglycerides & cholesterol, hepatitis

Androgenetic Alopecia

Genetically predetermined progressive loss of terminal hairs on scalp in a distribution pattern

MC hair loss in F & M, gradual in onset & occurs after puberty; type of non-scarring alopecia

Pathophysiology:
- Key androgen leading to AA: Dihydrotestosterone (DHT) – activation of the androgen receptor shortens the androgen (growth phase) in the normal hair growth cycle
- Pathologic specimens show decreased anagen to telogen ratio

Clinical Manifestations:
- Varying degrees of hair thinning and nonscarring hair loss
- Males: begins as bitemporal thinning of the frontal scalp then involves the vertex
- Females: thinning of the hair between the frontal and vertex of the scalp without affecting the frontal hairline

Diagnosis:
- Usually clinical
- Dermoscopy: miniaturized hair and brown perihilar casts
- In females: investigate the cause with labs such as DHEAS, testosterone levels, CBC, iron, TIBC, TSH, & vit D

Management:
- Topical Minoxidil: 5% OTC, best used if recent onset alopecia involves a smaller area, requires 4-6 month trial before noticing improvement & must be used indefinitely
  - Mechanism: widens blood vessels, allows more blood oxygen & nutrients to promote growth (anagen) phase
  - Adverse: pruritus & local irritation with flaking
- Oral Finasteride (Propecia): 5-alpha-reductase-type 2 inhibitor inhibits androgen (inhibits conversion of testosterone to DHT)
  - Adverse: decreased libido, sexual or ejaculatory dysfunction; increased risk of high-grade prostate ca; cat X
- Hair transplant may be effective

Atopic Dermatitis (Eczema)

Rash due to defective skin barrier susceptible to drying, leading to pruritus & inflammation

Pathophysiology:
- Disruption of the skin barrier (filaggrin gene mutation) and disordered immune response which manifests mostly in infancy or almost always by age 5
- Triggers: heat, perspiration, allergens, & contact irritants (wool, nickel, food, synthetic fabrics)
Genetics & environmental factors play a role, + hx of atopy
- IgE, eosinophils, Langerhans cell, T helper cells all play a role in atopic dermatitis
- TH2 prominent in acute lesions, TH1 found in chronic lesions

**Atopy triad:** **atopic dermatitis + allergic rhinitis + asthma** (3 A’s)

**Clinical Manifestations**
- **Hallmark:** pruritus*
- Erythematous, ill-defined blisters, papules or plaques → later the lesions dry, crust over & scale
- Older children & adults: MC in flexor creases (antecubital and popliteal folds)
- Infants: face and extensor part of extremities (from crawling & rubbing the skin)
- **Nummular eczema:** sharply defined discoid or coin-shaped lesions, especially on the dorsum of the hands, feet & extensor surfaces (knees, elbows)

**Diagnosis**
- Clinical, can also do a skin prick test
- Increased IgE and elevated eosinophilia supports diagnosis

**Acute Management**
- 1st line: topical CS – avoid class I & II in children [Mometasone, Fluticasone, Betamethasone, Triamcinolone]
- **Antihistamines** for pruritus, wet dressings, antibiotics if secondary infection (MC=staph aureus) develops
- Topical calcineurin inhibitors [Tacrolimus, Pimecrolimus] = steroid alternative
- Systemic: phototherapy (UVA, UVB, & narrow-band UVB) – used in children w/ mod to severe eczema, Cyclosporine, Azathioprine, Mycophenolate mofetil, Methotrexate, Dupilumab

**Chronic Management**
- Maintain skin hydration: hydration & skin emollients twice daily & within 3 min of exiting a lukewarm shower
- Oral antihistamines for pruritus (Cetirizine, fexofenadine, loratadine), Hydroxyzine, Diphenhydramine
- Avoid triggers (heat, low humidity), or irritants (soaps, detergents, washcloths, frequent baths)

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**Contact Dermatitis**

**Inflammation of the dermis & epidermis from direct contact between a substance & the skin surface**

**Irritants:** MC type, causes include: chemicals (solvents, cleaners, & detergents), alcohols, or creams

**Allergens:** Nickel (MC worldwide), poison ivy, oak, or sumac; other metals, chemicals (fragrances, glue, hair dyes), detergents, cleaners, acids, prolonged water exposure

**Pathophysiology:**
- Allergic: type IV hypersensitivity reaction (T cell lymphocyte-mediated), delayed by days
- Irritant: non-immunologic reaction (immediate)

**Clinical Manifestations**
- **Acute:** erythematous papules or vesicles (may be linear or geometric), often assoc. with localized pruritus, stinging, or burning; may ooze, develop edema, and progress to blisters or bullae
- **Chronic:** lichenification fissuring and scales

**Diagnosis**
- Clinical diagnosis
- Patch testing: may identify potential allergens to prevent future exposures
- Histology not usually needed but will show spongiosis (intercellular edema in the epidermis)

**Management**
- **Identification & avoidance** of irritants*

**Topical corticosteroids** = first-line medical treatment; use oral CS in severe/extensive reactions

**Topical calcineurin inhibitors** (Tacrolimus or Pimecrolimus) are alternatives

**General Measures**
- Cool saline or astringent compresses, cool baths, skin emollients
- Use drying agents if oozing or weeping
- Burrow’s solution, itching can be relieved with antihistamines or calamine lotion

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**Burns**

**Degree Involvement:**
- **1st degree** (sunburn): erythema of involved tissue, skin blanches with pressure, skin may be tender
  - Involves only **epidermis**
  - MCC: overexposure, heals uneventfully w/ no residual scarring
- **2nd degree** (partial thickness): skin is red & blistered, skin is **very tender**
  - Involves all epidermis + some dermis, painful w/ weeping & blisters
  - Superficial: blisters = expectant management
  - Deep: excise & graft, heals over 4-8 weeks; if infx it can lead to full thickness burn
• **3rd degree (full thickness):** burned skin is tough & leathery, skin non-tender, painless, nonblanching
  - Involves all epidermis + dermis + some fat
  - Requires skin grafting & escharotomy
• **4th degree:** into bone & muscle

**Minor Burns:** < 10% adults, < 5% children/elders, < 2% full thickness burns, must not involve face, hands, perineum, feet, cross major joints or be circumferential

**Major Burns:** > 25% TBSA adults, >20% children/elders, > 10% full thickness, or involving face, hands, perineum, feet, crossing major joints or circumferential

**Treatment**
- Monitor ABC’s, fluid replacement, topical antibiotic – cleanse w/ mild soap & water, no ice, irrigate chemical burns w/ running water x20 min, topical Bacitracin applied to superficial burns, wrap finger & toes individually to prevent maceration & gauze between, give antibiotics: silver sulfadiazine
- >10 % in children or >15% adults: formal fluid resuscitation w/ Lactated Ringers IV x 24 hours [1/2 in 1st 8 hours, with ½ in remaining 16 hours]
- Parkland Formula to determine how much LR: 4mL x %BSA x weight (kg)

**Diaper Dermatitis – Irritant**

**Pathophysiology**
- Irritant contact dermatitis d/t overhydration of the skin, maceration, prolonged contact with urine/feces

**Clinical Manifestations**
- Erythematous, scaly diaper area with papulovesicular or bullous lesions, fissures & erosions
- Genitocrural folds are spared in irritant dermatitis

**Diagnosis**
- Clinical, may use KOH prep

**Management**
- Zinc oxide ointment or Vitamin A/D ointment & leave area open to air or cover w/ topical emollient

**Diaper Dermatitis – Candidal**

**Pathophysiology**
- Infection occurs 48-72 hours after, MC in immunocompromised

**Clinical Manifestations**
- Isolated to perineal area & involves genitocrural folds
- Satellite lesions may be visible – tiny, red papules & papulovesicles

**Diagnosis**
- Clinical, may use KOH prep

**Management**
- Hydrocortisone 1% BID + antifungal (Nystatin cream)
  - Avoid high strength topical CS

**Drug Eruptions**

**Most cutaneous drug reactions are self-limited** if offending drug is discontinued
- **Triggers:** Antigen from foods, insect bites, drugs, environmental, exercise-induced, & infections

**Pathophysiology**
- Type I: IgE mediated, immediate – urticaria & angioedema
- Type II: cytotoxic, antibody-mediated (drugs in combo w/ cytotoxic antibodies → cell lysis)
- Type III: immune antibody-antigen complex – drug-mediated vasculitis & serum sickness
- Type IV: delayed [cell-mediated] morbilliform reaction – Erythema Multiform
- Non-immunologic: cutaneous drug reactions d/t genetic incapability to detoxify certain meds (sulfa, anticonvulsants)

**Drug Eruption: Exanthematous Drug Eruption**

**Pathophysiology**

**Dermatitis – Perioral**

**Pathophysiology**
- MC in young woman w/ hx of prior topical steroid use in area

**Clinical Manifestations**
- Papulopustules on erythematous base → confluent plaques, and scales around the mouth
- May see satellite lesions, & vermilion border spared

**Diagnosis**
- Clinical
- Culture to rule out staphylococcal infection

**Management**
- Topical metronidazole; can also use erythromycin or Pimecrolimus
- If no clearance: systemic tx w/ minocycline, doxycycline or tetracycline

**General Measures**
- Avoid topical steroids! C/I d/t → flare of lesions

**Diaper Dermatitis**

**Pathophysiology**
- Irritant contact dermatitis d/t overhydration of the skin, maceration, prolonged contact with urine/feces

**Clinical Manifestations**
- Erythematous, scaly diaper area with papulovesicular or bullous lesions, fissures & erosions
- Genitocrural folds are spared in irritant dermatitis

**Diagnosis**
- Clinical, may use KOH prep

**Management**
- Zinc oxide ointment or Vitamin A/D ointment & leave area open to air or cover w/ topical emollient
- Type IV delayed hypersensitivity reaction that most commonly occurs 5-14 days after initiation of offending medication or within 1-2 days in previously sensitized individuals
- Any drug can cause it but Penicillin, sulfa-containing meds, NSAIDs, & Allopurinol are common causes

**Clinical Manifestations**
- Generalized distribution of bright red macules & papules that coalesce to form plaques, primarily involving trunk & proximal extremities
- Systemic symptoms include low-grade fever & pruritus

**Management**
- Prompt withdrawal = mainstay of treatment
- Symptomatic treatment: oral antihistamines (H1 blockers) – second or first-generation
- Oral corticosteroids are reserved for severe cutaneous reactions

**Drug Eruption: Angioedema**

*Self-limited localized subcutaneous (or submucosal) swelling resulting from extravasation of fluid into interstitium*

- Affects mucosal tissues of the face, lips, tongue, larynx, hands, feet & genitalia
- Onset in minutes to hours with spontaneous resolution in hours to a few days

**Types**
- **Mast-cell (histamine) mediated** – allergic reactions
  - Angioedema that may be accompanied w/ other allergic reaction symptoms (urticaria, flushing, generalized pruritus, bronchospasm, stridor, throat tightness, & hypotension)
- **Bradykinin-mediated**: ACE inhibitor-induced or hereditary (d/t C1 esterase inhibitor deficiency)
  - Angioedema without allergic reaction symptoms

**Diagnosis**
- No information to suggest an external cause & the patient has isolated angioedema without pruritus or urticaria
- ? Obtain C4 levels & C1 inhibitor antigenic level

**Management**
- Immediate assessment & ongoing airway protection – epinephrine if severe
- **Mast-cell (histamine) mediated** – epinephrine (if severe), glucocorticoids, and antihistamines
- **Bradykinin-mediated**:
  - C1 inhibitor concentrate, Ecallantide (kallikrein inhibitor), Icatibant (bradykinin-beta2 receptor antagonist), FFP if other therapies aren’t available
  - Danazol @ lowest dose may be needed for long-term management in hereditary causes

**Erythema Multiforme**

*Type IV hypersensitivity reaction assoc. w/ certain infections, medications (sulfa drugs), & other various triggers*

**Risk factors:**
- MC: HSV, Mycoplasma in children, S. pneumoniae
- Meds: sulfa drugs, beta-lactams, Phenytoin, Phenobarbital, Allopurinol
- Malignancy, autoimmune, idiopathic

**Clinical Manifestations**
- Target lesions w/ 3 components on trunk & extremities: (1) dusky, central area or blister + (2) dark red inflammatory zone surrounded by pale ring of edema + (3) erythematosus halo on extreme periphery of lesion
- (-) Nikolsky sign = no epidermal detachment, often febrile
- Minor: target lesions distributed acrally w/ no mucosal membrane involvement
- Major: target lesions acrally progressing centrally + mucosal membrane involvement (oral, genital, or ocular) & no epidermal detachment

**Diagnosis**
- Clinical, bx if dx not clear

**Management**
- Symptomatic: d/c offending drug, give antihistamines, analgesics, skin care
- Oral lesions: Corticosteroid + Lidocaine + Diphenhydramine mouthwash
- Severe: systemic corticosteroids
- Mycoplasma related: antibiotics
- HSV related: Acyclovir
**Drug Eruption: Dermatitis Medicamentosa**

**Pathophysiology**
- Simple
  - Exanths typically appear in 2nd week
  - MCC: antibiotics (penicillins & quinolones)
- Complex
  - Drug eruptions eosinophilia & systemic symptoms typically present in 3rd week of drug therapy
  - Most common: sulfonamides, allopurinol, anticonvulsants

**Clinical Manifestations**
- Abrupt onset of eruption of widespread, symmetric, pruritic erythematous lesions w/ many types
- MC skin reaction to drugs: erythema
- Fever & other syx may be present – HA, malaise, arthralgias, &/or myalgias

**Diagnosis**
- Clinical Exam
- Labs: no value in simple reactions – get CBC, CMP in complex reactions

**Management**
- Withdraw drug, consider antihistamines
- Anaphylaxis treatment – airway, IV fluids, EKG, epinephrine

**Stevens-Johnson Syndrome & Toxic Epidermal Necrolysis**

*Severe mucocutaneous reactions characterized by detachment of the epidermis & extensive necrosis*

**Risk factors:**
- MCC: medications – sulfa drugs, anticonvulsants, lamotrigine, allopurinol, NSAIDs, antipsychotics, abx
- Infections less common – Mycoplasma, HIV, HSV
- Malignancy, idiopathic

**Clinical Manifestations**
- Prodrome: fever, URI syx, sometimes asthenia
- Followed by widespread flaccid bullae beginning on trunk & face before spreading to other areas (palms and soles rarely involved)
- Pruritic targetoid lesions *(erythematous macules w/ purpuric centers)* or diffuse erythema w/ involvement of at least 1 mucous membrane + involvement with epidermal detachment (+ Nikolsky sign), skin often tender to touch
- Ocular involvement common (corneal ulceration or uveitis)
- Pulmonary – bronchitis, pneumonitis

**Diagnosis**
- Clinical
- Biopsy: full thickness skin necrosis, (+) eosinophilia, & atypical lymphocytes

**Management**
- **Discontinue causative agent**
- **Supportive:** treat like severe burns – burn unit admission, pain control, prompt withdrawal of offending meds, fluid & electrolyte replacement, wound care w/ gauze and petroleum

**General Measures**
- SJS: sloughing involving <10% of body surface
- TEN: >30% body surface area

**Impetigo**

*Highly contagious, superficial vesiculopustular skin infection*

- MC bacterial skin infection in children 2-6
- **Risk factors:**
  - Poor personal hygiene, poverty, crowding, warm & humid weather, skin trauma

**Clinical Manifestations**
- **Type: Nonbullous:** MC
  - Impetigo contagiosa: papules, vesicles & pustules with weeping & later development of “honey-colored, golden crusts” w/ pruritis, NO pain
  - @ sites of superficial skin trauma, primarily on exposed surfaces on the face & arms assoc. w/ regional lymphadenopathy
  - MCC: S. auereus, 2nd MCC: Group A Streptococcus
- **Type: Bullous:**
  - Vesicles form large bullae (rapidly) w/ rupture & development of thin “varnish-like crusts,” fever, diarrhea
  - MCC: S. aureus; rare, seen in newborns/young children & commonly on the trunk w/ less lymphadenophy
**Type:** Ecthyma:
- Ulcerative pyoderma caused by group A strep, not common, heals w/ scarring

**Diagnosis**
- Clinical
- Gram stain and wound culture if needed

**Management**
- **Mild:** Mupirocin topically TID X10d, may use Bacitracin or Retapamulin; good skin hygiene, wash area with soap & water to prevent recurrence @ distant sites
- **Extensive disease or systemic sx:** systemic antibiotics – Cephalexin or Dicloxacillin, Macrolides
- **Community acquired MRSA?**: Doxycycline, Clindamycin, Bactrim or Linezolid PO x7days

**Complications**
- Cellulitis=MC, acute glomerulonephritis, NOT RHEUMATIC FEVER

### Lice (Pediculosis)

**Head lice:** *Pediculus humanus capitis*

**Transmission**
- Person-to-person, fomites (hats, clothing, bedding)
- Girls > Boys, 3-12 y/o, warm humid weather, less common in African Americans

**Clinical Manifestations**
- Intense itching, popular urticaria near lice bites
- Visualization of crawling nymphs or adult lice, presence of nits does not confirm infestation
- **Nits:** white, oval-shaped egg capsules @ base of hair shafts

**Diagnosis**
- Clinical

**Management**
- Drug of choice: Permethrin topical, shampoo left x10min & use of a fine tooth cone to remove nits, reapply 7-10d
- Alternative: Malathion – 8-12h tx period
- Oral Ivermectin in refractory cases

**Body lice:** *Pediculus humanus corporis*

**Transmission:** sexually transmitted, strongly related to poor body hygiene; can be a vector for diseases to humans like relapsing fever, epidemic typhus, & trench fever

**Pathophysiology:** unlike head & pubic, body lice do not live on skin; they live & lay eggs in seams of clothing/bedding & move to skin only to feed

**Clinical Manifestations:** pruritus & excoriations

**Diagnosis:** clinical, identification of nits/lice in clothing

**Management**
- Improve hygiene – first-line, clean clothes
- Permethrin cream 5% (8-10 hour application)

**Pubic Lice:** *Phthiriasis pubis*

**Transmission:** sexually transmitted

**Clinical Manifestations:** pruritus of involved area

**Diagnosis:** clinical, can do microscopic exam of shafts

**Management**
- **1st line:** topical Permethrin or Pyrethrins x8-10 hours
- Repeat tx if lice remains after 9-10 days
- Treat sexual partners & launder clothing & bedding

### Scabies

**Highly contagious skin infection d/t Sarcoptes scabiei**

**Pathophysiology**
- Female mites burrow into the skin to lay eggs, feed & defecate (scybala are fecal particles that precipitate a hypersensitivity reaction)

**Clinical Manifestations**
- Intense pruritus especially @ nights
- Infected patients may remain w/out sx for 4-6w

**Physical Examination**
- Multiple, small erythematous papules, excoriations
- **Linear burrows** (pathognomonic) – commonly found in intertriginous zones, including the scalp & web spaces between fingers & toes, spares neck & face
Red itchy pruritic papules or nodules on scrotum, glans or penile shaft, or body folds are pathognomonic. 

**Diagnosis**
- Clinical
- Skin scrapings will show mites, eggs, & feces

**Management**
- Drug of choice: **Permethrin topical** from neck down 8-14 hours before showering, repeat once after 1w
- Safe in pregnancy & lactation
- May use Lindane – cheaper, can cause seizures d/t incr. absorption through open pores, DON’T USE IN PREGNANT PATIENTS
- Infants/pregnant woman: 6-10% sulfur in petroleum jelly
- Extensive: Ivermectin

**General Measures**
- Treat close contacts
- Place clothing & bedding in bag x72h then wash w/ heat

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**Lichen Planus**

*Chronic, inflammatory autoimmune disease*

**Etiology**
- Increased incidence in Hepatitis C, drug reactions, graft v. host, malignant lymphoma
- More common in adults

**Clinical Manifestations**
- 6 P’s: **Purple, Polygonal, planar, pruritic, papules or plaques** w/ irregular borders
- **Wickham Striae**: lacy striation [fine white lines] on lichen planus lesion or on oral mucosa
- **Koebner’s phenomenon**: new lesions at site of trauma [may see in psoriasis also]
- Nail dystrophy which may cause scarring alopecia
- Location: **flexor surfaces of extremities, mucous membranes** on skin, mouth, scalp, genitals & nails

**Diagnosis**
- Clinical
- Confirmatory w/ biopsy & immunofluorescence: sawtooth lymphocyte infiltrate @ dermal epidermal junction

**Management**
- 1st line: Topical steroid ointment
- Antihistamines for pruritus
- 2nd line: PO/intralesional CS, topical Tretinoin or photossensitizing Psoralen + UV light therapy

**General Measures**: will resolve spontaneously in 8-12 months

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**Pityriasis Rosea**

**Etiology**
- Uncertain, may be associated with viral infections (HSV6 or 7)
- Older children & young adults, increased incidence in Spring & Fall

**Clinical Manifestations**
- **Herald Patch**: solitary salmon-colored macule on the trunk, 2-6 cm in diameter
- Followed by general exanthem 1-2 weeks later: smaller, very pruritic 1 cm round or oval salmon-colored papules w. white circular (collarette) scaling in a Christmas tree pattern along skin folds (Langer lines)
- Confined to trunk and proximal extremities w/ spared face, palms, and soles
- May have upper respiratory prodrome before the rash

**Diagnosis**
- Clinical
- Young adults – RPR should be ordered to r/o secondary syphilis

**Management**
- Self-limiting lasting 3-8 weeks and disappearing spontaneously
- Pruritus? Topical or systemic steroids and antihistamines, if necessary
- Emollients may be used to soften scales

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**Tinea**

*Fungal skin infections that infect keratinized tissues in stratum corneum of skin, hair & nails by ingesting keratin*

**Etiology**: Trichophyton, Microsporum, Epidermophyton

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**Risk Factors:** Increased skin moisture, immunodeficiency (HIV, DM), peripheral vascular disease

**Diagnosis:** KOH prep
- Dermatophytes: arthrospores around/within hair shaft; long, branching fungal hyphae with septations
- Candidiasis: budding yeast, pseudohyphae
- Tinea versicolor: short hyphae & clusters of spores (spaghetti & meatballs)

*Nystatin not effective for treatment*

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**Tinea Capitis**

*Infection of the hair scalp*

**Etiology**
- 90% caused by *Trichophyton tonsurans*, 10% Microsporum

**Risk Factors:**
- Poor hygiene, direct contact, preadolescents, more common in African Americans

**Clinical Manifestations**
- **Patches of alopecia w/ black dots**: multiple black dots are d/t broken hair shafts d/t endothrix infection
- **Scaly patches w/ alopecia**: single or multiple patches w/ hair loss, erythema & pruritus may be present
- **Kerion**: severe manifestation characterized by inflammatory plaque w/ pustules & thick crusting, often painful
- **Favus**: less common form – cup-like shaped yellow crusts composed of dried scalp secretions, fungi, skin cells & dead inflammatory cells

**Diagnosis**
- Clinical
- KOH Prep – most common initial test, fungal element inside or surrounding the hair
- Wood’s lamp: no fluorescence w/ Trichophyton spp., (+) fluorescence with Microsporum

**Definitive Diagnosis:** Culture

**Management**
- Oral Griseofulvin: **first line treatment** x6-12 weeks, can cause hepatitis, GI, headache, & Disulfiram rxn; better absorption w/ fatty food; may add topical 2.5% selenium sulde/ketoconazole shampoo 2x/week to suppress spores
- 2nd line: Oral Terbinafine, less common: Itraconazole or Fluconazole

**General Measures**
- Asymptomatic carriers common & contribute to spread; MC in prepubescent children 3-7 y/o

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**Tinea Barbae**

*Papules, pustules & hair follicles on beards*

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**Tinea Unguium**

*Dermatophyte onychomycosis – infection of the nail*

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**Tinea Pedis**

*“Athlete’s foot” – most common dermatophyte infection*

**Etiology**
- Trichophyton rubrum, Trichophyton interdigitale, & Epidermophyton floccosum

**Transmission**
- Direct contact, most common in adolescents & young men

**Clinical Manifestations**
- **Interdigital**: MC – pruritic, erythematous erosions or scales between the toes
- **Hyperkeratotic**: diffuse hyperkeratotic rash involving the soles, lateral & medial surfaces of the feet w/ “moccasin” distributive pattern
- **Vesiculobullous**: pruritic vesicular or bullous eruption w/ underlying erythema, especially involving medial surfaces of the foot, may be painful

**Diagnosis**
- Same as tinea capitis

**Management**
- First-line: topical antifungals – Butenafine, Tolnaftate, Ciclopirox, azoles – 4 week duration, Terbinafine 1% x1w
- Hyperkeratotic lesions: add Burrow’s solution
- PO Terbinafine, Fluconazole, or Itraconazole if topical meds ineffective, or Griseofulvin

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**Tinea Crucis**

*Superficial fungal infection of groin or inner thighs, “jock itch”*

**Etiology**
- Trichophyton spp (T. rubrum MC) & Epidermophyton floccosum

**Risk Factors**
- Males, copious sweating, immunocompromised, may be d/t tinea pedis

**Clinical Manifestations**

- **Hallmark:** pruritus
- Annular patches or plaques, diffuse erythema to the inner thighs or groin w/ sharply demarcated raised border that may have tiny vesicles & often spares the scrotum & mucosa

**Diagnosis**

- Clinical, KOH prep is the best initial test and reveals segmented hyphae
- Fungal cultures: definitive diagnosis

**Management**

- First-line: topical antifungals – Butenafine, Terbinafine, Clotrimazole, Ketoconazole
- PO Terbinafine or Griseofulvin if topical is ineffective

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### Tinea Corporis

**Etiology**

- MCC: T. rubrum, usually seen in younger children or young adolescents w/ close physical contact to others

**Clinical Manifestations**

- One/more, asymmetrically distributed, annular, well-demarcated erythematous scaling plaques w/ central clearing
- Lesions may occur anywhere on the body
- Inflammatory forms may be frankly pustular or vesicular at the borders

**Diagnosis**

- Clinical

**Management**

- First-line: topical azole antifungals – 1% clotrimazole, 2% ketoconazole or 1% terbinafine cream applied 2x/d x2-4w

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### Tinea/Pityriasis Versicolor

**Fungal skin infections d/t overgrowth of Malassezia furfur, commonly in adolescents & young adults**

**Risk Factors**

- Hot, humid weather, excess sweating, oily skin

**Clinical Manifestations**

- Hyper/hypopigmented, well-demarcated round or oval macules w/ fine scaling – the lesions often coalesce into patches most common on upper trunk & proximal extremities (less often the face & intertriginous areas)
- Involved skin fails to tan w/ skin exposure

**Diagnosis**

- KOH prep from skin scraping: hyphae & spores = “spaghetti & meatballs”
- Wood’s lamp: yellow-green fluorescence (enhanced color variation)

**Management**

- First-line: topical Selenium sulfide, sodium sulfacetamide, zinc pyrithione, & “azoles,” daily for 7-10 days
- Systemic therapy: Itraconazole or Fluconazole [adults if widespread or failed topical treatment]
  - Ketoconazole & Fluconazole are associated with hepatotoxicity
  - Fluconazole delivered to skin via sweat so patients should not shower few hours after oral administration

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### Urticaria

**Edema of the superficial layers of skin d/t histamine-related increased vascular permeability**

**Pathophysiology**

- Type I [IgE] immediate, hypersensitivity reaction leading to superficial localized edema & erythema of the dermis, mucous membranes & subcutaneous tissues d/t release of vasodilators (histamine, bradykinin, kallikrein, & prostaglandins) from mast cells & basophils degranulation in the skin

- Triggers: Food, medications, hot/cold, stress, insect bites, environment, infection
- Chronic: idiopathic, 6+ weeks

**Clinical Manifestations**

- Sudden onset of circumscribed hives or wheals – **blanchable raised, erythematous** areas on skin or mucous membranes that may coalesce
- Associated with intense pruritis, and may have angioedema [painless, deeper form of urticaria affecting lips, tongue, eyelids, hands and genitals]
- Usually transient – disappears within 24 hours & new crops occur
- (+) Darier’s sign: localized urticaria appearing where the skin is rubbed (histamine release)

**Diagnosis**

- Clinical
• Skin or IgE testing should be limited to specific history of provoking allergen

Management
• Initial TOC: **Antihistamines (H1 Blockers):** 2ND gen preferred [Cetirizine, Loratadine, Fexofenadine] over 1st generation [Diphenhydramine, Hydroxyzine, Chlorpheniramine] because of less anticholinergic effects, minimal sedation, & less drug-drug interactions
  - No response to H1 antagonist? Add **H2 blocker** – Ranitidine
  - Severe, recurrent, or persistent case? Add **glucocorticoids** – Prednisolone 20-50mg/day x 10 days
  - Severe or concern for airway compromise/anaphylaxis? Epinephrine 0.3-0.5 mg; use 1:1,000 IM or 1:10,000 IV (PEDI: 0.01mg/kg SC/IV)

General Measures: Eliminate known precipitants, NSAIDs & alcohol may exacerbate syx

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**Verrucae**

Etiology
• Human Papillomavirus (HPV)

Clinical Manifestations
• Verruca vulgaris (common warts) [bottom picture]: skin colored papillomatous papules
• Verruca plana (flat warts) [middle picture]: face, arms, legs
• Verrucae plantaris (plantar warts) [top picture]: bottom of the foot. Rough surface. Dark spot (thrombosed capillaries)
• Condyloma acuminatum (venereal warts): flesh-colored, cauliflower appearance genital warts d/t HPV types 6 & 11
• Epidermodysplasia verruciformis: a rare, lifelong hereditary disorder characterized by chronic infection with HPV
• Cardinal sign of warts: absence of skin lines crossing their surface & presence of pinpoint black dots (thrombosed capillaries) or bleeding when warts are shaved

Diagnosis
• Clinical

Management
• Most resolve without treatment in 2 years
• Self-administered topical therapy – salicylic acid
• Cryotherapy w/ liquid nitrogen may be applied

General Measures: Freezing & other destructive treatment modalities don’t kill virus but destroy the cells that harbor HPV

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ENT/OPHTHALMOLOGY – 15%

**Acute Otitis Media**

*Inflammation of the middle ear, temporal bone & mastoid air cells w/ rapid onset + s/sx of inflammation*

Risk Factors: age 6-18 months, day care, pacifier or bottle use, second-hand smoke, bottle-fed infants

Organisms: *Strep pneumoniae* (MC), *H. Influenza*, *Moraxella Catarrhalis*, group A *Streptococcus*

Pathophysiology: **Preceded by viral URI** leading to blockage of Eustachian tube

Clinical Manifestations
• Fever, *otalgia*, *ear tugging* (infants), stuffiness, conductive hearing loss
• Tympanic membrane rupture: rapid relief of pain + otorrhea (heals in 1-2 days)
• Bulging & *erythematous tympanic membrane w/ effusion*, loss of landmarks
• Doctor says: if there is effusion – *H. influenza* is the more likely cause
• *Pneumatic otoscopy: decreased TM mobility* (most sensitive)

Diagnosis
• Clinical – may use tympanogram
  - Recurrent cases: tympanocentesis for a sample of fluid for culture definitive

Management
• **TOC:** *Amoxicillin* 80-90 mg/kg/day x 10-14 days (HIGH DOSE)
  - 2nd line: Amoxicillin-Clavulanic acid, Cefuroxime, Cefdinir, Cefpodoxime
• **Penicillin allergy? Azithromycin,** Clarithromycin, Erythromycin-Sulfisoxazole, Bactrim
• **Severe or recurrent?** Myringotomy (surgical drainage) w/ tympanostomy tube insertion
  - **Recurrent otitis media:** workup for IDA & CT scan
  - Over age 2, certain dx, severe infection: Antibiotics
  - Observation can be done depending on age & severity

Complications: TM rupture, mastoiditis, bacterial meningitis, brain abscess or dural sinus thrombosis
**Acute Pharyngotonsillitis - Viral**

**Etiology:**
- MC overall cause of pharyngitis (viral): adenovirus, rhinovirus, enterovirus, Epstein-Barr virus, respiratory syncytial virus, Influenza A & B, Herpes zoster virus

**Clinical Manifestations**
- Sore throat, pain or swallowing and may have phonation
- **Viral** often associated w/ cough, hoarseness, coryza, conjunctivitis, diarrhea, fever

**Diagnosis**
- Clinical but may perform rapid strep or throat culture to r/o bacterial cause

**Management**
- Mainstay: symptomatic treatment – fluids, warm saline gargles, topical anesthetics, lozenges, NSAIDs
- If EBV: malaise, fever, sore throat, splenomegaly; dx: atypical lymphocytes, heterophile agglutination test; be conscious about risk of splenic rupture and avoid sports for 3w after onset (4w if strenuous)

**Acute Pharyngotonsillitis - Fungal**

**Etiology:**
- Common in patients using inhaled steroids

**Clinical Manifestations**
- Sore throat, dysphagia, cheesy white patches in the oropharynx
- Seen in AIDS patients and small children

**Diagnosis**
- Clinical or endoscopy

**Management**
- **Clotrimazole** troches (one 10-mg troche dissolved slowly 5x daily)
- **Miconazole** mucoadhesive buccal tablets (50 mg qd applied to mucosal surface over canine fossa)
- **Nystatin** swish and swallow (400,000-600,000 units 4x/d)
- HIV+ patient: Fluconazole

**Acute Pharyngotonsillitis - Bacterial**

**Etiology:**
- Group A Streptococcus (Streptococcus pyogenes)

**Clinical Manifestations**
- Dysphagia, fever – not usually associated with viral symptoms (ie. no cough)
- **On exam:** pharyngeal edema/exudate (white/yellow), tonsillar exudate &/ petechiae, anterior cervical adenopathy

**Diagnosis**
- **Rapid antigen detection test:** best initial test (if negative then obtain throat culture (esp. children 5-15))
- **Throat culture:** definitive diagnosis (gold standard)
- **C**entror Criteria: GABHS-suggestive manifestations: fever 100.4+, tender anterior cervical lymphadenopathy, lack of cough, pharyngotonsillar exudate

**Management**
- **First line:** Penicillin (PCN G or VK, Amoxicillin); PCN Allergy? Macrolides, Clindamycin, Cephalosporins

**General Measures**
- Rare in children under 3 years old, highest incidence of rheumatic fever if untreated in children ages 5-15 – preventable with antibiotics
- May lead to acute glomerulonephritis or peritonsillar abscess, also

**Scarlet Fever**

**Diffuse skin eruption that occurs in the setting of Group A Streptococcus (S. pyogenes) infection**

**Pathophysiology**
- Type IV (delayed) hypersensitivity reaction to a pyrogenic strain (erythrogenic toxin A, B, or C)

**Clinical Manifestations**
- Fever, chills, pharyngitis
- **Rash:** diffuse erythema that blanches with pressure + multiple small (1-2mm) popular elevations w/ a *sandpaper texture*
  - Rash usually starts in the axillae & groin & spreads to trunk & extremities (spares palms & soles)
  - Flushed face w/ *circumoral pallor* & *strawberry tongue*
  - Pastia’s lines: linear petechial lesions seen at pressure points, axillary, antecubital, abdominal or inguinal areas

**Diagnosis**
- Clinical or testing for GABHS (rapid strep, anti-streptolysin titer, throat culture)

**Management**
- **Penicillin G or VK = first line**, Amoxicillin
- **Macrolides if penicillin-allergic**
- Children may return to school after 24 hours of antibiotic administration

**Allergic Rhinitis**

**Immunoglobulin E (IgE)-mediated mast cell histamine release due to airborne antigens [allergens]**

**Clinical Manifestations**
- Sneezing, nasal congestion, itching, **clear, watery rhinorrhea**
- Eyes, ears, nose and throat may be involved & may have bluish discoloration around the eyes
• Pale of violaceous **boggy turbinates, nasal polyps w/ cobblestone mucosa, allergic shiners** (edematous, dark circles under eyes) & **allergic salute** (transverse nasal crease from pushing up on the nose)

**Diagnosis**
- History & occasional skin testing

**Management**
- **Intranasal corticosteroids = first-line** [*Mometasone, Fluticasone*]
- Antihistamines, mast cell stabilizers, & short term decongestants may also be used
- Anticholinergics for rhinorrhea, avoidance & environmental control, exposure reduction

**General Measures**
- Commonly occurs in patients w/ other atopic disease [asthma, eczema, atopic dermatitis] & those w/ FHx
- MC type of rhinitis overall
- Nasal polyps – most commonly found d/t allergic rhinitis, can cause obstruction/anosmia if large; Dx: pale boggy mass on nasal mucosa, tx with Intranasal CS but if large – may need surgical removal

**Epiglottitis – MEDICAL EMERGENCY**

**Supraglottic inflammation/obstruction of the airway**

**Pathophysiology**
- **MCC: H. influenza type B** (HiB) – kids in underserved areas or without vaccinations
- Immunized? Suspect Streptococcal species (Group A Strep or S. pneumoniae), H. influenza, or S. aureus
- Assoc. with cocaine use in adults, MC in children 3 months-6 years, M> 2:1, DM increases risk; any season

**Clinical Manifestations**
- 3 D’s: **drooling, dysphagia, distress**
- Fever, odynophagia, inspiratory stridor, dyspnea, hoarseness, muffled “hot potato” voice, restlessness
- **Tripod/Sniffing dog position**: leaning forward, elbow on lap, neck hyperextended, chin protruding

**Diagnosis**
- Definitive diagnosis: **Laryngoscopy** (cherry-red epiglottis w/ swelling) performed when securing airway
- Soft tissue lateral cervical XR: **thumb/thumbprint sign** – d/t swollen, enlarged epiglottis
- Do not use a tongue depressor to visualize in children

**Management**
- Most important: maintain airway – keep child calm, OR best place to intubate, Dexamethasone for airway edema
- 2nd or 3rd gen-cephalosporin (Ceftriaxone/Cefotaxime); Penicillin, Ampicillin or anti-staph coverage (Vanco) may be added
- Prevention: Rifampin to close contact, routine use of HiB vaccine

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### Bacterial Conjunctivitis

**Inflammation of conjunctiva**

**Etiology**
- S. aureus = MC, S. pneumoniae, M. catarrhalis
- N. gonorrhoea, C. trachomatis
- Transmitted by direct contact & autoinoculation
- H. influenza: MCC in preschool children
- MCC neonates: Chlamydia trachomatis

**Clinical Manifestations**
- Purulent discharge, lid crusting (eye “stuck shut” in morning), conjunctival erythema w/ no ciliary injection (limbal flush)
- No significant visual changes
- Chlamydia trachomatis – presence of **acute follicular conjunctivitis** consistent w/ inclusion conjunctivitis

**Diagnosis**
- Clinical
- Fluorescein stain: for keratitis/corneal abrasion
- Culture & gram stain discharge
- C. trachomatis: **Giemsas stain** shows inclusion body & scant mucopurulent discharge
- Gonorrhea: gram stain & culture

**Management**
- Topical abx: **Erythromycin ointment**, Trimethoprim-Polymyxin B (Poltrim), Fluoroquinolones – Moxifloxacin or Ofloxacin

### Viral Conjunctivitis

**Inflammation of conjunctiva**

**Etiology**
- MC: Adenovirus
- Highly contagious from direct contact
- Swimming pool MC source during outbreaks – MC in children

**Clinical Manifestations**
- Foreign body or gritty sensation, ocular erythema & itching
- Normal vision
- Starts unilateral and progresses to bilateral involvement in 1-2 days
- May have accompanying viral syx

**Physical Exam**
- Ipsilateral preauricular lymphadenopathy (~both)
- Copious watery discharge, may have mucoid discharge
- Cobblestoning of palpebral conjunctiva (tarsal conjunctiva)

### Allergic Conjunctivitis

**Inflammation of conjunctiva**

**Etiology**
- Contact of allergen w/ the eye causes mast cell degranulation & histamine release

**Clinical Manifestations**
- Bilateral conjunctival erythema (red eye) w/ normal vision
- Allergy syx distinguish allergy from viral: nasal congestion, sneezing, **pruritus [Hallmark*], atopy history
- Cobblestone mucosa appearance to inner upper eyelid, erythema, watery or mucoid discharge, chemosis (conj. edema)

**Diagnosis**
- Clinical

**Symptomatic:**
- Topical antihistamines (H1-blockers):
• Contact lens? Treat for pseudomonas – topical Ciprofloxacin or Ofloxacin
• Alt: Tobramycin/Gentamicin
• Chlamydia: Oral erythromycin or tetracycline x3weeks – common regimen is 1% silver nitrate, 1% tetracycline ointment, or 0.5% erythromycin ointment, assess STD/child abuse
• Gonorrhea: prompt referral & topical + systemic abx

General Measures:
• Suspect Moraxella/ Gonococcal if copious discharge not responding to conventional tx

Red flags:
• Reduction of visual acuity – concerns about inflx keratitis, iritis, angle closure glaucoma
• Ciliary flush: pattern of injection in which redness more pronounced @ limbus (transition zone btw cornea & sclera) – concerns about infectious keratitis, iritis, angle closure glaucoma
• Photophobia – concerns about infectious keratitis, iritis
• Severe foreign body sensation or corneal opacity – concerns about infectious keratitis
• Fixed pupil or severe headache with nausea – concerns about AGC

### Conjunctivitis

<table>
<thead>
<tr>
<th>Clinical Finding</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Allergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>50%</td>
<td>25%</td>
<td>Mostly</td>
</tr>
<tr>
<td>Discharge</td>
<td>Mucopurulent</td>
<td>Watery</td>
<td>Rare</td>
</tr>
<tr>
<td>Redness</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Rare</td>
<td>Rare</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Anterior Epistaxis

**Etiology**
- Kiesselbach’s venous plexus = MC site
- MC associated with nasal trauma (nose picking MC in children, blowing nose forcefully), low humidity, hot environments (dried nasal mucosa), rhinitis, alcohol, cocaine use

**Management**
- **Direct pressure:** first-line therapy in most cases, apply 5-15 minutes seated position, leaning forward [to reduce vessel pressure]
- Untreated septal hematomas can lead to septum destruction if not evacuated
- **Adjunct medications:** topical vasoconstrictors (Oxymetazoline nasal, lidocaine w/ epinephrine, 4% cocaine) – cautious use in patients w/ HTN
- Cauterization: electrocautery or silver nitrate if the above measures fail & the bleeding site can be visualized
- Nasal packing: if direct pressure, vasoconstrictors & cautery are unsuccessful or in severe bleeding
- May consider antibiotic (Cephalexin or Clindamycin) to prevent toxic shock syndrome if packed (controversial)
- Septal hematomas are associated with loss of cartilage if the hematoma is not removed
- Post treatment care: avoid exercise for a few days, avoid spicy foods (they cause vasodilation), Bacitracin, petroleum gauze & humidifiers helpful to moisten the nasal mucosa

### Posterior Epistaxis

**Etiology**
- Sphenopalatine artery branches & Woodruff's plexus = most common site (may cause bleeding in both nares & posterior pharynx)
- **Risk factors:** hypertension, older patients, nasal neoplasms

**Management**
- **Balloon catheters = most common initial management**
- Foley catheter, cotton packing
- Diagnose with direct visualization – if recurrent or severe get a CBC, PT, & PTT
- CT if foreign body, tumor or sinusitis suspected
- *Always ask patients with epistaxis about aspirin & ibuprofen use*

### Sensorineural Hearing Impairment

**Etiology**
- Occurs secondary to lesions in the inner ear (sensory) or the auditory (8th) nerve (neural)
- Important to determine between sensory & neural because sensory is sometimes reversible & seldom life-threatening, a neural loss is rarely recoverable &

### Conductive Hearing Impairment

**Etiology**
- 2ary to lesions in external auditory canal, TM, or middle ear which prevent sound from being conducted to the inner ear
- External or middle ear disorders
- Eustachian tube dysfunction (secondary to viral URI or allergic rhinitis)
may be d/t a potentially life-threatening brain tumor (commonly a cerebellopontine angle tumor)
- Inner ear disorders:
  - Presbycusis, chronic loud noise exposure, CNS lesions (acoustic neuroma), Labyrinthitis, Meniere syndrome
- MCC: Presbycusis

Clinical Manifestations
- Normal Ear
  - Weber: no lateralization
  - Rinne: normal air conduction > bone conduction
- SensoriNeural:
  - Weber: lateralization to normal ear
  - Rinne: normal air conduction > bone conduction
  - Difficulty hearing their own voice & deciphering words

*MCC: SensoriNeural lateralizes to Normal ear + Normal Rinne - your ear has been fucked too many times – Marielle

MCC: Cerumen impaction
- Defect in sound conduction (obstruction from a foreign body or cerumen impaction), damage to ossicles (otosclerosis, cholesteatoma), mastoiditis, otitis media

Clinical Manifestations
- Conductive:
  - Weber: lateralization to abnormal ear
  - Rinne: abnormal (negative) bone conduction > air conduction

Mixed loss (conductive + sensorineural): may be caused by severe head injury w/ or without fracture of the skull or temporal bone, by chronic infection or by one of many genetic disorders. It also may occur when a transient conductive hearing loss, commonly due to otitis media, is superimposed on a sensorineural hearing loss.

Mastoiditis

Inflammation of the mastoid air cells of the temporal bone

Pathophysiology
- Complication from preceding acute otitis media or recurrent acute otitis media
- S. pneumoniae, H. influenzae, M. catarrhalis, S. aureus, S. pyogenes

Clinical Manifestations
- Deep ear pain (worse @ night), fever, lethargy, malaise
- Signs of otitis media (bulging & erythematous TM), mastoid (postauricular)
  - tenderness w/ edema & erythema
- Forward protrusion of the auricle

Diagnosis
- First-line diagnostic test: CT scan w/ contrast of temporal bone

Management
- IV antibiotics [IV Vancomycin + Ceftazidime/Cefepime/Piperacillin-Tazobactam] + middle ear or mastoid drainage (myringotomy) w/ or without tympanostomy tube placement
- Tympanocentesis for cultures
- Complicated or refractory? Mastoidectomy

General Measures
- May develop cutaneous abscess (fluctuance) & narrowed auditory canal

Oral Candidiasis

Overgrowth of Candida Albicans due to local or systemic immunosuppressed states

Risk Factors
- Immunocompromised states [HIV, chemotherapy, diabetics], use of inhaled CS without a spacer. Antibiotic use, xerostomia, or denture use

Clinical Manifestations
- Asymptomatic
- Loss of taste or cotton-like feel in the mouth, loss of taste, throat or mouth pain w/ eating or swallowing
- White curd-like plaques on buccal mucosa, tongue, palate & the oropharynx that are easily scraped off (may leave behind erythema & friable mucosa if scraped)
- Denture form – may be associated w/ erythema only

Diagnosis
- Clinical, fungal culture – rarely done
- KOH prep: budding yeast, pseudohyphae – smear performed on scrapings

Management
- Topical therapy: 1st line therapy – Nystatin liquid swish & swallow, Clotrimazole troches or Miconazole mucoadhesive buccal tablets
- Oral Fluconazole reserved for refractory cases or patients w/ both oropharyngeal + esophageal Candidiasis

Orbital (Septal) Cellulitis

Infection of the orbit (fat & ocular muscles) posterior to the orbital septum

Pathophysiology
- Often polymicrobial: S. aureus, Streptococci, GABHS, H. influenzae
- MC secondary to untreated sinus infections (ethmoid), in children 7-12 years old
• Less commonly due to: untreated blepharitis, facial trauma, ophthalmic surgery, facial or dental infections

**Clinical Manifestations**

- **Ocular pain especially with eye movement, ophthalmoplegia** (extraocular muscle weakness) w/ diplopia, proptosis (bulging) & visual changes
- Eyelid edema & erythema

**Diagnosis**

- Clinical diagnosis that is confirmed with CT
- CT scan with contrast: infection of the fat & ocular muscles behind the septum

**Management**

- Ophthalmology evaluation
- Admit + IV antibiotics = Vancomycin + Ceftriaxone or Cefotaxime

**General Measures**

*Periorbital cellulitis is only an infx of the skin & NOT the fat behind and won’t have worsening pain w/ eye movements

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**Peritonsillar Abscess**

**Abscess between the palatine tonsil & the pharyngeal muscles**

**Pathophysiology**

- Results from a complication of tonsillitis or pharyngitis
- Most common in adolescents & young adults 15-30 years

**Etiology**

- Polymicrobial – predominant species is **Group A Streptococcus (S. pyogenes)**, S. aureus, & respiratory anaerobes (Bacteroides)

**Clinical Manifestations**

- Dysphagia, severe unilateral pharyngitis, high fever
- Muffled “hot potato” voice, difficulty handling oral secretions (drooling), trismus (lockjaw)
- Swollen or fluctuant tonsil → **uvula deviation to the contralateral side**, bulging of the posterior soft palate, & anterior cervical lymphadenopathy

**Diagnosis**

- Primarily clinical, can do U/S
- Needle aspiration: culture, and differentiate abscess from cellulitis

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**Otitis Externa**

**Inflammation of the external auditory canal**

**Pathophysiology**

- Often secondary to trauma (Q-tips, ear wax, 7-12 years old) or a moist environment (swimmer’s ear)
- Excess moisture raises pH from the normal acidic pH → facilitating bacterial overgrowth
- If the canal is closed, Weber lateralizes to the abnormal ear (blocked canal)

**Etiology**

- Pseudomonas aeruginosa = MC
- S. aureus, S. epidermis, GABHS, Proteus, anaerobes; Aspergillus, fungi

**Clinical Manifestations**

- Ear pain, pruritus in the ear canal
- Auricular discharge, ear pressure or fullness, hearing loss
- Physical exam: pain on traction of the ear canal or tragus, purulent auricular discharge that causes TM to be unseen sometimes

**Diagnosis**

- Clinical + otoscopy: edema of the external auditory canal w/ erythema, debris or discharge

**Management**

- Protect the ear against moisture (drying agents = isopropyl alcohol & acetic acid) + removal of debris & cerumen + topical antibiotics w/ coverage against Pseudomonas & Staphylococcus (w/ or w/out glucocorticoids for inflammation)
- Fungal source: Topical therapy – 2% acetic acid 3-4 drops QID, or clotrimazole 1% solution, or Itraconazole oral
- Topical antibiotics: Ciprofloxacin-dexamethasone, Ofloxacin
- Aminoglycoside combination: Neomycin/Polymyxin-B/Hydrocortisone – not used if tympanic perforation suspected or if TM cannot be visualized – aminoglycosides are ototoxic

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CT scan is imaging test of choice if needed to differentiate abscess from cellulitis.

**Management**
- **Drainage (Aspiration [preferred] or I&D) + antibiotics**
  - Antibiotics: PO (Amoxicillin, Augmentin, clindamycin); parenteral (Ampicillin-sulbactam, Clindamycin)
- Tonsillectomy: for patients who fail to respond to drainage, PTA w/ complications, hx of prior episodes, or recurrent severe pharyngitis
- Secure the airway early in a severe infection

**Prevention:** Prompt treatment of streptococcal infections

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**Strabismus**

*Misalignment of one or both eyes*

**General**
- Stable ocular alignment is not usually present until 2-3 months
- Referral is needed if it persists over 4-6 months of age – to reduce incidence of amblyopia (lazy eye)

**Major Types**
- **Esotropia:** convergent strabismus – deviated inward (nasally) “cross-eyed”
- **Exotropia:** divergent strabismus – deviated outward (temporally)

**Clinical Manifestations**
- Diplopia, scotomas, or amblyopia
- Asymmetric corneal reflex

**Diagnosis**
- **Hirschberg corneal light reflex testing:** initial testing – asymmetric deflection of the corneal light reflex in one eye is seen in strabismus
- **Cover test:** refixation of the uncovered eye is consistent w/ manifest strabismus (tropia)
- **Cover-uncover test:** looks for latent strabismus (phoria) – misalignment will appear to deviate inward or outward, convergence testing

**Management**
- First-line: patch (occlusive) therapy – cover the normal eye to stimulate & strengthen the affected eye, typically used for amblyopia and not strabismus → but may improve vision and improve prognosis
- Eyeglasses = primary treatment for accommodative esotropia
- Corrective surgery: severe or unresponsive to conservative therapy

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**Tympanic Membrane Perforation**

**Pathophysiology**
- Most commonly occurs d/t penetrating or noise trauma (@ the pars tensa) or otitis media
- May lead to cholesteatoma development

**Clinical Manifestations**
- Acute ear pain, hearing loss, tinnitus, vertigo
- Patients w. otalgia prior to rupture may develop sudden pain relief w/ bloody otorrhea

**Diagnosis**
- Otoscopic examination: perforated TM – DO NOT perform pneumatic otoscopy
- May have conductive hearing loss: Weber lateralization to affected ear, Rinne bone > air

**Management**
- Most heal spontaneously, surgery may be needed if TMP 2m+
- Topical antibiotics if there is infection – **Ofloxacin drops**
- Avoid water & topical aminoglycosides in the ear whenever there is a TM rupture

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**INFECTION DISEASE – 12%**

**Atypical Mycobacterial Disease**

*Lungs are the MC site of disease (most involve MAC)*

**Mycobacterium Avium Complex**

**Etiology**
- *Mycobacterium avium & intracellulare*
- **Transmission:** present in soil & water (NOT person to person)

**Risk Factors**
- Symptoms seen in patient w/ underlying pulmonary disease (Bronchiectasis, COPD) &/ immunocompromised patients (HIV with CD4 count less than or equal to 50cells/uL)
- Symptoms rarely occur in immunocompetent patients without underlying lung disease, inc. risk in bronchiectasis

**Clinical Manifestations**
- **Pulmonary:** presents similar to TB – cough, chest pain, fever, weight loss. **upper lobe infiltrates & cavities**
• **Disseminated:** fever or unknown origin (MC), sweating, weight loss, fatigue, diarrhea, dyspnea, RUQ pain, hepatosplenomegaly – MC in HIV patients
• **Lymphadenitis in children** – children, submandibular, & maxillary

**Diagnosis**
- Acid-fast stain & culture of samples

**Management**
- MAC is treated with clarithromycin + ethambutol + Rifampin/Rifamycin/Rifabutin fort at least 12 months
- Life threatening disease? Add a parenteral aminoglycoside to above regimen
- Second line: Ethambutol + Rifamycin (or Rifabutin) + Aminoglycoside
- Surgical excision of infected lymph nodes = curative in 90% of patients w/ lymphadenitis

**Prevention**
- Prophylaxis for HIV patients w/ single drug (azithromycin or clarithromycin) if CD4 < 50

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**Mycobacterium Marinum** – Fish Tank Granuloma

**Etiology**
- Atypical Mycobacterium – found in fresh & salt water **MARINUM = AQUARIUM = WATER**
- Transmission: Inoculation of a break in skin barrier (laceration, abrasion, etc.) with exposure to contaminated water
- Occupational hazard of aquarium handlers, marine workers, fisherman & seafood handlers

**Clinical Manifestations**
- **Localized cutaneous disease:** erythematous bluish papule or nodule at the site of trauma that can ulcerate (w/ history of exposure to non-chlorinated water 2-3w earlier)
- Subsequent lesions may occur along the path of lymphatic drainage over a period of months

**Diagnosis**
- Culture

**Management**
- No consensus on regimen or duration of therapy – Rifampin has been shown to be effective
- Doxycycline, Moxifloxacin have also been used

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**Leprosy** (Hansen’s Disease)

**Etiology**
- Chronic disease caused by *Mycobacterium leprae* & lepromatosis that primarily affects superficial tissues (especially skin & peripheral nerves)
- Endemic in subtropical areas – requires long exposure (few months to 20-50 years incubation period)

**Clinical Manifestations**
- **Lepromatous:** nodular, plaque, or popular skin lesions (lepromas) with poorly defined borders
  - Hypopigmented lesions can be seen in cooler areas of the body – face (leonine), ears, wrists, elbows, knees & buttocks; loss of eyebrows & eyelashes
  - Slowly evolving SYMMETRIC nerve involvement (sensation preserved), paresthesia in affected peripheral nerves
- MC seen in immunocompromised patients
- **Tuberculoid:** limited disease – sharply demarcated hypopigmented macular lesions numb to the touch (loss of sensation) w/ sudden onset of ASYMMETRIC nerve involvement
  - MC in immunocompetent patients (immune system rxn in the nerves causes the loss of sensation)
  - Mononeuritis multiplex: nerve damage – posterior tibial nerve, median & ulnar involvement (clawing), common peroneal nerve (foot drop), vibratory & proprioception preserved

**Diagnosis**
- Acid fast bacillus smear performed on tissue from skin bx

**Management**
- Lepromatous: Dapsone, Rifampin, Clofazimine x2-3 years
- Tuberculoid: Dapsone + Rifampin 6-12 months → then Dapsone x2 years

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**Epstein-Barr Disease**

**Pathophysiology**
- Epstein-Barr virus (part of Human herpesvirus family) infects B cells, incubation period 30-50 days
- Transmission: saliva (kissing disease), especially ages 15-25

**Clinical Manifestations**
- Fever, lymphadenopathy (especially posterior cervical), can be generalized
- Tonsillar pharyngitis – may be exudative; may have petechiae on the hard palate
- Associated with headache, fatigue, malaise, splenomegaly (inc. risk of splenic rupture), hepatomegaly
- Maculopapular rash seen in ~5%, especially if given Ampicillin

**Diagnosis**
- **Heterophile antibody** (Monospot) – test of choice (+ within 4 weeks)
- Rapid Viral Capsid Antigen test, increased LFTs
- **Peripheral Smear**: lymphocytosis >50% with >10% atypical lymphocytes

### Management

- **Mainstay of treatment:** supportive – rest, analgesics, antipyretics – symptoms may last for months
- Corticosteroids used ONLY if airway obstx d/t lymphadenopathy, hemolytic anemia, or severe thrombocytopenia – Strep & EBV can coexist
- Avoid trauma & contact sports x3-4 weeks if splenomegaly is present to **prevent splenic rupture**

### Complications

- Hodgkin lymphoma, Burkitt lymphoma, CNS lymphoma, nasopharyngeal carcinoma, gastric carcinoma

---

**Herpes Simplex 1: Oral Lesions**

### Transmission

- Direct contact with contaminated saliva or other infected bodily secretions (mouth to mouth contact, shared drinkware)

### Pathophysiology

- Herpes Simplex Virus I – MCC of oral lesions – lips, tongue
- Direct contact at mucosal or skin sites cause viral entry into the epidermis until it reaches the sensory & autonomic nerve endings

### Primary Lesions

- Most are asymptomatic, –may cause tonsillopharyngitis in adults & gingivostomatitis in children
- **Herpetic Whitlow:** can occur in dentists & health care workers exposed to infected secretions

### Secondary Lesions

- **Herpes labialis (cold sore):** reactivation of latent infection in ganglion neurons characterized by prodromal symptoms (pruritus, burning, tingling or pain) within 24 hours followed by the development of grouped vesicles on an erythematous base that undergoes crusting prior to healing

### Diagnosis

- Test of choice: PCR – most sensitive & specific
- Gold standard: HSV-1 serology
- Viral cultures, direct fluorescent antibody; Tzanck smear (nonspecific finding of multinucleated giant cells)

### Management

- Orolabial: oral Valacyclovir (2g BID x1 day), Alternative: Acyclovir
- Chronic suppression may be needed for recurrent outbreaks

---

**Herpes Simplex II: Genital lesions**

### Transmission

- Sexually transmitted via direct close contact w/ infected lesions
- Virus can enter & stay dormant in the sensory nerve ganglion where it can become activated

### Pathophysiology

- Herpes Simplex Virus I – MCC of oral lesions – lips, tongue
- Direct contact at mucosal or skin sites cause viral entry into the epidermis until it reaches the sensory & autonomic nerve endings

### Clinical Manifestations

- Painful genital ulcers often proceeded by prodromal symptoms (burning, paresthesia, numbness), dysuria, fever
- PE: Multiple, shallow, tender ulcers – grouped vesicles on an erythematous base, inguinal lymphadenopathy

### Diagnosis

- Test of choice: PCR – most sensitive & specific
- Gold standard: HSV-1 serology
- Viral cultures, direct fluorescent antibody
- Tzanck smear: multinucleated giant cells (intranuclear eosinophilic Cowdry A inclusions), classic but not specific

### Management

- Acyclovir – 800 mg PO 2x/day x5 days, Valacyclovir – 1g PO 2x/day x10d, Famciclovir – 250 mg PO TID x7-10d

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**Herpes Viruses**

- HSV 1 - Oral lesions (tongue, lips etc.)
- HSV 2 - Genital lesions (vulva, vagina, cervix, glans, prepuce, and penile shaft)
- HHV 3 - VZV (chickenpox or shingles)
- HHV 4 - EBV (infectious mononucleosis [mono or glandular fever])
HHV 5 - CMV (Cytomegalo Virus is the most common virus transmitted to a pregnant woman's unborn child)
HHV 6 - Roseolovirus (6th disease or Roseola Infatum)
HHV 7 - Similar to HHV6 (not yet classified)
HHV 8 - A type of rhadinovirus known as the Kaposi's sarcoma-associated herpesvirus (KSHV)

**Influenza**

**Transmission**
- Primarily via airborne respiratory secretions or contaminated objects
- Influenza A is associated with more severe outbreaks compared to B

**Risk Factors**
- Age 65+, pregnancy, immunocompromised
- Children = important vectors for disease (highest rates of infxn seen in children, highest complication rate in elders)

**Clinical Manifestations**
- **Abrupt onset** of a wide range of syx: HA, fever, chills, malaise, URI symptoms, pharyngitis, pneumonia
- **Myalgia** – most commonly involves legs & lumbosacral areas

**Diagnosis**
- Rapid influenza nasal swab or viral culture

**Management**
- Mild & healthy: **supportive** treatment, rest
- **Antivirals recommended in patients hospitalized or @ high risk of complications** – 65 y/o+, CVD, pulmonary disease, immunosuppression (malignancy, DM, HIV infxn, post-transplant), chronic liver dz, & hemoglobinopathies (sickle cell, thalassemia)
  - **Neuraminidase inhibitors**: Oseltamivir best if within 48 of syx onset (works for types A&B), alt: Zanamivir, Peramivir
  - Adverse reactions: skin reactions, N/V, transient neuropsychiatric events; egg allergy = C/I of Zanamivir
- **Adamantane derivatives**: Amantadine & Rimantadine are effective against influenza A only

**Complications**
- Pneumonia, respiratory failure, death, meningitis, myocarditis, encephalitis, rhabdomyolysis, & kidney failure

**Chemoprophylaxis**
- Oseltamivir – can be used in high-risk groups 1 y/o+ in cases of outbreaks or exposure
- Influenza outbreaks in long-term facilities → **all residents should receive chemoprophylaxis regardless of immunization status** – for general population, only individuals who didn’t receive annual influenza vaccine should be given chemoprophylaxis

**EXANTHEM: Measles (Rubeola) (1st Disease)**

**Etiology**
- Measles or rubeola virus (Paramyxovirus family)
- Transmission: respiratory droplets, airborne, ~6-21 day incubation period
- 3-phase progression: Prodrome → Enanthem → Exanthem

**Clinical Manifestations**
- **Prodrome**: URI syx + malaise, anorexia, fever + 3 C's!:
  - Cough, coryza, conjunctivitis
- **Enanthem**: Koplik spots: small 1-3mm pale white/blue papules w/ an erythematous base on buccal mucosa opposite the 2nd molars (pathognomonic)
- **Exanthem**: Rash: morbilliform (maculopapular), brick-red rash beginning @ hairline spreading cephalocaudally & centrifugally that darkens & coalesces, blanches
  - Rash lasts **7 days** w/ (+) lymphadenopathy & pharyngitis

**Diagnosis**
- Clinical
- IgM measles antibodies
- PCR of viral RNA from throat, nasopharyngeal or urine samples

**Management**
- Mainstay: supportive – PO hydration, Tylenol or Ibuprofen, isolate x1w
- Vitamin A: ↓ morbidity & mortality
- Measles immunoglobulin: for high risk children

**Complications**
- MC: Diarrhea
- MCC of death: Pneumonia
- AOM, conjunctivitis, encephalitis

Question may describe: pt with hx of fever, runny nose, conjunctivitis, & cough → rash from face spreading downward; exam is + for mild conjunctival injection & generalized macular rash with white macules on buccal mucosa

**Mumps**

**Etiology**
- Paramyxovirus
- Transmission: respiratory droplets, saliva, & household fomites ~12 day incubation period
- Increased in spring & most infectious 48h prior to onset of parotitis & infectious for 9 days after onset

Clinical Manifestations
- **Prodrome:** low-grade fever, myalgia, malaise, HA, earache → parotitis (bilaterally usually)
- **PE:** parotid swelling & tenderness, erythema & edema of Stensen’s duct

Diagnosis
- Clinical, serologies or PCR technology
- Increased amylase, leukopenia w/ relative lymphocytosis, decreased glucose

Management
- Supportive: antipyretics, analgesics, self-limited [syx last 7-10 days]
- Hospitalized: patient placed on droplet precautions & CDC recommends isolation for at least 5 days after syx onset

Complications
- Epididymo-orchitis (unilateral) = MC complication, esp in postpubertal males – may occur 5-10d after parotitis onset
- Neurologic: aseptic meningitis (MC), encephalitis, deafness
- Oophoritis, arthritis, infertility
- MCC of pancreatitis in children

---

**EXANTHEM: Rubella (German Measles)***

Etiology
- Rubella virus (Togavirus family)

Clinical Manifestations
- **Prodrome:** low grade fever, cough, anorexia, & posterior cervical/posterior auricular lymphadenopathy
- **Exanthem:** Rash: pink/red nonconfluent maculopapular rash that starts on face & spreads to trunk & extremities lasting 3 days [spreads more rapid than measles and much darker & confluent in measles]
- Forchheimer spots: small red macules/petechiae on soft palate
- Photosensitivity & joint pain

Diagnosis
- Clinical diagnosis
- Rubella-specific IgM antibody w/ enzyme immunoassay
- Rubella-virus specific IgM antibodies present – can be + up to one year after infection

Management
- Supportive: Tylenol/Ibuprofen, oral hydration

General Measures
- Forchheimer spots seen in Scarlet fever too
- Not assoc. w/ complications
- Teratogenic in first trimester (Question: Neonate born w/ hepatosplenomegaly, jaundice, continuous machinery-like murmur, cataracts, sensorineural hearing loss & thrombocytopenia [Blueberry muffin rash] – congenital rubella syndrome, causes deafness in newborn)

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**EXANTHEM: Erythema Infectiosum – Fifth Disease***

Etiology
- Parvovirus B-19: infects & destroys reticulocytes, leading to a decrease or transient alt in erythropoiesis (can lead to aplastic crisis [Sickle cell patients @ highest risk, & G6PD patients])
- MC in children <10 y/o
- Transmission: respiratory droplets, 4-14 day incubation period

Clinical Manifestations
- Nonspecific viral symptoms (coryza, malaise, fever) followed by erythematous malar rash w/ “slapped-cheek” appearance & circumoral pallor for 2-4 days
- Malar rash is followed by a lacy, reticular maculopapular rash on the extremities (especially upper) that usually spares palms & soles, resolving in 2-3 weeks – pruritic
- Older children & adults: arthropathy & arthralgias
- Associated w/ increased fetal loss during pregnancy (hydrops fetalis, CHF, spontaneous abortion)

Diagnosis
- Clinical
- Serology: associated w/ enlarged nuclei w/ peripherally displaced chromatin
- Parvovirus-specific IgM antibodies & PCR

Management
**EXANTHEM: Hand-foot-and-mouth Disease***

**Etiology**
- **Coxsackievirus type A** – this is an Enterovirus that is part of a Picornavirus family
- Commonly in children under 5 & in Summer/early Fall

**Clinical Manifestations**
- Mild fever, URI symptoms [sore throat, malaise, irritability], & decreased appetite starting 3-5 days after exposure
- **Oral exanthem**: erythematous macules that become painful oral vesicles surrounded by a thin halo of erythema that undergoes ulceration (esp on buccal mucosa & tongue) followed by exanthem
- Exanthem: greyish-yellow *vesicular, macular or maculopapular* lesions on the distal extremities (often including palms & soles) – less commonly vesicles are seen on face & torso
- Not painful or pruritic

**Diagnosis**
- Clinical
- Coxsackie-specific Immunoglobulin A, viral culture

**Management**
- Supportive: antipyretics (Acetaminophen, Ibuprofen), hydration, topical Lidocaine

**General Measures**
- Complications: Aseptic meningitis & Guillain-Barre syndrome
- Virus usually clears up within 10 days; good hand hygiene and cleansing of surfaces can decrease transmission

**EXANTHEM: Roseola Infantum – Exanthema Subitum – HSV 6/7 – Sixth Disease***

**Transmission**
- Respiratory droplets with a 10-day incubation period
- 90% occur in children, < 2 years of age

**Clinical Manifestations**
- **Fever prodrome**: high fever 3-5 days (may exceed 104) & lymphadenopathy – child appears well & alert during febrile phase, the *fever resolves abruptly before the onset of the classic rash**
- **Rash**: rose, pink, macular or maculopapular, blanchable rash *beginning on the trunk & neck before spreading to the face*
  - Macules 2-5mm & rash lasts hours up to 2 days
  - Only viral exanthem that starts on the trunk
- **Nagayama spots**: erythematous papules on the soft palate & uvula
- Erythematous tympanic membranes, respiratory symptoms, anorexia
- 15% risk of febrile seizures

**Diagnosis**
- Clinical

**Management**
- **Supportive – mainstay of treatment** (self-limited) – rest, maintain fluid intake, antipyretics
- Adequate handwashing important to prevent spread of infection

**Varicella - Chickenpox**

**Etiology**
- VZV, part of the Human herpes virus family (HHV-3) → causes 2 clinically distinct diseases: **Primary – varicella (chickenpox)** and **reactivation – herpes zoster (Shingles)**

**Transmission**
- Aerosolized droplets from nasopharyngeal secretions or direct contact w/ skin lesions – 10-20 day incubation period

**Clinical Manifestations**
- Prodrome: fever, malaise, anorexia, or pharyngitis followed by generalized vesicular rash, usually within 24 hours
- Evolution: classic evolution = *erythematous macules that become papules then vesicular then crust over*
  - Rash begins on the face, then goes to the trunk before spreading to the extremities – usually pruritic
- **PE: asynchronous rash in different stages of evolution** – including macules, papules, clusters of *vesicles on an erythematous base (“dew drops on a rose petal”) & crusted lesions*
  - More severe presentations may occur in adults

**Diagnosis**
- **Clinical** – serology & fluorescent microscopy will confirm the diagnosis
• **PCR** – highest yield when testing is needed, can be performed on fluid from lesions, skin scraping or CSF
  
• **Direct fluorescent antibody staining** largely replaced Tzanck smear
  
• **Tzanck smear**: multinucleated giant cells
  
• **Serologies**: anti-VZV IgM in response to an acute infection – IgG denotes immunity

**Management**

• **Previously healthy child 12 y/o or younger** – supportive & symptomatic treatment (Tylenol, Calamine lotion) – avoid acetylsalicylic acid d/t increased risk of Reye syndrome – NSAIDs may increase risk of superinfection!
  
• **Acyclovir** should be given to adolescents (13 years old +), adults, & immunocompromised patients (give IV) because they are susceptible to complications (pneumonia, encephalitis, hemorrhagic complications) – when given within 72 hours of onset. **Acyclovir** can limit both severity & duration - **Acyclovir resistant cases get Foscarnet!!**
  
• Hospitalized patients should be placed on **contact & airborne precautions**
  
• Chickenpox can be spread from 48 hours prior to the onset of the rash up until all the lesions have crusted over – during that time frame, patients should avoid contact with pregnant women & unvaccinated individuals

**Complications**

• **Bacterial superinfection** = MC complication in children
  
• **Varicella pneumonia** = leading cause of mortality & morbidity in adults (may develop within 3-7 days following rash)
  
• **Encephalitis. Reye syndrome** (rare)

---

**Enterobiasis – Pinworms**

_Nematode infection caused by Enterobius vermicularis (pinworm)_

• MC helminthic infection in the United States

**Transmission**

• Hand-mouth contact w/ contaminated fomites, autoinoculation, **fecal-oral contamination** (especially **school-aged children** 5-10 years old)

**Clinical Manifestations**

• **Perianal itching**, especially **nocturnal** (eggs are laid @ night)
  
• **Severe cases** – associated w/ abdominal pain, N/V

**Diagnosis**

• (+) **Cellophane tape test** or pinworm paddle test early in the AM to look for football shaped ova under microscope

**Management**

• Albendazole, Mebendazole, or Pyrantel
  
• Pregnancy – Pyrantel
  
• Treat entire household to reduce reinfection – wash hands, trim fingernails, take bath early in AM to reduce egg contamination

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**Pertussis (Whooping Cough)**

_Highly contagious infection secondary to Bordetella Pertussis, a gram-negative coccobacillus_

• Rarely seen d/t widespread vaccination – MC in children under 2 y/o

**Transmission**

• Respiratory droplets during coughing fits w/ a 7-10 day incubation period

**Clinical Manifestations**

• **Catarhal Phase**: URI sx lasting 1-2 weeks – most contagious during this phase
  
• **Paroxysmal Phase**: severe paroxysmal coughing fits with inspiratory whooping sound after cough fits – may have **post coughing emesis**, lasts 2-4 weeks
  
• **Convalescent Phase**: resolution of the cough (cough may last for up to six weeks)

**Diagnosis**

• Clinical – when available, order both **throat culture** & PCR; - **lymphocytosis** is common
  
• **Throat culture**: most sensitive during first 2 weeks of the illness
  
• **PCR of nasopharyngeal swab**: sensitive up to 4 weeks of illness

**Management**

• **Mainstay of treatment**: Supportive – oxygenation, nebulizers, mechanical ventilation as needed & droplet precautions if admitted
  
• **Macrolides = drug of choice** used to decrease contagiousness of affected patient
  
• **Azithromycin** – better tolerated & preferred in children <1 month of age, Erythromycin; second-line: Bactrim

**Complications**

• **Pneumonia**, encephalopathy, otitis media, sinusitis, & seizures; inc. mortality in infants d/t apnea/cerebral hypoxia associated w/ coughing fits
Acute bronchiolitis

**Inflammation of the bronchioles – the smallest air passages of the lungs which usually occurs in children under 2**

**Etiology**
- **Respiratory Syncytial Virus (RSV)** = MCC, Rhinovirus, Adenovirus, Influenza virus, parainfluenza virus, etc
- **At risk:** Infants 2 months to 2 years most commonly affected, exposure to cigarette smoke, lack of breastfeeding, prematurity, & crowded conditions

**Clinical Manifestations**
- **Viral prodrome** (fever, URI symptoms) for 1-2 days, followed by **respiratory distress** (wheezing, tachypnea, nasal flaring, cyanosis, retractions, rales)
- **Signs of severity:** hypoxemia, apnea, respiratory failure

**Diagnosis**
- Clinical diagnosis
- CXR: nonspecific – hyperinflation, peribronchial cuffing/thickening, atelectasis – not routinely performed but may be used to rule out other causes
- Nasal washings using monoclonal antibody testing for RSV culture & antigen assay
- Pulse oximetry single best predictor of disease in children

**Management**
- **Supportive measures mainstay of treatment** – humidified oxygen, IV fluids, nebulized saline, cool mist humidifier, antipyretics (Acetaminophen)
- Mechanical ventilation may be indicated if severe
- Medications play a limited role – beta-agonists, nebulized racemic epinephrine – CS NOT indicated unless (+) hx of an underlying reactive airway disease
- Ribavirin may be administered if severe lung or heart disease or in immunocompromised patients
- Hospitalization if low O2 saturation, age under 3 months, respiratory rate 70+, or atelectasis on CXR

**Prevention for High Risk**
- Palivizumab (1x/month x5 months start Feb) – during first year of life for children born under 29 weeks, syx chronic lung disease of prematurity, congenital heart disease, neuromuscular difficulties, immunodeficiency
- Handwashing = preventative

**Asthma**

**Chronic, reversible, often intermittent inflammatory obstructive disease of the small airways**

**Pathophysiology**
- 3 components – airway hyperreactivity, bronchoconstriction, & inflammation
  - Increased IgE binds to mast cells, initiating an inflammatory response, including increased Leukotrienes
  - Can present @ any age but initial occurrence is most common in childhood

**Risk Factors**
- **Atopy = strongest risk factor**, family history, air pollution, obesity, environmental tobacco smoke, male gender
- **Samter’s triad** (Aspirin-exacerbated respiratory disease) consists of asthma + chronic rhinosinusitis with nasal polyps + sensitivity to Aspirin &/ NSAIDs
- **Atopic triad** (patients with one condition are likely to develop one or two of the other) – Asthma + atopic dermatitis (eczema) + allergic rhinitis

**Triggers**
- Intrinsic (non-allergic): anxiety, stress, exercise, cold/dry air, hyperventilation, & viral infections
- Extrinsic (allergic): animal dander, pollen, mold, dust mites, cockroaches, etc. – associated with increased IgE
- Other: medications (ASA, NSAIDs, Beta-blockers, histamine), GERD

**Clinical Manifestations**
- **Classic triad:** dyspnea, wheezing & cough (especially @ night), may have chest tightness & fatigue
- Clues to severity: previous intubations, hospital admissions, ICU admission
- PE: **prolonged expiration with wheezing**, hyperresonance to percussion, decreased breath sounds, tachycardia, tachypnea, use of accessory muscles
- **Severe asthma & Status asthmaticus:** inability to speak in full sentences, “tripod” positioning, **silent chest** (no air movement), altered medical status – ominous, pulsus paradoxus (inspiratory blood drop >10 mmHg), PEFR <40% predicted
- **Findings of longstanding disease:** nasal polyps or atopic dermatitis may be seen

**Diagnosis – in the office**
- Pulmonary function tests: gold standard in making asthma dx. Reversible obstruction (decreased FEV1, decreased FEV1/FVC, increased RV, TLC, & RV/TLC)

FEV measures how much air a person can exhale during a forced breath. The amount of air exhaled during the first (FEV1), second (FEV2), and/or third seconds (FEV3) of the forced breath. Forced vital capacity (FVC) is the total amount of air exhaled during the FEV test.
• Bronchoprovocation: Methacholine challenge (>20% decrease on FEV1) followed by bronchodilator challenge (an increase of FEV1 12+% is expected)

Diagnosis – Acute Asthma Exacerbation

• **Peak expiratory flow rate:** best & most objective way to assess exacerbation severity & patient response to treatment
  - Discharge criteria: PEFR 70+% predicted or PEFR 15+% initial attempt, subjective improvement
  - Pulse oximetry: SaO2 less than 90% is indicative of respiratory distress
  - **ABG:** not usually ordered in most exacerbations, respiratory alkalosis is expected (from tachypnea)
  - Pseudonormalization (normal CO2) or respiratory acidosis may indicate impending respiratory failure
  - Chest radiograph: usually normal, generally not helpful in the diagnosis of asthma but may be used to rule out other causes of symptoms (pneumonia)

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**Symptoms**
- Intermittent: < 2 days/week
- Mild persistent: >2 days/week
- Moderate persistent: Daily
- Severe persistent: Throughout the day

**SABA use for syx**
- Intermittent: <2x/month
- Mild persistent: >2 days/week (not daily)
- Moderate persistent: Daily
- Severe persistent: Several times/day

**Nighttime awakenings**
- Intermittent: <2d/week
- Mild persistent: 3-4x/month
- Moderate persistent: >1x/week (not nightly)
- Severe persistent: Usually nightly

**Interference w/ normal activity**
- Intermittent: None
- Mild persistent: Minor limitation
- Moderate persistent: Some limitation
- Severe persistent: Extremely limited

**Lung function**
- Intermittent: nL FEV1 between exacerbations, FEV1 80+% predicted, FEV1/FVC normal
- Mild persistent: FEV1 80+% predicted, FEV1/FVC normal
- Moderate persistent: FEV1 60-80% predicted, FEV1/FVC reduced by 5%
- Severe persistent: FEV1 under 60% predicted, FEV1/FVC reduced by over 5%

**Recommended management**
- Intermittent: SABA PRN
- Mild persistent: SABA PRN + Low-dose ICS
- Moderate persistent: Low ICS + LABA or increased ICD dose (medium) or add LTRA
- Severe persistent: High dose ICS + LABA +/- Omalizumab (anti-IgE drug)

**Exacerbations requiring PO steroids**
- Intermittent: 0-1/year
- Mild persistent: 2+/year

Management

**Acute treatment of exacerbation:** Oxygen, nebulized SABA (Albuterol), anticholinergic (ipratropium bromide), & oral corticosteroids (prednisone, methylprednisolone, prednisolone) – side effects in PPP pg 111

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**Croup – Laryngotracheitis**

*Inflammation of the larynx & subglottic airway*

**Etiology**
- **MCC = parainfluenza virus type I**, RSV, Adenovirus, & Rhinovirus
- MC between 6 months-6 years; especially in fall & winter

**Clinical Manifestations**
• **Upper airway involvement**: harsh, “seal-like barking” cough – hallmark of the disease in infants & young children, inspiratory *stridor*, hoarseness (especially in older children & adults), dyspnea, low-grade fever – symptoms often worse @ night
• URI symptoms (coryza) prior, during, or after acute presentation
• Significant upper airway obstruction, respiratory distress, rarely death

**Diagnosis**
- **Clinical diagnosis**: once epiglottitis & foreign body aspiration are excluded
- **Frontal cervical radiograph**: Steeple sign (subglottic narrowing of the airway) – 50%, rarely done

**Management**
- Mild (no stridor @ rest, no respiratory distress)
  - **Supportive** (cool humidified air mist, hydration), O2 if O2sat under 92%, Dexamethasone/Prednisone provides relief as early as 6 hours after single dose (PO/IM) → faster resolution of syx, ↓ length of stay, & ↓ relapse
  - Moderate (stridor @ rest, with mild to moderate retractions):
    - Dexamethasone or Prednisone PO or IM + supportive treatment
  - Nebulized epinephrine, observe patient 3-4 hours after clinical intervention, may be discharged home if improvement is seen
- **Severe** (stridor @ rest, with marked retractions)
  - Dexamethasone + nebulized epinephrine & hospitalization

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**Cystic Fibrosis**

*Autosomal recessive exocrinopathy → abnormal mucus production → obstruction of glands & ducts*

**Pathophysiology**
- Mutation in the cystic fibrosis transmembrane conductance receptor (CFTR) gene leads to abnormal chloride & water transport across exocrine glands throughout the body, leading to a thick, viscous secretion of the lungs, pancreas, sinuses, intestines, liver & genitourinary tract
- MC in Caucasians & Northern Europeans

**Clinical Manifestations**
- **Infancy**: meconium ileus, failure to thrive, diarrhea from malabsorption (may lead to rectal prolapse)
- **Pulmonary**: CF is the MCC of Bronchiectasis in the US
- **GI**: malabsorption (especially fat-soluble vitamins [A, D, E, K], steatorrhea, diarrhea, recurrent pancreatitis (may lead to pancreatic insufficiency), distal intestinal obstruction, biliary cirrhosis
  - Infertility due to azoospermia; sinusitis

**Diagnosis**
- **Elevated sweat chloride**: test of choice (most accurate) – *NaCl 60mmol/L or greater* on 2 occasions after Pilocarpine administration (Pilocarpine is a cholinergic drug that induces sweating)
- **Chest radiograph**: Bronchiectasis common, hyperinflation of the lungs
- **Pulmonary function test**: obstructive pattern (usually irreversible)
- **DNA Analysis**: genotyping is not as accurate as sweat chloride testing because there are more types of mutations than those tested with genotyping

**Management**
- **Antibiotics are often needed** – Macrolides; Cephalosporins (Cefuroxime, Cefixime), Augmentin, Fluoroquinolones &/ inhaled aminoglycosides
- **Airway clearance treatment**: inhaled bronchodilators, decongestants, mucolytics, inhaled recombinant human deoxyribonuclease (breaks down large amounts of DNA in the respiratory mucous that clogs up the airways)
- **Supportive**: pancreatic enzyme replacement, supplementation of fat soluble vitamins, vaccinatinos – Pneumococcal, influenza
- Lung & pancreatic transplant in selected cases

**General Measures**
- Mean survival is 31 years old
- In the first few months of life, respiratory infection is common w/ Staph aureus & H. influenzae, after that → *Pseudomonas aeruginosa becomes the major causative organism of infection*

Questions will show: patient, young, growth retardation, long history of recurrent pneumonia/chroic diarrhea, foul smelling stools

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**Foreign Body Aspiration**

*Aspirated solid or semi-solid object, usually lodged in larynx or trachea*

- Aerodigestive foreign body causing varying amounts of obstruction to the airway
- Common items include: food, coins, toys, food & ballons (peanuts are MC foreign body aspirated in children)
- Mean age = 2 (incisors are used to bite the food but absence of molars make it difficult to grind food)
- Main cause of death is d/t hypoxic-ischemic brain injury & less commonly, pulmonary hemorrhage
Risk factors: institutionalization, advanced age, poor dentition, alcohol, sedative use

Complications: bronchiectasis, pneumonia, lung abscess, atelectasis

**Most common on the right side** (due to wider, more vertical & shorter right main bronchus) – 80% in mainstem or lobar bronchus, 20% in upper airway, **right > left**

- **Position may influence location:**
  - Supine: MC in **superior segment of right lower lobe**
  - Sitting/standing: MC in **posterobasal segment of right lower lobe**
  - Lying on right side: MC in **right middle lobe/posterior segment of right upper lobe**

**Clinical Manifestations**
- Asymptomatic or **sudden onset of choking, cough and dyspnea**
- **Physical examination:** wheezing or asymmetric breath sounds (may be normal)
  - Inspiratory stridor if FB high in the airway
  - Wheezing & decreased breath sounds if low in airway

**Diagnosis**
- **Chest XR:** air trapping most common finding in children, atelectasis, pneumothorax – normal CXR doesn’t rule out FB aspiration; may order additional neck films
- **CT chest:** may be indicated in symptomatic patients with negative XR
- **Rigid bronchoscopy:** definitive diagnostic test (also therapeutic because object can be removed) (preferred in children)
  - Flexible rather than rigid may be used for diagnostic purposes in cases when the diagnosis isn’t clear or if the FBA is known but location is unclear

**Management**
- **Rigid bronchoscopy:** removal of foreign object – thoracotomy if refractory to bronchoscopy
- In acute choking, the Heimlich maneuver should be performed → emergency tracheostomy if Heimlich unsuccessful

**Hyaline Membrane Disease – Neonatal/Infant Respiratory Distress Syndrome (IRDS)**

**Pathophysiology**
- Disease of preterm infants caused by a **lack of pulmonary surfactant production**
  - Surfactant production begins 24-28 weeks, by 35 weeks enough surfactant is produced, it helps to prevent the lungs from collapsing. As the airways collapse, infants will struggle more and more to breathe until they become acidotic and multisystem organ failure begins
- MC single cause of death in the first month of life

**Risk Factors**
- **Caucasians, males, multiple births, maternal diabetes, C-section delivery, perinatal infection**

**Clinical Manifestations**
- Usually presents @ birth or shortly after birth with respiratory distress – tachypnea (over 60 bpm), tachycardia, chest wall retractions, expiratory grunting, nasal flaring, cyanosis

**Diagnosis**
- **CXR:** diffuse bilateral reticular atelectasis (causes ground-glass appearance) opacities + air bronchograms, poor lung expansion, domed diaphragms
- **ABG:** hypoxia (unresponsive to oxygen supplementation), normal or slightly increased PCO2
- **Postmortem histopathology:** waxy-appearing layers lining the collapsed alveoli & airway distension

**Management**
- **Exogenous surfactant via endotracheal tube** to open the alveoli + mechanical ventilation (CPAP)
  - 2-3 day clinical course with or without treatment
  - 90% survival rate w/ treatment & normal return of lung function within 1 month

**Prevention**
- Antenatal glucocorticoids given to mature lungs if premature delivery is suspected (between 24-36 weeks)

**Pneumonia – Bacterial**

**Etiology**
- **Typical:** *Streptococcus pneumoniae* (most common), H. influenzae, Klebsiella pneumoniae, Staph aureus
- **Atypical:** Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila

**Clinical Manifestations**
- **Typical:** fever, productive cough, pleuritic chest pain, dyspnea
  - Rigors (severe chills w/ violent shaking): classically associated with Streptococcus pneumoniae
- **Atypical:** low-grade fever, dry nonproductive cough, extrapulmonary symptoms (myalgias, malaise, pharyngitis, nausea, vomiting, diarrhea)

**Physical Examination**

- **Ground-glass appearance on CXR**
• Typical: tachypnea, tachycardia, signs of consolidation: bronchial breath sounds, dullness to percussion, increased tactile fremitus, egophony, inspiratory rales (crackles)
• Atypical: pulmonary exam often normal (signs of consolidation usually absent) – may have crackles (rales)
• Elderly, diabetic, & immunocompromised patients may have minimal exam findings even with typical pneumonia

Presentation based on Etiology

**Streptococcus pneumonia**
- MCC of community-acquired pneumonia
- **Classic presentation:** sudden onset of one time chills & rigors (violent shivering), fever, productive cough w/ **blood-tinged (rusty) sputum** – (common in patients with a splenectomy)
- **Gram stain:** gram (+) diplococci

**Haemophilus Influenza**
- 2nd MCC of community-acquired pneumonia
- **Increased Risk:** extremes of age (under 6, elderly), immunocompromised (DM, HIV, chemotherapy), underlying pulmonary disease (asthma, COPD, bronchiectasis, CF), alcoholics
- Often a colonizer of the respiratory tract – gram (-) rod

**Staphylococcus Aureus**
- Associated as a superimposed infection after a viral infection – hospital-acquired pneumonia, seen with **salmon colored sputum**
- **Chest XR:** bilateral, multilobar infiltrates or abscesses (cavitary lesions)
- **Gram stain:** gram (+) cocci in clusters
- If MRSA → treat with Vancomycin

**Klebsiella pneumonia**
- Severe illness in **chronic alcoholism,** sick patients, patients with chronic illnesses (Diabetes)
- May present with **purple-colored (currant jelly) sputum**
- **Chest XR:** cavitary lesions are hallmark* (nonspecific) or lobar consolidations
- **Gram stain:** gram (-) rods

**Mycoplasmia pneumonia**
- MCC of atypical **walking pneumonia** – outbreaks in late summer & early fall
- **Risk factors:** young & healthy (school-age children, college students, military recruits)

Clinical Manifestations:
- **Extrapulmonary symptoms:** commonly presents w/ **pharyngitis & URI prodrome** (rhinorrhea, HA, malaise, low grade fever) followed by persistent dry (nonproductive) cough – physical exam often normal
- **Bullous myringitis** (fluid-filled blisters on the tympanic membrane) is a rare, nonspecific finding
- Complications included SJS, TENs, erythema multiforme, cold autoimmune hemolytic anemia (IgM)

Diagnostic Tests
- **Chest radiograph:** atypical pattern – **reticulonodular pattern most common,** diffuse, patchy or interstitial infiltrates
- **PCR** (test of choice), cold agglutinins, serology, special culture media (bc it is a short rod without a cell wall, gram-stain is NOT useful)

Management
- **Macrolides** (Azithromycin) or Doxycycline
- **Lacks a cell wall** so naturally resistant to beta-lactams

**Legionella Pneumophila**
- Aerobic, pleomorphic intracellular gram-negative bacterium
- **Transmission:** outbreaks related to contaminated water sources (air conditions, portable water, vents), no person-to-person
- **Risk factors:** immunosuppressed, smokers, elderly, chronic lung disease

Clinical Manifestations
- Fever, chills, dyspnea, dry cough, chest pain, malaise, myalgias
- **Extrapulmonary symptoms:** GI symptoms prominent – **diarrhea** (watery & non-bloodly), N/V
- Higher incidence of **hyponatremia & increased LFTs**
- **Neurologic symptoms:** headache, confusion, altered mental status
- Although “atypical,” patients can be very ill

Diagnostic Tests
- Nucleic acid detection (PCR preferred, urine antigen, culture)

Management
- **Macrolides** (Azithromycin) or respiratory Fluoroquinolones (Levofloxacin, Moxifloxacin, & Gemifloxacin)

**Pneumonia – Viral**
- **Causes of hospital-acquired pneumonia:** Pseudomonas, MRSA
- **CURB65 (ADMIT IF AT LEAST 2):** Confusion, Uremia (30+), RR 30+, BP low (under 90/60), age 65+
- Community-acquired, inpatient: beta-lactam (Ceftiraxone) + Macrolide
Etiology
- Adults: flu is MCC
- Kids: RSV, 1st episode of wheezing
- Adenovirus tends to cause symptoms fast, will present with GI symptoms and lasts about 1 week. May differentiate from bacterial mycoplasma pneumonia as mycoplasma is slow and insidious.

Diagnosis
- CXR: bilateral interstitial infiltrates
- → rapid antigen testing for influenza, → RSV nasal swab, → cold agglutinin titer that is negative

Management
- Symptomatic – beta-2-agonist, fluids, rest
- If influenza is the cause: oseltamivir/zanamivir for influenza A and B, or amantadine/rimantadine for influenza A

Respiratory Syncyial Virus Infection

Pathophysiology
- RSV is the MCC of lower respiratory tract infections worldwide – virtually all children will contract it by age 3
- Leading cause of pneumonia & bronchiolitis in infants & may play a major role in the pathogenesis of asthma bronchiolitis
- See above disorders*

CARDIOVASCULAR – 10%

Acute Rheumatic Fever

Acute autoimmune inflammatory multi-systemic illness sequela of a beta-hemolytic streptococcal infx of the pharynx

Pathophysiology
- Symptomatic or asymptomatic infection with Group A Streptococcus (aka Strep pyogenes) stimulates antibody production to host tissues & damages organs directly
- Children 5-15 years old

Clinical Manifestations
- Polyarthritis: (75%) 2 or more joints affected (simultaneous more diagnostic) or migratory (lower → upper joints) – lasts 3-4 weeks
  - Medium/large joints most commonly affected (knees, hips, wrists, elbows, shoulders)
  - Heat, redness, swelling, & severe joint tenderness must be present
  - Joint pain (arthralgia) without other symptoms doesn’t classify as major
- Active carditis: (40-60%) can affect valves (especially mitral & aortic), myocardium (myocarditis) &/or pericardium (pericarditis) – carditis confers great morbidity & mortality
- Sydenham’s chorea: (<10%) “Saint Vitus dance” may occur 1-8 months after initial infection
  - Manifestations include sudden involuntary, jerky, non-rhythmic, purposeless movements especially involving the head/arms, usually resolves spontaneously & MC in females
- Erythema marginatum: macular, erythematosus, non-pruritic annular rash with rounded, sharply demarcated borders (may have central clearing) – crops last hours → days before disappearing
  - Often accompanies carditis
  - MC on trunk & extremities – not the face
- Subcutaneous nodules – rare, seen over joints (extensor surfaces), scalp, and spinal column
- Other findings not associated w/ jones criteria: abdominal pain, facial tics/grimaces, epistaxis

Diagnosis
- Jones criteria for rheumatic fever – 2 Major OR 1 Major + 2 Minor PLUS Supporting evidence of recent strep infx

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
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<tbody>
<tr>
<td>Joint (migratory polyarthritis)</td>
<td>Arthralgia</td>
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<tr>
<td>Oh my heart (active carditis)</td>
<td>Fever – 101.3+</td>
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<tr>
<td>Nodules (subcutaneous)</td>
<td>EKG: prolonged PR interval</td>
</tr>
<tr>
<td>Erythema marginatum</td>
<td>Elevated CRP &amp;/ESR</td>
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<tr>
<td>Sydenham’s chorea</td>
<td>Leukocytosis</td>
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- Supporting evidence of a recent group A streptococcal infection:
  - Positive throat culture for GAS or
  - Positive rapid streptococcal antigen or
  - Elevated/increased streptococcal antibody titers (antistreptolysin O, anti-DNase B

Management
- Anti-inflammatory: Aspirin (2-6 weeks with taper) +/- corticosteroids in severe cases & carditis
- Penicillin G – antibiotic of choice (or erythromycin if PCN allergic) both in acute phase & after acute episode
  - Prevention is the most important therapeutic course – therefore all patients should be treated w/ abx

Complications
- Rheumatic valvar disease – mitral (75-80%), aortic (30%), tricuspid & pulmonic (5%)
Atrial Septic Defect

Abnormal opening in the atrial septum between the right & left atrium → volume overload of right atrium & ventricle

Pathophysiology
- Allows for a left to right shunt (noncyanotic) because the foramen ovale fails to close
- Types: ostium secundum (MC type), ostium primum (assoc. w/ mitral valve abnormalities [regurg]), sinus venosus, coronary sinus
- 2nd MC congenital heart disease

Clinical Manifestations
- Most pts asyx or minimally syx in childhood; syx often occur in 3rd decade
- Infants & young children: recurrent respiratory infx, failure to thrive, DOE
- Adolescents & young adults: exertional dyspnea, easy fatigability, palpitations, atrial arrhythmias, syncope, heart failure
- Over 30 – dyspnea & chest pain, over 50 – afib & RVF
- May develop paradoxical emboli (stroke from venous clots) or dysrhythmias later in life
- Larger shunts may cause exercise intolerance DOE, fatigue & atrial arrhythmias w/ palpitations

Physical Examination
- Systolic ejection crescendo-decrescendo flow murmur @ pulmonic area (LUSB – 2nd or 3rd intercostal space)
- Wide, fixed split S2 that does not vary with respirations, loud S1 & hyperdynamic right ventricle

Diagnosis
- Echocardiogram: best test to make the diagnosis
- ECG: incomplete RBBB, Crochetage sign (notching of the peak of the R wave in the inferior leads)
- CXR: cardiomegaly & inc. cardiovascular markings
- Cardiac catheterization: definitive but rarely needed

Management
- Small ASD < 5mm may be observed (most small ASD spontaneously close in the first year of life)
- Symptomatic treatment: Diuretics, ACE inhibitors, digoxin
- Surgical correction: 1cm+/symptomatic (between 2-4 y/o) → perQ transcatheter closure v. surgical intervention

Patent Ductus Arteriosus

Persistent communication between the descending thoracic aorta & main pulmonary artery after birth

Pathophysiology
- Associated with a left to right shunt (noncyanotic)
- Continued prostaglandin E1 production & low arterial oxygen content promotes patency
- Risk factors: prematurity, female (2x>), fetal hypoxia

Clinical Manifestations
- Most are asymptomatic – infants may develop poor feeding, weight loss, frequent lower respiratory tract infections, pulmonary congestion, infective endocarditis
- Eisenmenger syndrome: pulmonary hypertension & cyanotic heart disease occurring when a left-to-right shunt switches & becomes a right-to-left shunt (cyanotic)
- Patients may develop cyanotic lower extremities (cyanosis & clubbing of feet)

Physical Examination
- Continuous machine-like or “to and fro” murmur loudest @ pulmonic area (LUSB – 2nd intercostal space)
- Wide pulse pressure (bounding peripheral pulses) with low DB, loud S2

Diagnosis
- Echocardiogram: best test to make the diagnosis
- ECG: LVH, left atrial enlargement
- CXR: normal or cardiomegaly
- Cardiac catheterization: definitive but rarely needed

Management
- NSAIDs = 1st line medical treatment (IV Indomethacin, Ibuprofen)
- Surgical correction (percutaneous catheter occlusion/surgical ligation) if no closure w/ indomethacin, best if done before 1-3 y/o

Coarctation of the aorta

Congenital narrowing of the aortic lumen at the distal arch & descending aorta, 2x M>F

Pathophysiology
- Narrowing of the aorta, MC @ the insertion of the ductus arteriosus distal to the origin of the left subclavian vein results in HTN in the arteries proximal (primary arteries supplying the upper extremities) with relative hypotension in the lower extremities
- Over time, the body compensates by developing collaterals around the coarctation
- Often associated with **bicuspid aortic valve (50% of patients)**, mitral valve defects, patent ductus arteriosus & Turner syndrome

**Types**
- **Post-ductal**: (adult type) – narrowing occurs distal to the ductus arteriosus
- **Pre-ductal**: (infantile type) – narrowing occurs proximal to the ductus arteriosus

**Clinical Manifestations**
- May range from asymptomatic to heart failure or shock after birth with closure of the patent ductus arteriosus
- **Bilateral claudication**, dyspnea on exertion, syncope
- **Neonatal presentation**: failure to thrive in infants, poor feeding 1-2 weeks after birth

**Physical Examination**
- **Upper extremity systolic HTN with lower extremity hypotension &/or diminished/delayed lower extremity pulses** (femoral & dorsalis pedis pulse)
- Late systolic ejection murmur/continuous murmur **radiating to the left back, left scapula or chest**, heard in the **aortic area**

**Diagnosis**
- **Echocardiography**: confirmatory test (narrowing of aorta seen)
- **CXR**: posterior rib notching (d/t increased intercostal artery collateral flow), **3 sign** (narrowed aorta looks like the notch of a number 3
- **ECG**: left ventricular hypertrophy
- **Angiography**: gold standard

**Management**
- **Corrective surgery or transcatheter-based intervention** (eg. Balloon angioplasty w/ or w/out stent placement) preferably in early childhood (between 2 and 4 years)
- Emergent surgical repair performed in cases of circulatory shock, cardiomegaly, severe HTN, severe CHF
- **Prostaglandin E1 (Alprostadil) preoperatively** to stabilize the condition – maintains a patent ductus arteriosus, reducing symptoms @ improves lower extremity blood flow
- Untreated? Most adults die by 50 y/o d/t aortic rupture, CVA, or aortic dissection

**General Measures**
- Rule out COA in a young adult with HTN

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### Tetralogy of Fallot

**Pathophysiology**
- Constellation of: 1) pulmonary stenosis (RV outflow obstruction) 2) RV hypertrophy 3) large unrestrictive VSD 4) overriding aorta
- **MC cyanotic congenital heart disease** (associated with a right-to-left shunt d/t pulmonary stenosis)
- **Risk factors**: genetic & environmental factors – associated with chromosome 22 deletion

**Clinical Manifestations**
- **Infancy**: cyanosis most common presentation (blue baby syndrome)
  - Tet spells relieved with putting knees to chest in infancy
  - **Older children**: exertional dyspnea, cyanosis that worsens with age
  - **Tet spells** – paroxysms of cyanosis **relieved with squatting** (squatting decreases right-to-left shunting, improving oxygenation); develop during crying/feeding
- **Physical exam**: **harsh systolic murmur @ left mid to upper sternal border (VSD), right ventricular heave (RVH)**, digital clubbing, cyanosis

**Diagnosis**
- **Echocardiogram**: test of choice
- **CXR**: boot-shaped heart (d/t prominent right ventricle)
- **EKG**: RVH, right atrial enlargement – check QRS width annually to reduce sudden cardiac death risk

**Management**
- **Surgical repair** – ideally in first 4-12 months of life
- **Prostaglandin infusion prior to surgery to maintain a patent ductus arteriosus** – improve circulation
- **Prophylaxis** for bacterial endocarditis

**Complications**
- **MC causes of death** are sudden cardiac death & heart failure
- Complications after surgery: arrhythmias, pulmonary regurgitation, residual outflow obstruction, heart failure

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### Hypertrophic cardiomyopathy

*Autosomal dominant genetic disorder of inappropriate LV&/or RV hypertrophy with diastolic dysfunction*
Pathophysiology

- **MCC of sudden cardiac death in young athletes in the US**
- Subaortic outflow obstruction due to asymmetrical septal hypertrophy & systolic anterior motion of the mitral valve
- The obstruction worsens with:
  1. increased contractility (exercise, Digoxin, beta agonists)
  2. decreased LV volume (dehydration,Valsalva, decreased venous return)

Clinical Manifestations

- **Dyspnea** most common symptom, fatigue, angina, presyncope, syncope, dizziness, arrhythmias (may be asymptomatic initially)
- **Sudden cardiac death**, especially in adolescent & preadolescent children during times of extreme exertion usually d/t Vfibb
- Medium-pitched harsh mid-systolic crescendo-decrescendo murmur heard @ left sternal border;
  - Increased murmur intensity with decreased venous return (Valsalva, standing) or decreased afterload (Amyl nitrate)
  - Decreased murmur intensity with increased venous return (squatting, supine, leg raise) or increased afterload (handgrip)
  - Increased LV volume preserves outflow
- May have loud S4 gallop w/ apical lift, mitral regurgitation, S3, or pulsus bisferiens

Diagnosis

- **Echocardiography**: asymmetric ventricular wall thickness (especially septal) 15mm+, systolic anterior motion of mitral valve, & small LV chamber size
- **EKG**: left ventricular hypertrophy, anterolateral & inferior pseudo q waves, enlarged atria

Management

- Focus on early detection, medical tx, surgical tx, & or ICD placement
- **Medical**: beta blockers 1st line medical management
- **Surgical**: Myomectomy usually performed in young patients refractory to medical therapy
- **Alcohol septal ablation**: an alternative to surgical myomectomy
- Consider an implantable cardioverter-defibrillator for patients with syncope or sudden cardiac arrest

General Measures

- Patients should avoid dehydration, extreme exertion, and exercise. Cautious use of Digoxin, Nitrates & diuretics (Digoxin ↑ contractility, nitrates & diuretics ↓ LV volume)

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**Ventricular Septal Defect**

*Hole in the ventricular septum, assoc. w/ left-to-right shunt*

Pathophysiology

- MC type of congenital heart disease in childhood
- Small to moderate associated w/ a left to right shunt
- Large (unrestricted) defects may eventually develop a right to left shunt – **Eisenmenger syndrome**

Types

- **Perimembranous**: most common type – hole in the LV outflow tract near the tricuspid valve
- **Muscular**: usually multiple holes in a “swiss cheese” pattern
- **Inlet (posterior)**: located posterior to the septal leaflet of the tricuspid valve
- **Supracristal (outlet)**: beneath the pulmonic valve, may have aortic valve insufficiency

Clinical Manifestations

- Small (restrictive): asymptomatic or mild symptoms, normal pressure differences between the ventricles are maintained; usually asy @ birth & develop syx after a few weeks
- Moderate: excessive sweating or fatigue, especially during feeds, lack of adequate growth, frequent respiratory infxs
- Large (unrestricted): severe symptoms, no pressure difference between the ventricles
- **Eisenmenger syndrome**: right-to-left shunt occurring w/ large (unrestricted) VSDs

Physical Examination

- **High-pitched harsh holosystolic murmur** best heard @ lower left sternal border
- Smaller VSDs usually louder & associated w/ more palpable thrills than larger ones
- May be associated w/ a thrill or diastolic rumble @ the mitral valve

Diagnosis

- **Echocardiography**: determines the size & location of VSD, echocardiogram preferred over catheterization
- **EKG**: LVH in mild to moderate disease, combines RVH + LVH (Katz-Wachtel phenomenon)
- **Chest radiograph**: may be normal, show left atrial enlargement or right ventricular hypertrophy

Management

- **Observation**: in small, symptomatic VSDs (must close within 12 months)
- **Patch closure**: symptomatic infants or uncontrolled CHF, growth delay, recurrent respiratory infections
**Kawasaki Disease – aka mucocutaneous lymph node syndrome**

Medium & small vessel necrotizing vasculitis including the coronary arteries

**Pathophysiology**
- Mucocutaneous vasculitis d/t vessel wall infiltration w/ mononuclear cells & later IgA secreting plasma cells → destruction of tunica media & formation of aneurysms
- Unknown cause: increased risk with advanced maternal age, mother of foreign birth, group B strep, early infancy hospitalization d/t infx for bacterial cause, an unidentified respiratory agent/viral pathogen with propensity towards vascular tissue

**Risk factors**
- Children (especially under 5), boys, & Asians (highest risk)

**Clinical Manifestations**

*Warm + CREAM* = Fever >5 days + 4 out of 5 of the following:
- Conjunctivitis
- Rash (erythematous or morbilliform or macular)
- Extremity changes: edema, erythema, or desquamation of palms & soles; Beau’s lines (transverse nail grooves), arthritis
- Adenopathy (cervical)
- Mucositis: strawberry tongue, lip swelling, fissures, pharyngeal erythema

**Diagnosis**
- Labs: nonspecific – elevated WBC and platelet count, anemia, increased ESR & CRP, sterile pyuria
- EKG & echocardiogram: recommended to look for complications

**Management**
- IV immunoglobulin + aspirin for fever, joint pain, & prevention of coronary complications; Recurrent: 2nd dose IVIG + CS x 3d

**Complications**
- **Coronary vessel arteritis: coronary artery aneurysm** (20% of pts not given tx), MI, pericarditis, myocarditis

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**Syncope**

*Sudden, brief loss of consciousness with loss of postural tone followed by spontaneous revival*

**Pathophysiology**
- Most syncope results from **insufficient cerebral blood flow**
  - Most deficiencies in cerebral blood flow result from **decreased cardiac output** (CO) which can be caused by:
    - Cardiac disorders that obstruct outflow, disorders of systolic or diastolic dysfunction, or arrhythmias
  - Some cases involve inadequate flow but with insufficient cerebral substrate (O2, glucose, or both) – CNS requires O2 & glucose to function & a deficit in either will cause LOC (usually hypoglycemia is cause)
  - Conditions that decrease venous return:
    - Outflow obstruction exacerbated by exercise, vasodilation, & hypovolemia (aortic stenosis, hypertrophic cardiomyopathy)
    - Arrhythmias cause syncope when HR is too fast to allow adequate filling or too slow to provide adequate output
    - Hemorrhage, increased intrathoracic pressure, increased vagal tone, loss of sympathetic tone (all of these except hemorrhage is termed vasovagal (aka neurocardiogenic) and is common & benign)
    - Orthostatic hypotension
    - Cerebrovascular disorders (strokes, TIA)
- **MC causes are: vasovagal, or idiopathic**

**Clinical Manifestations**
- Patient is motionless & limp, usually has cool extremities, weak pulse & shallow breathing
- May have brief involuntary muscle jerks occur, resembling a seizure

**Diagnosis**
- Depends on a careful history, eyewitness accounts, or fortuitous exams during the event
- Testing done includes: EKG, pulse ox, sometimes echo or tilt table testing, blood tests, CNS imaging is rarely indicated

**Management**
- Identify & fix the underlying cause

**General Measures**
- Seizures can cause sudden LOC but are not considered syncope – however, must consider in patients presenting with apparent syncope because hx may be unclear & some seizures do not cause tonic-clonic seizures
- Sometimes a brief (under 5 second) seizure occurs with true syncope
- **Red flags suggest a more serious etiology**: syncope during exertion, multiple recurrences within a short time, older age, heart murmur or other findings suggesting structural heart disease, injury during syncope, FHx of sudden unexpected death

---

**GASTROINTESTINAL – 10%**

**Appendicitis**

*Obstruction of the lumen of the appendix, resulting in inflammation & bacterial overgrowth*

**Etiology**
• **Fecalith & lymphoid hyperplasia most common**, inflammation, malignancy or foreign body
  • Lymphoid hyperplasia due to infection = MCC in children
  • MC age 10-30, MCC of acute abdomen in children 12-18, perforation rate highest in young children

**Clinical Manifestations**

- **Classic presentation:** anorexia & periumbilical or epigastric pain followed by RLQ abdominal pain (12-18 hours), N & V (vomiting usually occurs after the pain)
  - Pts w/ a retrocecal appendix may have an atypical pattern (diarrhea), & (+) rectal/gyn exam – appendix may also be pelvic
  - Appendiceal inflammation stimulates nerve fibers around T8-T10, causing vague periumbilical pain
  - Once the parietal peritoneum becomes irritated, it radiates to right lower quadrant
  - Rebound tenderness, rigidity & guarding – retrocecal appendix may have atypical findings
  - Tests for appendicitis:
    - **Rovsing sign:** RLQ pain w/ LLQ palpation
    - **Obturator sign:** RLQ pain with internal & external hip rotation with flexed knee
    - **Psoas sign:** RLQ pain with right hip flexion/extension (raise leg against resistance)
    - **McBurney’s point tenderness:** point 1/3 the distance from the anterior sup. iliac spine & navel

**Diagnosis**

- In adults: CT scan is the preferred imaging of choice & is more sensitive in confirming dx
  - In children: U/S image of choice → surgical consult obtained prior to imaging to determine if it is needed
  - Leukocytosis (10-20,000/uL), if higher: – suspect perforation & peritonitis; ~see microscopic hematuria & pyuria

**Management**

- Appendectomy (laparoscopic preferred when possible) – give a 3rd generation cephalosporin preoperatively
- Appendix perforated? Continue abx postoperatively

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**Colic**

*Frequent complex of paroxysmal abdominal pain & severe crying*

- Usually seen in infants under 3 months old, unknown etiology

**Clinical Manifestations**

- Sudden onset of loud crying (paroxysms may persist for several hours) with facial flushing & circumoral pallor
- Abdomen is distended, tense – legs drawn up
- Temporary relief with passage of feces or flatus

**Diagnosis**

- Clinical

**Management**

- No single treatment provides satisfactory relief – improve feeding techniques (burping), avoid over/underfeeding
- Careful exam is important to rule out other causes
- Resolves spontaneously with time

---

**Constipation**

- 2 of the following: Infrequent bowel movements (<2/week), straining, hard stools, feelings of incomplete evacuation, use of digital maneuvers, sensation of anorectal obstruction/blockage w/ 25% of BMs
  - Above must be fulfilled for last 3 months with symptom onset 6 months prior to diagnosis

**Etiology**

- Disordered movement of stool through colon/anus/rectum (usually proximal GI tract is intact)
- Slow colonic transit: idiopathic, motor disorders (colorectal cancer, DM, hypothyroid), adverse effects of drugs (Verapamil, opioids) – Outlet delay: Hirschsprung’s disease

**Clinical Manifestations**

- Bloating, abdominal pain, straining & pain with BM
- On physical exam: assess rectum for hard stool, masses, anal fissures, hemorrhoids, sphincter tone, push effort, prostatic hypertrophy in males, posterior vaginal masses in females

**Diagnosis**

- Lab testing: CBC, CMP. TSH to identify secondary causes

**Management**

- **Fiber** – increase to 20-25 grams per day. Add water & exercise
  - MOA: retains water & improves GI transit
- **Bulk forming laxatives:** Psyllium, Methylcellulose, Polycarbophil, Wheat dextran
  - **MOA:** absorbs water & increases fecal mass – ↑ frequency & softens the stool consistency w/ minimal effects
  - Dietary fiber + bulk forming laxatives the most physiologic & effective approach to constipation
  - **Adverse effects:** flatulence, bloating
- **Osmotic laxatives:** polyethylene glycol (PEG), lactulose, sorbitol, saline laxatives (milk of magnesia, magnesium citrate)
  - **MOA:** causes H2O retention in the stool (osmotic effect pulls H2O into gut)
• **Adverse effects:** flatulence & bloating
• Lactulose: Synthetic disaccharide (sugar) not absorbed (pulls water into gut), also used in hepatic encephalopathy
• Sorbitol: Synthetic sugar
• Saline laxatives – adverse: hypermagnesemia (especially with chronic renal disease)

**Stimulant laxatives:** Bisacodyl, Senna

• **MOA:** increases acetylcholine-regulated GI motility (peristalsis) & alters electrolyte transport in the mucosa
• **Adverse:** diarrhea, abdominal pain

---

**Dehydration**

*Body fluid depletion d/t poor intake or excessive loss (vomiting, diarrhea) leading to hypovolemia & affecting each organ system*

**Clinical Manifestations**

<table>
<thead>
<tr>
<th>% Body weight loss</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Consolable</td>
<td>Irritable</td>
<td>Lethargic/obtunded</td>
</tr>
<tr>
<td>Heart rate</td>
<td>Regular</td>
<td>Increased</td>
<td>More increased</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Normal/low</td>
<td>low</td>
</tr>
<tr>
<td>Urine</td>
<td>Normal</td>
<td>Reduced</td>
<td>None</td>
</tr>
<tr>
<td>Skin turgor</td>
<td>Normal</td>
<td>Tenting</td>
<td>None</td>
</tr>
<tr>
<td>Anterior fontanelles</td>
<td>Flat</td>
<td>Soft</td>
<td>Sunken</td>
</tr>
<tr>
<td>Capillary refill</td>
<td>Less than 2 seconds</td>
<td>2-3 seconds</td>
<td>3+ seconds</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Moist</td>
<td>Dry</td>
<td>Parched/cracked</td>
</tr>
</tbody>
</table>

**Diagnosis**

• Clinical

**Management**

• Goal: rapidly expand ECF volume & restore tissue perfusion, replenish fluid & electrolyte deficits, meet patient’s nutritional needs & replace ongoing losses

---

**Duodenal Atresia**

*Complete absence or closure of a portion of the duodenum, leading to a gastric outlet obstruction*

**Risk Factors**

• Polyhydramnios (increased amniotic fluid), Down syndrome
• Associated with other congenital defects

**Clinical Manifestations**

• **Neonatal intestinal obstruction:** shortly after birth (within 1st 24-48 hours of life) with bilious vomiting (may be nonbilious), abdominal distention
• Associated anomalies include: malrotation, esophageal atresia, congenital heart disease

**Diagnosis**

• Abdominal XR: **double bubble sign** (distended air-filled stomach + smaller distended duodenum separated by the pyloric valve)
• Upper GI series: often performed preoperatively to assess the GI tract

**Management**

• Decompression of the GI tract, electrolyte and fluid replacement
• Duodenoduodenostomy = definitive management

---

**Encopresis**

• Repeated passage of feces into inappropriate places (clothing or floor) whether involuntary or intentional
• Individual must be at least 4 years old, & one such event must occur once a month x3 months

**Etiology**

• Anxiety about defecating in a particular place – a more generalized anxiety in response to stressful environmental factors
• Oppositional behavior
• Physiologic conditions – lack of sphincter control, constipation with overflow incontinence

**Epidemiology**

• Incidence decreases with age, M>F, 1% prevalence in 5 y/o child
• Associated with other conditions such as conduct disorder & ADHD

**Management**

• Enlist child in cure, positive reinforcement – do not punish
• Older children should participate in cleaning up
• Timed bowel movements, if related to constipation give stool softeners, psychotherapy, family therapy, & behavioral therapy
• Perform a psychosocial evaluation and treat according to specific causative factors

**General Measures**

• R/o influence of a medication or a general medical condition (hypothyroidism, lower GI problems, dietary factors)

<table>
<thead>
<tr>
<th>Foreign body ~ GI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathophysiology</td>
</tr>
<tr>
<td>• Ingestions are often <strong>unwitnessed</strong> &amp; a child may not develop symptoms</td>
</tr>
<tr>
<td>• MC in children 6 months – 3 years</td>
</tr>
<tr>
<td>• Usually radio-opaque objects – coins, screws, buttons, batteries, small toys; aspiration of gastric contents, inert material, toxic material or poorly chewed food</td>
</tr>
</tbody>
</table>

**Clinical Manifestations**

• Degree of injury depends on the substance
• Choking, coughing, wheezing, hemoptysis
• Once beyond the esophagus, objects **typically pass** but with **an increased risk of complications** such as bowel obstruction, perforation, erosion to adjacent organs – abdominal pain, N/V, fever, hematochezia, melena
• Common obstruction locations: cricopharyngeal, middle 1/3 of esophagus, LES, pylorus, ileocecal valve

**Diagnosis**

• Radiographs: chest, neck, upper abdomen – regional hyperinflation caused by check valve effect
  • Normal CXR doesn’t exclude FB object
  • CXR: may show radio-opaque foreign bodies, obstructive hyperinflation (asymmetric), collapse/atelectasis, normal
• Bronchoscopy indicated for all patients with a suspected inhaled foreign body (consider radiolucent)

**Management**

• Object is in the esophagus
  • **Observe for 24 h** w/ serial XR & **remove endoscopically** if *object doesn’t pass distally* within that time-frame
  • **If the object causes symptoms or time-point of ingestion is unknown** attempt **immediate endoscopic removal**
  • If the ingested item appears relatively benign & has already progressed inferior to the diaphragm on imaging, **observe and wait for spontaneous passage**
  • **If the ingested object is sharp** then **remove immediately with endoscopy**
  • **Batteries** in esophagus have the potential to cause **severe tissue damage** & should be **removed immediately with endoscopy**
    • Consider using a Foley catheter to remove retrograde from esophagus or bougienage to pass the object distally into the stomach
• Object distal to the esophagus (in stomach MC)
  • Symptomatic: **remove immediately w/ endoscopy**
  • Asymptomatic:
    • **Small blunt object** - follow with serial XR; **remove endoscopically** if *it doesn’t advance past pylorus in 3-4 w*
    • **Large object (> 3 cm)** - beyond pylorus? **monitor** with serial imaging; in stomach? **remove endoscopically**
    • **Sharp object** - before pylorus? **remove endoscopically**; beyond pylorus? monitor with serial imaging & remove if no progress for 3 days
  • **Always remove button/disc batteries ASAP** for their risk of causing corrosive burns or tissue damage to GI tract (unless already passed through pylorus)
  • If an **acid/alkali** is ingested: do NOT induce emesis, monitor ABCs, endoscopy 2-3 weeks later to assess damage

**Complications**

• Asphyxia, pneumonia, acute gastric aspiration

**Gastroenteritis**

**NONINVASIVE (ENTEROTOXIN) INFECTIOUS DIARRHEA**

• Noninvasive: vomiting, watery, voluminous (involves small intestine), no fecal WBCs or blood

**Norovirus Gastroenteritis**

• Most common overall cause of gastroenteritis in adults in N. America & MC cause of viral GE worldwide
• Peak incidence in Winter but can occur at any time

**Transmission**

• Fecal-oral route, contaminated food & water, fomite contamination
• Often associated with outbreaks – **cruise ships**, hospitals, restaurants

**Clinical Manifestations**

• 24-48 hour incubation period, symptoms last 2-3 days
• **Vomiting predominant symptom** – nausea, non-bloody diarrhea that lacks mucus & fecal leukocytes (noninvasive), generalized symptoms

**Management**

• Fluid replacement
**Rotavirus Gastroenteritis**
- Most common in young unimmunized children between 6 months – 2 years of age

**Transmission**
- Fecal-oral route, incubation period under 48 hours

**Clinical Manifestations**
- Children: vomiting, nonbloody diarrhea & fever
- Adults: symptoms usually less severe

**Diagnosis**
- PCR Testing

**Management**
- Oral rehydration is mainstay of treatment

**Staphylococcus Aureus Gastroenteritis**
- Infection due to heat-stable enterotoxin B, IP within 6 hours

**Transmission**
- Food contamination most common source (dairy, mayo, meat, egg, salad) especially @ room temperature

**Clinical Manifestations**
- Prominent vomiting & nausea, abdominal cramps are the usual symptoms
- Fever, headache & diarrhea are seen in a small amount of cases

**Management**
- Fluid replacement (oral preferred), IV if unable to tolerate oral

**Bacillus Cereus Gastroenteritis**
- Enterotoxin that can survive reheating, IP within 6 hours

**Transmission**
- Food contamination (fried rice)

**Clinical Manifestations**
- Prominent vomiting & nausea, abdominal cramps are the usual symptoms
- Fever, headache & nonbloody diarrhea are seen in a small amount of cases

**Management**
- Fluid replacement (oral preferred), IV if unable to tolerate oral

**Enterotoxin E. Coli Gastroenteritis**
- MCC of **traveler’s diarrhea**

**Transmission**
- Contaminated food & water – contaminated water includes unpeeled fruits washed in the water, untreated drinking water/ice produces heat-stable toxins & heat-labile toxins, IP 24-72 hours

**Clinical Manifestations**
- Abrupt onset of watery nonbloody diarrhea, abdominal cramping, vomiting

**Diagnosis**
- Gram-stain & cultures

**Management**
- Oral rehydration therapy first line, usually self-limiting
- Loperamide, bismuth subsalicylate
- Antibiotics: Tetracyclines first-line antibiotic if needed, fluoroquinolones, or macrolides – antibiotics may shorten the disease course in patients who are severely ill, other comorbid conditions, or with high fever
- Prevention: in areas where it is endemic, use bottled water, wash hands often, use chemical toilets, cook food through

**Vibrio Cholerae Gastroenteritis**
- Gram (-), comma-shaped rod transmitted via contaminated food & water – **shellfish**
- Outbreaks may occur during poor sanitation & overcrowding conditions (especially abroad)

**Pathophysiology**
- Exotoxin causes a secretory diarrhea (inhibition of water, sodium & chloride absorption) which may cause profound dehydration & hypovolemia

**Clinical Manifestations**
- Vomiting, abdominal pain, borborygmi, cramping & copious watery diarrhea = “rice water stools” (gray with flecks of mucus & has a “fishy odor” but no fecal odor, blood or pus)

**Diagnosis**
- Clinical diagnosis, stool cultures, PCR rapid testing

**Management**
- Oral rehydration therapy & electrolyte replacement = mainstay of treatment (self-limited)
Gram-negative rods transmitted via raw or undercooked shellfish consumption and seawater (direct contact of water with wounds or shucking oysters), especially during warm summer months

- *V. parahaemolyticus*: gastroenteritis
- *V. vulnificus*: gastroenteritis, necrotizing fasciitis, cellulitis – MCC of death from seafood consumption in US

**Risk Factors for Bacteremia**

- Underlying liver disease (cirrhosis, alcoholism, hemochromatosis)
- Immunocompromised (DM)

**Clinical Manifestations**

- Gastroenteritis: diarrhea, abdominal cramps, nausea, vomiting, fever
- Cellulitis: d/t exposure of wound to seawater or estuarine water
- Necrotizing fasciitis: hemorrhagic bullae & may rapidly progress to shock

**Diagnosis**

- Clinical, stool studies, wound & blood cultures

**Management**

- Gastroenteritis: rehydration therapy
- Cellulitis: tetracyclines
- Necrotizing fasciitis: emergent surgical debridement + broad-spectrum antibiotics

**Clostridioides Difficile Gastroenteritis**

- Spore-forming, toxin-producing gram-positive anaerobic bacterium

**Risk Factors**

- **Recent antibiotic use (Clindamycin), advanced age, gastric suppression therapy (PPI, H2 blockers)**

**Pathophysiology**

- Organism overgrowth secondary to alteration of the normal GI flora, most commonly seen after course of antibiotics (Anoxicillin in children) or chemotherapy – can be a healthcare associated infection

**Clinical Manifestations**

- Watery non-bloody diarrhea, abdominal cramps, fever & abdominal tenderness
- Complications include: pseudomembranous colitis, bowel perforation & toxic megacolon

**Diagnosis**

- C. difficile toxin (stool) – initial test of choice
- Leukocytosis
- Sigmoidoscopy in select patients: pseudomembranous

**Management**

- Discontinuing the offending antibiotic = initial step to management
- Contact precautions & hand hygiene (NO sanitizer – hands are resistant to killing by alcohol)
- Oral Vancomycin or oral Fidaxomicin = 1st line agents, Metronidazole = alternative
- 2nd recurrent CDI episode: pulse-tapered oral Vancomycin or Fidaxomicin
- Recurrent disease treated with metronidazole: oral Vancomycin
- Frequently recurrent disease (at least 3 recurrences) – fecal microbiota transplant

**INVASIVE INFECTIOUS DIARRHEA**

- **Invasive**: high fever, (+) blood & fecal leukocytes, not as voluminous (large intestine), mucus
- DO NOT give anti-motility drugs w/invasive diarrhea (may cause toxicity)
- Includes: Campylobacter, Shigella, Salmonella, Yersinia, Enterohemorrhagic E Coli, Campylobacter

**Yersinia Enterocolitica**

- Gram-negative coccobacillus with bipolar staining (“safety pin” appearance)
- Sources: contaminated port MC in the US, milk, water, & tofu

**Clinical Manifestations**

- Fever, abdominal pain mimics acute appendicitis (can cause mesenteric lymphadenitis, producing abdominal tenderness or guarding)

**Diagnosis**

- Cultures from stool, pharynx or mesenteric nodes

**Management**

- Fluid & electrolyte replacement mainstay of treatment
- Severe: Fluoroquinolones, Bactrim

**Campylobacter Enteritis**

- MCC of bacterial enteritis in the US, MC antecedent event in post-infectious Guillain-Barre syndrome
- MC affects children & young adults, IP = 3 days

**Sources:**
- Contaminated food – **raw or undercooked poultry** most common, raw milk, contaminated water, dairy cattle – puppies important source in children

**Clinical Manifestations**
- Fever, crampy periumbilical abdominal pain (may mimic acute appendicitis), nausea
- Diarrhea initially watery progressing to bloody

**Diagnosis**
- Stool culture: gram-negative, “S, comma or seagull shaped” organisms
- Enzyme immunoassay or PCR

**Management**
- Fluid & electrolyte replacement mainstay of treatment (usually mild & self-limiting w/ peak of illness lasting 24-48 hours)
- Severe or high-risk patients: Macrolides first-line antibiotic of choice when needed (Azithromycin/Erythro), fluoroquinolones, Doxycycline
- Loperamide & other anti-motility agents generally avoided in invasive diarrheas

**Prevention**
- Proper food handling & handwashing can prevent spread

→ **Enterohemorrhagic E. Coli O157:H7**

**Sources:**
- Ingestion of undercooked beef, unpasteurized milk or apple cider, day care centers & contaminated water
- Incubation period average 4-9 days

**Pathophysiology**
- Shiga-like toxin (verotoxin) causes endothelial damage, leading to hemorrhage
- MC seen in children & elderly

**Clinical Manifestations**
- Watery diarrhea early on before becoming bloody, crampy abdominal pain, vomiting, fever usually absent/low-grade

**Management**
- Fluid replacement mainstay of treatment & supportive measures, avoid anti-motility drugs → ↑ complications
- Avoid antibiotics in children d/t increased incident of hemolytic uremic syndrome (increased release of shiga-like toxins) (if abx needed, you would give Bactrim)

→ **Typhoid (Enteric) Fever**

- Diarrheal illness most caused by the gram-negative rod *Salmonella typhi* and *paratyphi*
- More common in children & young adults – IP 5-21 day

**Transmission**
- Fecal-oral, contaminated food or water
- History of travel to areas where sanitation is poor (South-Central Asia) or contact with carrier

**Pathophysiology**
- Crosses intestinal epithelium barrier through M cells overlying the lymphoid follicles of Peyer’s patches
- May colonize the gallbladder in chronic carriers

**Clinical Manifestations**
- Headache, intractable fever, chills, abdominal pain, constipation initially followed by non-bloody diarrhea (may be “pea-soup” green in color), malaise & anorexia
- Fever with relative bradycardia (classic but rare)
- Rose spots (faint pink or salmon-colored macular rash that spreads from trunk to extremities) occurs in 2nd week, abdominal tenderness
- Hepatosplenomegaly, GI bleeding, signs of dehydration, & delirium may be seen in later stages

**Diagnosis**
- Culture of the stool &/or blood

**Management**
- Oral rehydration & electrolyte replacement first-line management, antibiotics often given

→ **Nontyphoidal Salmonella**

- Other Salmonella species (*S enteriditis, typhimurium*)
- One of the MCC of foodborne disease in US (**poultry and pork, eggs, milk products, fresh produce**) & contacts w/ reptiles
- Incubation period 8-72 hours

**Clinical Manifestations**
- N, V, fever, abd cramping, diarrhea (may be “pea soup” brown-green in color or may be bloody), malaise, HA

**Diagnosis**
- Stool cultures

**Management**
- Oral rehydration & electrolyte replacement therapy mainstay of treatment, usually self-limited
**Antibiotics**: Fluoroquinolones first-line when needed (severe disease)

**Shigellosis**
- Diarrheal illness MCC by gram (-) rods – *Shigella sonnei* (MC in US), *flexneri & dysenteriae* (produces most toxin)

**Pathophysiology**
- *S. dysenteriae* produces a “Shiga” enterotoxin that is neurotoxic, cytotoxic, and enterotoxic

**Transmission**
- Fecal-oral contamination, ingestion of contaminated food or water
- **Highly virulent**, incubation period 1-7 days

**Clinical Manifestations**
- Lower abdominal pain, abdominal cramps, high fever, tenesmus, **explosive watery diarrhea** that progresses to **mucoid & bloody diarrhea**
- Neurologic manifestations especially in young children (**febrile seizures**)
- Complications: reactive arthritis (Reiter syndrome), hemolytic uremic syndrome (esp children), & toxic megacolon

**Diagnosis**
- Stool cultures, positive fecal WBCs & RBCs
- CBC: **Leukemoid reaction** (WBC 50,000+)
- Sigmoidoscopy: punctate areas of ulceration

**Management**
- **Oral rehydration & electrolyte replacement therapy** mainstay of treatment,
- In general, anti-motility drugs should be avoided (can worsen the illness d/t retained toxins)
- Antibiotics indicated if severe: Fluoroquinolones, 3rd gen cephalosporins, azithromycin, Bactrim are options

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**DO NOT USE ANTI-MOTILITY DRUGS IN BLOODY DIARRHEA** – ↑ likelihood of hemolytic uremic syndrome

- Diarrhea in poorly canned home foods, think: C. perfringens
- Diarrhea after drinking fresh mountain stream water: Giardia lamblia – incubates for 1-3 weeks, causes foul-smelling bulky stool that may wax and wane over weeks before resolving
- Aeromonas – prolonged diarrhea, use Bactrim for tx

**Gastroesophageal Reflux Disease**

**Pathophysiology**
- Reflux of gastric contents into the esophagus due to an **incompetent lower esophageal sphincter**
- **Transient relaxation of LES (incompetency)**  ➔ gastric acid reflux  ➔ esophageal mucosal injury

**Risk factors**
- Weight gain, fatty foods, caffeine or carbonated beverages, alcohol, tobacco smoke, drugs

**Clinical Manifestations**
- Typical: **heartburn (pyrosis) hallmark** – often retrosternal & postprandial, increased with supine position & may be relieved with antacids; regurgitation: water brash, sour taste in mouth, cough, sore throat
- Atypical symptoms: hoarseness, aspiration pneumonia, wheezing, chest pain
- **“Alarm” symptoms**: dysphagia, odynophagia, weight loss, bleeding

**Complications**
- 4 complications may present w/ alarm syx: esophagitis, stricture, barrett’s esophagus, esophageal adenocarcinoma

**Diagnosis of typical GERD**
- Clinical diagnosis based on history
- **24-hour ambulatory pH monitoring**: gold standard if confirmation is needed
- Esophageal manometry: decreased LES pressure

**Diagnosis of persistent symptoms or alarm symptoms**
- **Endoscopy**: first-line diagnostic test if persistent symptoms or complication of GERD is suspected

**Management**
- **Lifestyle modifications**: elevate head, avoid recumbency 3 hours after eating, avoid foods that delay gastric emptying (fatty/spicy food, chocolate, peppermint, caffeine), smoking cessation, decreased alcohol intake, weight loss
- **Stage 2**: intermittent/mild (under 2 episodes/week) – “as needed” pharmacologic therapy – antacids & H2 receptor antagonists
- **Stage 3**: PPI in moderate to severe disease (2+ episodes/week)
- Nissen fundoplication in medication-refractory patients

- Patients with typical symptoms of GERD given a trial of therapy

---

**Autoimmune Hepatitis**

*Idiopathic chronic inflammation of the liver d/t circulating autoantibodies, MC in young women*

**Clinical Manifestations**
• Asymptomatic, nonspecific symptoms (fatigue, nausea, malaise, abdominal pain, arthralgia)
• Physical exam: may be normal – hepatosplenomegaly & jaundice

**Diagnosis**
• Autoantibodies: Type I: **positive ANA, smooth muscle antibodies**, Type II: anti-liver/kidney microsomal antibodies, increased IgG
• LFTs: hepatocellular pattern (increased ALT 1000+)
• Liver biopsy: definitive diagnosis – bridging necrosis or multiacinar necrosis

**Management**
• Corticosteroids, CS + Azathioprine, or 6-Mercaptopurine

**Complications**
• Cirrhosis, pericarditis, myocarditis, proliferative glomerulonephritis, uveitis

---

**Acute Viral Hepatitis**

**Clinical Manifestations**
• Prodromal phase: malaise, arthralgia, fatigue, URI symptoms, anorexia, **decreased desire to smoke**, N/V, abdominal pain, loss of appetite, alcoholic stools; Hepatitis A is associated with a spiking fever
• Icteric phase: **jaundice** (most don’t develop this time), if present, jaundice usually develops once the fever subsides
• Fulminant: **encephalopathy, coagulopathy**, hepatomegaly, jaundice, edema, ascites, asterixis, hyperreflexia

**Diagnosis**
• Increased ALT & AST (both usually 500+ if acute, under 500 if chronic) – may have hyperbilirubinemia

**Management**
• Clinical recovery usually within 3-16 weeks, 10% HBV & 80% HCV become chronic
• **Chronic hepatitis**: disease 6 months+ duration – only HBV, HCV, HDV associated with chronicity, chronic may lead to end stage liver disease or hepatocellular carcinoma (HCC)
• **Fulminant**: encephalopathy, coagulopathy, jaundice, edema, ascites, asterixis, hyperreflexia

---

**Fulminant Hepatitis**

**Acute hepatic failure in patients with hepatitis**

**Etiology**
• Acetaminophen toxicity most common in the US
• Viral hepatitis, autoimmune hepatitis, drug reactions (Tolcapone), sepsis
• **Reye Syndrome**: fulminant hepatitis in children given ASA after a viral infection

**Clinical Manifestations**
• **Encephalopathy**: vomiting, coma, AMS, seizures, asterixis (flapping tremor of the hand with wrist extension), hyperreflexia, cerebral edema, increased ICP
• **Coagulopathy**: increased PT, INR 1.5+, & eventually increased PTT d/t hepatic production of coagulation factors
• Hepatomegaly, jaundice (not usually seen in Reye syndrome)
• **Reye Syndrome**: may develop rash (hands & feet), intractable vomiting, liver damage, encephalopathy, dilated pupils with minimal response to light & multi-organ failure

**Diagnosis**
• Combination of symptoms, hepatic encephalopathy, abnormal LFTs, and increased INR 1.5 or greater
• **Hypoglycemia common** (d/t hepatic gluconeogenesis), increased ammonia (encephalopathy)
• Labs to look for cause (Acetaminophen levels, viral serologies)

**Management**
• Supportive: IV fluids, electrolyte repletion, Mannitol if ICP elevation, PPI stress ulcer prophylaxis
• Active bleeding coagulopathy? Blood products of platelets or cryoprecipitate
• **Definitive**: liver transplant

---

**Hepatitis A - RNA**

**Acute viral infection of the liver due to HAV infection, usually a mild acute illness w/ recovery in a few weeks**

**Transmission**
• Fecal-oral (similar to HEV) – fecal contaminated food & water, especially with **international travel** (Asia), close contact w/ an infected individual, day care workers, men who have sex with men, homeless, shellfish, illicit drug use

**Clinical Manifestations**
• Most patients asy or mildly syx – may be associated with **spiking fever**
• Malaise, anorexia, nausea, vomiting, abdominal pain – RUQ
• **Physical examination**: jaundice, hepatomegaly

**Diagnosis**
• LFT: elevated AST, ALT, bilirubin
• **Acute**: IgM anti-HAV
• Past exposure: IgG HAV Av with negative IgM
**Management**
- **No treatment needed** (self-limiting infection similar to HEV)
- Not usually associated with a chronic state (like HEV), fulminant is rare

**Prevention**
- **Handwashing & improved sanitation greatest impact to reduce transmission**, food safety, immunization

**Preexposure Prophylaxis**
- Increased risk of HAV infection – give 2 doses 6 months apart
- HAV vaccination for international travelers 6 months of age or older

**Postexposure Prophylaxis**
- **Healthy individuals 1-40 years old**: HAV vaccine **preferred over immunoglobulin** (within 2 weeks of exposure)
- **Healthy individuals 40 + y/o**: HAV vaccine (w/ or w/out immune globulin) rather than IG alone (within 2w exposure)
- **Immunocompromised/chronic liver disease 1+ y/o**: HAV vaccine + HAV immunoglobulin (within 2w exposure)

**General Measures**
- Contagious until 1 week of jaundice; once exposed they have lifelong immunity

---

**Hepatitis E – RNA**

**Transmission**
- Fecal-oral (similar to HAV) – fecal contaminated food & water, blood transfusions, **mother-to-child transmission**

**Clinical Manifestations**
- Most patients are asy or mildly syx
- Malaise, anorexia, nausea, vomiting, fever, abdominal pain
- **Physical examination**: jaundice, hepatomegaly
- Increased risk of fulminant hepatitis in pregnant women, malnourished, or patients with preexisting liver disease

**Diagnosis**
- **LET**: elevated AST, ALT, bilirubin
- **Acute**: IgM anti-HEV

**Management**
- **No treatment needed** (self-limiting infection similar to HAV), not associated with chronic state (like HAV)
- **Highest mortality d/t fulminant hepatitis during pregnancy**, especially during 3rd trimester

---

**Hepatitis D**

*Defective virus that requires Hepatitis B virus antigen to cause co- or superimposed infection*

**Pathophysiology**
- HDV uses the HBsAg as its envelope protein – HDV has a direct cytopathic effect – more severe hepatitis & faster progression to cirrhosis

**Transmission**
- Primarily parenteral (exposure to blood or blood products)

**Clinical Manifestations**
- Most are asymptomatic – fatigue, myalgia, nausea, RUQ pain, jaundice, dark urine, clay-colored stools

**Diagnosis**
- **Screening**: total anti-HDV confirmed by immunohistochemical staining of liver biopsies for HDAg or RT-PCR assays for HDV RNA in serum
- Also perform Hepatitis B serology

**Management**
- No FDA approved management
- Interferon alpha has been used in management of chronic HDV
- Definitive: liver transplant

**General Measures**
- **Prevention**: Hep B vaccination

---

**Hepatitis C – RNA**

**Transmission**
- **Parenteral**: IV drug use MC in US, needlestick injuries, increased risk if blood transfusion before 1992
- Sexual or perinatal not common, not associated with breastfeeding (unless in a child presenting w/ HCV)

**Clinical Manifestations**
- Most asyx
- **Acute**: fatigue, myalgia, nausea, RUQ pain, jaundice, dark urine, clay-colored stools

**Diagnosis**
• **Screening test**: anti-HCV antibodies usually becomes (+) within 6 weeks, does NOT imply recovery (may become negative after recovery), increased LFTs
• **Confirmatory**: HCV RNA quant more sensitive than HCV antibody (may be (+) in pts with negative ab testing) – HCV RNA best way to determine viral replication activity
• **Genotyping**: most effective to determine effective treatment options

**Management**
- The newer regimens all have nearly equal efficacy (95%+ cure rate within 12 weeks of oral therapy) – response to tx determined by PCR-RNA viral load at 12 & 24 weeks after therapy; Options:
  - Ledipasvir-Sofosbuvir, Ekbasvir-Grazoprevir, Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir +/- Ribavirin, Simeprevir or Daclatasvir + Sofosbuvir
  - Older regimen: Pegylated interferon alpha 2b + Ribavirin
  - AE Interferon: psychosis, depression, thrombocytopenia, leukopenia, arthralgias
  - AE Ribavirin: anemia

**General Measures**
- **85% of patients with HCV develop chronic infection**
- MC infectious cause of chronic liver disease, cirrhosis, & liver transplantation in the US
- Some newer treatments may reactive Hepatitis B so perform HBV testing prior to treatment
- Increased risk of cirrhosis, hepatocellular carcinoma & liver failure

**Hepatitis B - DNA**

**Transmission**
- Percutaneous, sexual, parenteral, perinatal (maternal-fetal route)

**Clinical Manifestations of Acute**
- Most are asymptomatic, 3 possible states:
  - **Subclinical (anicteric)**: constitutional symptoms (malaise, arthralgia, fatigue, URI symptoms, N, V, abdominal pain, anorexia, decreased desire to smoke in smokers)
  - **Icteric**: Jaundice (only 30%)
  - **Fulminant**: acute hepatic failure (encephalopathy, coagulopathy, jaundice, edema, ascites)

**Clinical Manifestations of Chronic**
- **Chronic hepatitis**:
- **Chronic (carrier) state**: asymptomatic, normal LFTs, low viral load, & **undetectable HBsAg**

**Diagnosis**
- Hepatitis B serologies: HB surface antigen, surface antibody, and core antibody (see below)
- Chronic hepatitis = surface antigen positivity & failure to produce surface antibodies 6m+

<table>
<thead>
<tr>
<th>Marker</th>
<th>Meaning</th>
<th>Acute infection</th>
<th>Window period</th>
<th>Chronic infection</th>
<th>Remote infection (cleared)</th>
<th>Immunization</th>
<th>Inactive chronic carrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBcAb</td>
<td>Exposure</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Infection</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>HBsAb</td>
<td>Immunity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

**LFTs**: acute -AST & ALT in thousands range, chronic: ALT & AST in hundreds range or normal – increased bilirubin in icteric phase

**HBV DNA**: best way to assess viral replication activity

**Liver biopsy** can be used to determine extent of damage
Management of Acute HBV
  • Supportive = mainstay of treatment (majority of patients will not progress to chronic infection)

Management of Chronic HBV
  • Antiviral therapy may be indicated if persistent, severe symptoms, marked jaundice (bilirubin 10m+), inflammation on liver bx, increased ALT, or (+) HB envelop antigen persistence
    - Alpha-interferon 2b
    - Options: Entecavir, Tenofovir, Lamivudine (CHILD), Adefovir, Telbivudine
  • Treatment can be stopped after confirmation (2 consecutive tests 4 weeks apart) that the patient has cleared HBsAg

General Measures
  ➔ 3 step approach to Hepatitis B serologies
    1. Look @ surface antigen (NOT ANTIBODY) – if surface antigen is positive: acute OR chronic
    2. If surface antigen is (+), then look @ core antibody: If IgM is (+) = acute, if IgG is (+) = chronic
    3. Step 3 ONLY IF Surface Antigen negative – Now look at surface ANTIBODY –
      - If surface Ab is the only thing (+) = vaccinated
      - If core IgG is positive + surface Ab (+) = recovery (distant/resolved infx)

Hirschsprung Disease

Congenital megacolon d/t absence of ganglion cells, leading to a functional obstruction
  • MC in the distal colon & rectum; M>F 4:1, Down syndrome, Chagas disease, MEN II

Pathophysiology
  • Failure of complete neural crest migration leads to an absence of enteric ganglion cells (Auerbach & Meissner plexuses) which leads to failure of relaxation of the aganglionic segment & subsequent functional obstruction

Clinical Manifestations
  • Neonatal intestinal obstruction: meconium ileus (failure of meconium passage 48+ hours) in a full-term infant
    - Bilius vomiting, abdominal distention, no stool in rectal vault, failure to thrive
    - (Abdominal distention → decreased blood flow → deterioration of mucosal barrier → bacterial proliferation →..)
    - Enterocolitis: vomiting, diarrhea, signs of toxic megacolon (presents similar to sepsis)
    - Chronic constipation in older children with milder disease

Diagnosis
  • Contrast enema: transition zone (caliber change) between normal & affected bowel, also helpful for sx planning
  • Anorectal manometry: as a screening test (measures anal sphincter pressure); increased anal sphincter pressure & lack of relaxation of the internal sphincter with balloon rectal distention
  • Rectal biopsy: definitive, rectal suction biopsy usually performed with full thickness biopsy (need submucosa)
  • Abdominal XR: decreased or absence of air in rectum + dilated bowel loops

Management
  • Resection of the affected bowel segment

Toxic Megacolon

Nonobstructive, extreme colon dilation >6cm + signs of systemic toxicity

Etiology
  • Complications of IBD (UC), infectious colitis (C. difficile, CMV), ischemic colitis, volvulus, diverticulitis, radiation & obstructive colorectal cancer

Clinical Manifestations
  • Profound bloody diarrhea, abdominal pain & distention, N/V, tenesmus
  • Lower abdominal tenderness & distention
  • Signs of toxicity: AMS, tachycardia, hypotension, dehydration, & may have signs of peritonitis (rigidity, guarding, rebound tenderness)

Diagnosis
  • Initial imaging of choice: abdominal radiograph – evidence of colon 6cm+, can use CT to assess complications
  • 3 or more of the following:
    • Fever 38C+, Pulse 120+, Neutrophilic leukocytosis 10,500+/Ul, Anemia
    • Plus at least one: hypotension, dehydration, electrolyte abnormalities, AMS

Management
  • Mainstay: Supportive – bowel rest, bowel decompression w/ NG tube, broad-spectrum antibiotics (Ceftriaxone + Metronidazole), fluid & electrolyte replacement
  • Manage underlying cause (if UC = CS)

Inguinal Hernia

Indirect Inguinal Hernia
  • Type of inguinal hernia with bowel protrusion through the *internal inguinal ring* down the inguinal canal (may pass into the scrotum)
  • Often congenital & presents before 1 year old
• The origin of the sac is LATERAL to the inferior epigastric artery
• MC type of hernia in both sexes (M>F), young children & young adults

**Pathophysiology**

• Often congenital d/t a persistent patent process vaginalis, an increase in abdominal pressure may force the intestines through the internal ring into the inguinal canal & may follow the testicle tract into the scrotum

**Direct Inguinal Hernia**

• Type of inguinal hernia with bowel protrusion through the *external inguinal ring* (rarely enters the scrotum)
• The origin of the sac is MEDIAL to the inferior epigastric artery **within** Hesselbach's triangle
  • Hesselbach’s triangle (RIP) – *Rectus abdominis @ Medial border, *Inferior epigastric vessels @ lateral border, *Poupart’s (inguinal) ligament @ inferior border

**Pathophysiology**

D/t a weakness in the floor of the inguinal canal

**Clinical Manifestations of both Direct + Indirect**

• **Asymptomatic:** swelling/fullness at the hernia site, enlarges with increased intraabdominal pressure &/or standing. (Indirect: may develop scrotal swelling)
• **Incarcerated:** painful, enlargement of an irreducible hernia (unable to return the hernia contents back into the abdominal cavity), N & V if bowel obstruction present
• **Strangulated:** ischemic incarcerated hernias with systemic toxicity (irreducible hernia w/ compromised blood supply) – severe painful bowel movement (may refrain defection)

**Diagnosis** (both)

• Clinical, groin U/S often initial imaging of choice of an occult uncomplicated inguinal hernia
• Alternatives: CT/MRI

**Management** (both)

• Inguinal hernias often require surgical repair, Strangulated hernias are surgical emergencies

**Umbilical Hernia**

• Hernia through the umbilical fibromuscular ring – congenital (failure of umbilical ring closure) usually d/t loosening of the tissue around the ring in adults

**Management**

• Observation (usually resolves around 2 y/o), surgical repair indicated if 5 years+ to avoid incarceration/strangulation

**Intussusception**

*Telescop*ing (invagination) of a proximal intestinal segment into adjoining distal lumen ➔ bowel obstruction

**Risk factors**

• Children (2/3 seen between 6-18months), males, common after viral infections
• In adults: most always caused by a neoplasm
• **Lead points:** idiopathic MC, Meckel diverticulum, enlarged mesenteric lymph nodes, hyperplasia of Peyer’s patches, tumors, submucosal hematomas, foreign body

**Clinical Manifestations**

• **Classic triad:** vomiting + abdominal pain + passage of blood per rectum – “currant jelly” stools (stool mixed with blood + mucus), abdominal pain is colicky in nature occurring every 15-20 minutes
• Onset is sudden, child appears well between episodes (may appear lethargic)
• **Physical examination:** sausage-shaped mass in the right upper quadrant or hypochondrium + emptiness in the right lower quadrant (Dance’s sign) due to telescoping of the bowel

**Diagnosis**

• **Ultrasound:** best initial test – donut or target sign
• Abdominal radiograph: lack of gas in the bowels, “Crescent sign”/“Bull's eye/target sign/coiled spring lesion” representing layers of the intestine within the abdomen.
• **Air or contrast enema:** both diagnostic & therapeutic, air enema more commonly used than barium, especially if peritonitis is present – water-soluble contrast preferred over barium
Management

- Fluid & electrolyte replacement most important initial steps, followed by NG decompression
- Intussusception reduction: pneumatic (air) or hydrostatic (saline or contrast) decompression (air preferred), admit for observation (rule out occult perforation, 10% recurrence within 24 hours of treatment)
- Surgical resection if refractory to insufflation or if intestine has perforated

Neonatal Jaundice

Yellowish discoloration of the skin, sclera & conjunctiva due to elevated plasma bilirubin in a newborn

- Usually a transient 7 milk condition but in severe cases it may lead to kernicterus (cerebral dysfunction & encephalopathy)
- Physiologic jaundice presents on days 3-5 & bilirubin levels fall in about 50% of the neonates during the first week of life

Etiology

- Physiologic: transient decrease in UGT activity (UGT = enzyme that conjugates bilirubin)
  - Breastfeeding failure – caused by insufficient breast milk consumption (inadequate amounts of bowel movements to excrete bilirubin from the body)
  - Breast milk jaundice – infant liver is not mature enough to process lipids, occurs around 4th and 7th day of life (mom should keep breastfeeding)
- Pathologic: Crigler-Najjar syndrome, Gilbert syndrome, cretinism, hemolytic anemia, Dubin-Johnson syndrome
  - May occur in first 24 hours of life, persists 10-14+ days, bilirubin increases 5+mg/dL/day associated with a bilirubin over 12 in a term infant, conjugated bilirubin 2mg/dL+ or 20%+ of total bilirubin

Clinical Manifestations

- Jaundice: yellowing of skin, sclera & conjunctiva – in neonates, jaundice usually progresses from head to toe with increasing bilirubin levels, associated with bilirubin levels 5.0mg/dL +
- Kernicterus: cerebral dysfunction and encephalopathy due to bilirubin deposition in brain tissue – can manifest as seizures, lethargy, irritability, hearing loss, mental developmental delays – associated with bilirubin levels 20 mg/dL +

Diagnosis

- Bilirubin levels, Coombs test to distinguish between immune-mediated (ABO incompatibility) from non-immune-mediated hemolytic disorders, blood smear if hemolysis, LFTs, alkaline phosphatase

Management

- No management needed in physiologic jaundice
- Phototherapy = initial management of choice of all types
  - For term infants without risk factors: phototherapy is initiated based on total bilirubin: 24 hours of age 12+, 48 hours 15+ or 72 hours of age 18+ – values lower can be used in preterm or at-risk infants
- Exchange transfusion in severe cases (hemolysis, ABO incompatibility, Rh isoimmunization), IV immunoglobulin may be needed with iso-immune hemolysis

Dubin-Johnson Syndrome

- Hereditary conjugated (direct) hyperbilirubinemia d/t decreased hepatocyte excretion of conjugated bilirubin d/t gene mutation MRP2
- Think Ds: Dubin, Direct bilirubinemia, Dark liver

Clinical Manifestations

- Usually asymptomatic – may present with generalized constitutional symptoms & mild icterus

Diagnosis

- Mild, isolated conjugated (direct) hyperbilirubinemia (often between 2-5 mg/dL) but can increase with concurrent illness, pregnancy or OCPs
- Biopsy: grossly black liver, & dark granular pigment in the hepatocytes

Management

- None needed

Crigler-Najjar Syndrome

- Hereditary unconjugated (indirect) hyperbilirubinemia

Pathophysiology

- Decreased activity of UGT enzyme needed to convert indirect → direct bilirubin

Types

- Type I: no UGT activity, autosomal recessive…!!!!
- Type II (Arias Syndrome)

Diagnosis

- Mild, isolated conjugated (direct) hyperbilirubinemia (often between 2-5 mg/dL) but can increase with concurrent illness, pregnancy or OCPs
- Biopsy: grossly black liver, & dark granular pigment in the hepatocytes

Management

- None needed
## Gilbert Syndrome

- Hereditary unconjugated (indirect) hyperbilirubinemia, relatively common (5-10% of US population)
- **Pathophysiology**
  - Reduced UGT activity (10-30% of normal) & decreased bilirubin uptake, leading to increased indirect bilirubin
  - UGT = enzyme responsible for conjugation of bilirubin
- **Clinical Manifestations**
  - Asymptomatic in most cases, may develop transient episodes of jaundice during periods of stress, fasting, alcohol, or illness
- **Diagnosis**
  - Usually an incidental finding: slight increase in isolated indirect bilirubin level with otherwise normal LFTs
- **Management**
  - No treatment needed (mild, benign disease)

## Lactose Intolerance

- **Pathophysiology**
  - Inability to digest lactose due to low levels of lactase enzyme – lactase enzyme production normally declines in adulthood (especially African Americans, Asians, & South Americans)
- **Clinical Manifestations**
  - Loose stools, abdominal pain, flatulence & borborygmi after ingestion of milk or milk-containing products
- **Diagnosis**
  - **Clinical diagnosis** – symptom improvement after a trial of a lactose-free diet
  - **Hydrogen breath test:** test of choice, hydrogen produced when colonic bacteria ferment the undigested lactose – usually performed after a trial of a lactose free diet if the diagnosis is uncertain
- **Management**
  - Lactose-free diet or use of enzymes: lactase enzyme preparations
  - Lactaid (prehydrolyzed milk)

## Pyloric Stenosis

- **Hypertrophy & hyperplasia of the pyloric muscles causing a functional gastric outlet obstruction**
- **Clinical Manifestations**
  - Hallmark*: Nonbilious, projectile vomiting (after feeding)
  - Signs of dehydration, weight loss & malnutrition may be present
  - **PE:** palpable pylorus (“olive-shaped” nontender, mobile hard mass on right of epigastrium) esp. after emesis, hyperperistalsis, succession splash on auscultation
- **Diagnosis**
  - **Initial test of choice:** Abdominal U/S – elongated, thickened pylorus (more sensitive test) – will see “double-track”
  - Barium upper GI series:
    - **String sign:** (thin column of barium through narrow pyloric channel), delayed gastric emptying
    - **Railroad track sign:** excess mucosa in the pyloric lumen → 2 columns of barium
  - Labs: hypokalemia & hypochloremic metabolic alkalosis from vomiting
- **Management**
  - Initial: Rehydration (IV fluids) & electrolyte repletion (eg, potassium replacement)
  - Definitive: Pyloromyotomy [surgical incision of the hypertrophied pyloric muscle – Ramstedt procedure]
- **General Measures**
  - **MCC of intestinal obstruction in infancy**
  - Risk Factor: MC in first 3-12 weeks of life, associated w/ erythromycin use, Caucasians, M> 4:1, first-borns

## Niacin/Nicotinic Acid (B3) Deficiency

- **Sources of B3:** meats, grains, legumes
- **Etiology**
  - Often due to **diets high in untreated corn** (lacks niacin & tryptophan), diets which lack tryptophan, alcoholism, anorexia, malabsorption, INH therapy
  - **Carcinoid syndrome:** increased tryptophan metabolism due to the production of serotonin
  - **Hartnup disease:** decreased tryptophan absorption in the kidneys & small intestine
- **Clinical Manifestations**
  - **Pellagra (3Ds):** dermatitis, diarrhea, & dementia
    - Dermatitis: photosensitive hyperpigmented dermatitis (especially on sun-exposed areas)
  - **Diabetes**
    - Dementia (disorientation, delusions & encephalopathy)
- **Management**
  - Vitamin replacement/supplementation
### Vitamin A Deficiency

**Vitamin A Function:**
- Vision, immune function, embryo development, hematopoiesis, skin, and cellular health (epithelial cell differentiation)

**Sources**
- Found in the kidney, liver, egg yolk, butter, green leafy vegetables

**Risk Factors**
- Patients with liver disease, alcoholics, fat-free diets, fat malabsorption (Cystic fibrosis, Crohn ileitis, short bowel syndrome, bariatric surgery)

**Clinical Manifestations**
- **Visual changes: especially night blindness**, xerophthalmia (dry eyes), retinopathy
- Impaired immunity: (impaired wound healing, frequent infections), dry skin (follicular hyperkeratosis), poor bone growth, taste loss
- **Squamous metaplasia** (conjunctiva, respiratory epithelium, urinary tract)
- **Bitot’s spots**: white spots on the conjunctiva due to squamous metaplasia of the corneal epithelium

**Diagnosis**
- Clinical, decreased serum retinol levels

**Management**
- Vitamin replacement/supplementation

### Vitamin C (Ascorbic Acid) Deficiency - Scurvy

**Risk Factors**
- Diets lacking raw citrus fruits & green vegetables (excess heat denatures vitamin C), smoking, illicit drug use, alcoholism, malnourished individuals, elderly – symptoms can occur after 3 months of deficient intake

**Clinical Manifestations**
- Scurvy – 3 H’s: hyperkeratosis, hemorrhage, hematologic
  - **Hyperkeratosis**: hyperkeratotic follicular papules (often surrounded by hemorrhage), coiled hairs
  - **Hemorrhage**: vascular fragility (d/t abnormal collagen production) with recurrent hemorrhages in the gums, skin (perifollicular) & joints; impaired wound healing
  - **Hematologic**: anemia, glossitis, malaise, weakness, increased bleeding time

**Diagnosis**
- Clinical, serum ascorbic acid levels
- Leukocyte ascorbic levels more accurate

**Management**
- Ascorbic acid replacement – hematologic symptoms improve within weeks, generalized symptoms can improve within days

### Vitamin D Deficiency

**Pathophysiology**
- Low bone turnover + decreased osteoid mineralization (osteomalacia) &/or cartilage @ epiphyseal plates (Rickets)

- **Osteomalacia**

**Etiology**
- **Severe vitamin D deficiency most common** – leads to decreased serum calcium & phosphate with subsequent demineralization of the bone osteoid only (“soft bones”)
- Malabsorption (eg. chronic liver or kidney disease, gastric bypass, celiac sprue)
- **Disease in children = Rickets** & osteomalacia. **Adults = osteomalacia**

**Clinical Manifestations**
- Asymptomatic initially → diffuse bone pain & tenderness, muscular weakness (proximal)
- Hip pain may cause antalgic (waddling) gait
- **Bowing of long bones**, symptoms of hypocalcemia

**Diagnosis**
- **Classic**: decreased calcium, phosphate & 25-hydroxyvitamin D levels
- Increased alkaline phosphatase & PTH
- **XR**: Looser lines (zones) – transverse pseudo-fracture lines (narrow radiolucent lines from visible osteoid)

**Management**
- **Vitamin D supplementation first-line (Ergocalciferol)**

- **Rickets**

**Etiology**
- Vitamin D deficiency most commonly seen between 3 months – 3 years when growth (calcium) needs are high + decreased sunlight exposure (prolonged breastfeeding without vitamin D supplementation)
- **Calcipenic**: calcium deficiency &/or vitamin D deficiency including dietary deficiency, celiac disease, cystic fibrosis or extensive bowel resection
- **Phosphopenic** d/t renal phosphate wasting (Fanconi syndrome)
**Clinical Manifestations**
- Delayed fontanel closure, growth delays, delayed dentition & genu varum (lateral bowing of the femur & tibia)

**Diagnosis**
- Depends on cause but classic labs are decreased calcium, phosphate & 25-hydroxyvitamin D levels (Calcipenic)
- Increased alkaline phosphatase & PTH
- XR: widening of the epiphyseal plate, costochondral junction enlargement (rachitic rosary), long bones appear to have a less distinct “fuzzy” cortex

**Management**
- Vitamin D supplementation first-line (Ergocalciferol)

### NEUROLOGY/DEVELOPMENTAL – 6%

<table>
<thead>
<tr>
<th>Age</th>
<th>Injury Prevention</th>
<th>Violence Prevention</th>
<th>Nutritional Counseling</th>
<th>Fostering Optimal Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth &amp; 3-5 days</td>
<td>Crib safety Hot water heaters &lt;120° F Car safety seats Smoke detectors Back to sleep</td>
<td>Assess bonding and attachment Identify family strife, lack of support, pathology Educate parents on nurturing</td>
<td>Exclusive breastfeeding encouraged (should breastfeed every 2-3 hours) Formula as a second-best option (every 3-4 hours)</td>
<td>Discuss parenting skills Refer for parenting education</td>
</tr>
<tr>
<td>2 weeks → 1 month</td>
<td>Falls, Back to sleep Tummy time when awake: 5-10 min 2-3 times per day</td>
<td>Discuss sibling rivalry Assess if guns in the home</td>
<td>Assess breastfeeding &amp; offer encouragement, problem-solving Should be back to birth weight at 2-weeks</td>
<td>Recognize and manage postpartum blues Child care options</td>
</tr>
<tr>
<td>2 months</td>
<td>Burns/hot liquids Back to sleep</td>
<td>Reassess firearm safety</td>
<td>After 3 they do not need to eat during the night</td>
<td>Parent getting enough rest and managing returning to work</td>
</tr>
<tr>
<td>4 months</td>
<td>Infant walkers Choking/suffocation Back to sleep</td>
<td>Reassess</td>
<td>Introduction of solid foods</td>
<td>Discuss central to peripheral motor development</td>
</tr>
<tr>
<td>6 months</td>
<td>Burns/hot surfaces Place on back to sleep, but once infant can roll no need to worry about rolling to tummy.</td>
<td>Reassess</td>
<td>Start water and baby food</td>
<td>Consistent limit-setting versus “spoiling” an infant Praise good behavior</td>
</tr>
<tr>
<td>9 months</td>
<td>Water safety Home safety review Ingestions/poisoning</td>
<td>Assess parents’ ideas on discipline and “spoiling”</td>
<td>Avoiding juice Begin to encourage practice with cup drinking No honey until 1 yo</td>
<td>Assisting infants to sleep through the night if not accomplished Praise good behavior</td>
</tr>
<tr>
<td>12 months</td>
<td>Firearm hazards Auto-pedestrian safety</td>
<td>Discuss timeout versus corporal punishment Avoiding media violence Review firearm safety</td>
<td>Introduction of whole cow’s milk (and constipation with change discussed) Assess anemia, discuss iron-rich foods →3x birth weight</td>
<td>Safe exploration Proper shoes Praise good behavior</td>
</tr>
<tr>
<td>15 months</td>
<td>Review &amp; reassess topics</td>
<td>Encourage nonviolent punishments (timeout or natural consequences)</td>
<td>Discuss decline in eating with slower growth Assess food choices and variety</td>
<td>Fostering independence Reinforce good behavior Ignore annoying but not unsafe behaviors</td>
</tr>
<tr>
<td>18 months</td>
<td>Review and reassess topics Rear-facing seat until 2 yo</td>
<td>Limit punishment to high yield (not spilled milk!) Parents consistent in discipline</td>
<td>Discuss food choices, portions, “finicky” feeders</td>
<td>Preparation for toilet training Reinforce good behavior</td>
</tr>
<tr>
<td>2 years</td>
<td>Falls—play equipment Forward-facing car seat</td>
<td>Assess and discuss any aggressive behaviors in the child</td>
<td>Assess body proportions and recommend low-fat milk Assess family cholesterol and atherosclerosis risk →4x birth weight</td>
<td>Toilet training and resistance</td>
</tr>
<tr>
<td>3 years</td>
<td>Review &amp; reassess topics</td>
<td>Review, especially avoiding media violence</td>
<td>Junk food versus healthy eating</td>
<td>Read to the child Socializing with other children Head Start if possible</td>
</tr>
<tr>
<td>Age</td>
<td>Topics</td>
<td></td>
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<tr>
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</tr>
</tbody>
</table>
| 4 years | Booster seat versus seat belts  
Bike helmet |
| 5 years | Bicycle safety  
Water/pool safety  
Developing consistent, clearly defined family rules and consequences  
Avoiding media violence |
| 6 years | Fire safety  
Reinforce consistent discipline  
Encourage nonviolent strategies  
Assess domestic violence  
Avoiding media violence |
| 7-10 years | Sports safety  
Firearm hazard  
Lap and shoulder safety belt in back seat (8-12 y/o) |
| 11-13 years | Review and reassess  
Child can start sitting in the front seat at 13 y/o |
| 14-16 years | Motor vehicle safety  
Avoiding riding with substance abuser  
Establish new family rules related to curfews, school, and household responsibilities |
| 17-21 years | Review & reassess  
Establish new rules related to driving, dating, and substance abuse |

### Down Syndrome

**Genetic disorder d/t 3 copies of chromosome 21 (trisomy 21) or 3 copies of a region of the long arm of chromosome 21**

- MC chromosomal disorder & cause of mental developmental disability

**Clinical Manifestations**

- **Head and neck:** low-set small ears, flat facial profile, flat nasal bridges, open mouth, protruding tongue, upslanting palpebral fissures, folded/dysplastic ears, brachycephalic, prominent epicanthal folds, excessive skin @ the nape of the neck, short neck, almond-shaped eyes, Brushfield spots (white, gray or brown spots on the iris)

- **Extremities:** transverse, singular palmar crease (Simian crease), hyperflexibility of the joint, short broad hands, increased space between the first & second ties (sandal gap deformity)

- **Neonates:** poor Moro reflex, hypotonia, dysplasia of the pelvis, hypotonia, may develop transient neonatal leukemia

- **Congenital heart disease:** atrioventricular septal defects, tetralogy of Fallot, PDA

- **GI:** duodenal/esophageal atresia, Hirschsprung disease

- **Complications:** atlantoaxial instability (C1-C2), Acute lymphocytic leukemia, early onset of Alzheimer disease

**Diagnosis**

- History, PE, genetic testing to confirm dx

**Prenatal Screening**

- **Biochemical screening:** free beta hCG: abnl high/low ~indicative of chromosomal abnormalities, PAPP-A: low with fetal DS

- **Nuchal Translucency Ultrasound** @ 10-13 weeks – increased thickness can be seen with trisomy 13, 18, & 21

- If increased thickness, chorionic villous sampling or amniocentesis is offered
**Febrile Seizure**

Convulsion associated with an elevated temperature greater than 38°C with absence of CNS infection or inflammation

**Pathophysiology**
- The MC seizure disorder during childhood, occur in 2-5% of children 6 months – 6 years
- Risk of recurrence is 30% after first episode, and 50% after second, no long-term sequelae, & children will outgrow by age 6
- Autosomal dominant inheritance pattern demonstrated in some families

**Clinical Manifestations**
- Present as a brief tonic-clonic seizure associated with fever

**Diagnosis**

**Management**
- If more the 5 minutes, treat with an IV benzodiazepine – Diazepam or Lorazepam

**General Measures**
- Increased risk of epilepsy (2% as opposed to 1% in general population)

**Immunization Guidelines**

<table>
<thead>
<tr>
<th>Ages</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>B – birth</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>2 months</td>
<td>– 2 B DR HIP</td>
</tr>
<tr>
<td>4 months</td>
<td>– 4 DR HIP</td>
</tr>
<tr>
<td>6 months</td>
<td>– 6 DR HIP in 6 MONTHS</td>
</tr>
<tr>
<td>1-1.5 years</td>
<td>– 1 MAD HPV</td>
</tr>
<tr>
<td>4-6 years</td>
<td>– 4 VERY DIM</td>
</tr>
<tr>
<td>11-12 years</td>
<td>– TADA HUMAN MEN</td>
</tr>
<tr>
<td>16-18 years</td>
<td>– MEN</td>
</tr>
<tr>
<td></td>
<td>Meningococcal Booster</td>
</tr>
</tbody>
</table>

*Types of Vaccines:*

1. Live attenuated vaccines – live weakened version of the organism, not given to immunocompromised/pregnant pt
   - MMR, Varicella Zoster, Rotavirus
   - Smallpox, yellow fever, oral typhoid, oral polio
2. Killed (inactivated vaccines) – weaker immune response than live & only induce humoral (antibody) immunity
   - Influenza, rabies, polio SaIK, Vibrio cholerae, Hepatitis A
3. Subunit Conjugate Vaccines – present only essential antigens needed to induce a response
   - S. pneumococcal, H. influenzae, N. meningitides, PCV13 (pneumococcal)
4. Subunit recombinant vaccines – DNA recombinant technology is used to manufacture
   - Hepatitis B (HBsAg), HPV vaccine
5. Toxoid Vaccines – chemically modified inactivated toxins to allow body to recognize the harmless toxin
   - Tetanus, Diphtheria, Pertussis

**Vaccine Contraindications**

- Baker’s yeast: Avoid hepatitis B
- Gelatin: avoid varicella & influenza vaccines
- Thimerosal: preservative used in vaccines so should be avoided in multi-dose vaccines
- Neomycin & Streptomycin allergy: avoid MMR & inactivated Polio vaccine

**Acute Bacterial Meningitis**

*Bacterial infection of the meninges*

**Etiology**

- *Streptococcus pneumoniae: MCC in adults* all ages & children aged 3m-10y
- *Neisseria meningitidis: MCC in older children* (10-19 y/o), 2nd MCC in adults, may be assoc. w/ petechial rash
- *Group B Streptococcus (S. agalactiae): MCC in neonates under 1m* (part of vaginal flora) & infants under 3m
- *Listeria monocytogenes*: Increased incidence in neonates, 50+ y/o, immunocompromised states (hx of glucocorticoid use, alcoholism, pregnancy, AIDS/HIV, chemotherapy)
- *Neonates*: Group B Streptococcus, Escherichia coli, & gram negative rods are common causes of neonatal meningitis, Listeria monocytogenes, also – H. influenzae incidence reduced d/t Hib vaccine

**Clinical Manifestations**

- Meningeal symptoms: HA, neck stiffness, photosensitivity, fever, chills, N, V – may have AMS changes & seizures
- Meningeal signs: nuchal rigidity, (+) Brudzinski (neck flexion produces knee &/hip flexion, (+) Kernig sign (inability to extend the knee/leg with hip flexion); look for bulging fontanelle in babies
- Focal neurologic findings (30%), 25% have a recent history of otitis or sinusitis
- Neisseria menigitidis: petechial rash on trunk, legs, conjunctivae

**Diagnosis**

- **Lumbar puncture + CSF examination** = best initial test & definitive diagnosis: decreased glucose (under 45), increased neutrophils, increased protein & increased pressure
- **Head CT scan** = best initial test PRIOR TO LP ONLY if needed to rule out mass effect if any of these are present: papilledema, seizures, confusion, focal neuro findings, 60y/o+, immunocompromised, or history of CNS disease

**Clinical Manifestations**

- **Management**
  - **Antibiotics**, along with Dexamethasone when indicated – should be started ASAP after LP is performed, if LP is C/I, or prior to head CT if needed before LP (basically ASAP after blood cultures are obtained or LP done)
  - **Dexamethasone has been shown to reduce mortality & sequelae of S. pneumo, H. influenza, & N. menigitidis**
  - Give if suspect H. influenza type B in children
  - Do not be continued for 24 hours after ignition of abx with suspected/confirmed infx
  - **Post-exposure prophylaxis**: Ciprofloxacin (500mg PO x1 dose) or Rifampin (600 mg PO q12h x 2 days) – **prophylaxis is only needed for “close contacts” with prolonged exposure (8+ hours) or direct exposure to respiratory secretions** (household contacts, roommates, kissing, sharing utensils, mouth to mouth resuscitation)
  - **Prophylaxis is not recommended for healthcare workers who haven’t had direct exposure to respiratory secretions**

**General Measures**

- **Empiric for 1m+ to 50 years**: Vancomycin + Ceftriaxone (or Cefotaxime)
- **Empiric for 50 years +**: Vanco + Ceftriaxone + Ampicillin (for Listeria)
- **Empiric for neonates (up to 1m)**: Ampicillin + either Gentamicin &/or Cefotaxime

**Aseptic Meningitis**

- Clinical & laboratory evidence of meningitis with (-) routine bacterial cultures

**Etiology**

- **Enteroviruses** = MCC (Coxsackivirus & Echovirus)
- Other viruses, mycobacteria, fungi, spirochetes, medications, and malignancies

**Clinical Manifestations**

- **Classical symptoms of meningitis but milder**
- **Meningeal symptoms**: HA, neck stiffness, photosensitivity, fever, chills, nausea, vomiting
- **Meningeal signs**: nuchal rigidity, (+) Brudzinski, (+) Kernig sign
- **No focal deficits in aseptic meningitis** helps to distinguish from encephalitis

**Diagnosis**

- **Diagnosis of exclusion** after ruling out bacterial meningitis (negative blood cultures)
- **Lumbar puncture** best initial test & most accurate if no symptoms of mass effect
  - **CSF**: Classic findings are normal glucose, lymphocyte predominance, protein count usually less than 200

**Management**

- **Supportive** (antipyretics, IV fluids, analgesics), if HSV – IV acyclovir
- Most patients have a self-limited course with resolution even without specific therapy

**Normal Growth & Development**

**Neonate**: 0-3 months, **Infant**: 3-12 months, **Toddler**: 12-24 months, **Preschool**: 3-6 years, **School Age**: 6-11 years, **Adolescence – girls**: 11 years, boys: 13 years

<table>
<thead>
<tr>
<th>Age</th>
<th>Motor</th>
<th>Language</th>
<th>Social</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 month</td>
<td>Moro &amp; grasp reflex, visual tracking Reacts to pain @ 1 month</td>
<td>Crying, responds to noise</td>
<td>Minimal – regards human face, establishes eye contact</td>
</tr>
<tr>
<td>2 months</td>
<td>Holds head up prone, wipes at objects Eyes follow object to midline</td>
<td>Cooing, vocalizes</td>
<td>Social smile, recognizes parent</td>
</tr>
<tr>
<td>3 months</td>
<td>Lifting head &amp; chest, Moro reflex disappears</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Normal**
4 months | Rolls from prone to supine, grasp objects | Orient to voice, colic resolves in most babies by this age | Regards hand, laughs 
& squeals
6 months | Sits upright unsupported, rolls prone to supine, transfers objects hand to hand | Babbles | Stranger anxiety (6 strangers switch sitting @ 6 months)
9 months | Crawls, pull-to-stand, pincer grasp (10m), eats w/ fingers | Mama-dada (nonspecific) | Waves bye, responds to name
12 months | Stands | Mama-dada (specific) | Picture book
15 months | Walks, uses cup | Several words | Temper tantrums
18 months | Walks up stairs, throws ball | Names objects | Toilet-training begins
24 months | Runs | 2-word sentences, several hundred word vocabulary | Follows 2-step commands
36 months | Rides a tricycle, eats with utensils | 3-word sentences | Knows first & last name
6-11 years | Development of conscience (super-ego), has same-sex friends
F-11, M-13y/0 | | | Abstract reasoning, formation of personality, may have friends of opposite sex

### Seizure Disorders

**Focal (Partial) Seizure**
- Abnormal neuronal discharge from one discrete section of one hemisphere
- **Simple:** with** retained awareness** (consciousness fully maintained)
- **Complex:** with** impaired awareness** (consciousness impaired)

#### Clinical Manifestations
- **Focal sensory, motor or autonomic symptoms** depending on the lobe affected – may be followed by a neurologic deficit (Todd’s paralysis) lasting up to 24 hours
- **Motor:** jerky, rhythmic movements, may start in one area (focal) & then spread to other parts of the affected limb/body (Jacksonian March), may be tonic (muscular rigidity) or tonic (rhythmic jerking)
- **Sensory:** paresthesia, numbness, pain, heat, cold, sensation of movement, olfactory, flashing lights (photopsia)
- **Autonomic:** abdominal (pain, N, V, hunger), cardiovascular (sinus tachycardia), BP changes, bronchoconstriction – **psychologic:** fear, déjà vu, hallucinations
- **Auras:** may precede, accompany or follow seizure onset
- **Automatisms:** repetitive behaviors (lip smacking, facial grimacing, chewing, manual picking, patting, coordinated movements or repeating words or phrases) that **may accompany partial seizures**

#### Diagnosis
- Initial workup is to r/o reversible causes (CBC, electrolytes, liver & renal function, & RPR) – MRI to r/o focal mass
- **Electroencephalogram**
  - Simple partial: focal discharge at the onset of the seizure
  - Complex partial: interictal spikes or with slow waves in the temporal or frontotemporal area

**Absence (Petit Mal) Seizure**
- Generalized seizure (involving both hemispheres)
- **MC seen in childhood** – age @ onset is 4-10 years (often ceases by early puberty or 20 y/o in most patients)

#### Clinical Manifestations
- **Pause/stare:** sudden, marked impairment of consciousness without loss of body tone (patient remains upright), staring episodes with pauses (behavioral arrest)
- **Episodes typically last 5-10 seconds,** if more than 10 seconds, can be associated with eyelid twitching & lip smacking
- No postictal phase, may occur tens of time daily – may be associated with automatisms (predominantly oral) or myoclonus, may be provoked by hyperventilation

#### Diagnosis
- **EEG:** bilateral symmetric 3 Hertz spike & wave activity (2.5-5Hz)

#### Management
- Ethosuximide first-line medical management, Valproic acid 2nd line, Lamotrigine
- Carbamazepine or Gabapentin can exacerbate absence seizures

**Generalized (Grand Mal) Seizure**
- Simultaneous neuronal discharge of both hemispheres (diffuse brain involvement)
- Generalized tonic clonic (grand mal) is the most common

#### Clinical Manifestations
- **Tonic-clonic (grand mal):** sudden loss of consciousness with tonic activity (contraction & rigidity) that may be associated with respiratory arrest followed by 1-2 minutes of clonic activity (repetitive, rhythmic, symmetric jerking usually lasting under 3 min) followed by postictal confusion phase – cyanosis & urinary incontinence may occur
• **Clonic:** repetitive rhythmic jerking (usually lasting less than 2-3 minutes) often associated w/ postictal state

• **Myoclonic:** sudden, brief, sporadic involuntary twitching – may be one muscle or group of muscles, no LOC

• **Tonic:** loss of consciousness followed by rigidity

• **Atonic:** sudden partial or complete loss of muscle and postural tone (“drop attacks”)

• **Absence:** nonconvulsive brief lapse of consciousness with brief staring episodes or without loss of postural tone

**Diagnosis**

• **Initial workup is to r/o reversible causes** (CBC, electrolytes, liver & renal function, RPR)

• **Increased prolactin & lactic acid immediately after seizures** helpful to r/o pseudoseizures – MRI to r/o focal mass

• **EEG:** bilateral symmetric 3 Hertz spike & wave activity (2.5-5Hz)

**Management**

• Treat underlying causes if known

• Long-term options for epilepsy are: Levetiracetam, Phenytoin, Valproic acid, Carbamazepine, Lamotrigine, Phenobarbital, Topiramate – if pregnant: Levetiracetam & Lamotrigine

• Ethosuximide 1st line for absence, valproic acid 2nd line

→**Status Epilepticus**

• A single, continuous epileptic seizure lasting 5 minutes or greater, or more than 1 seizure within a 5 minute period w/out recovery in between episodes – a neurologic emergency

**Etiology**

• Structural abnormalities, infections (meningitis, encephalitis), metabolic abnormalities, medications, toxins

**Diagnosis**

• Neuroimaging: once stabilized to determine if intracranial mass or hemorrhage is present

**Management**

• **Benzodiazepines are preferred initial agents** (Lorazepam usually preferred) – associated with rapid control of seizure & additional doses can be given

• Midazolam can be used as initial IM therapy if IV access cannot be established

• **Second line: Phenytoin or Fosphenytoin if no response to benzos** – can also be used to prevent recurrence

• Alternatives: Valproate and Levetiracetam

• **3rd line: Phenobarbital if no response to Phenytoin** (refractory)

• General anesthesia: Midazolam & Propofol can be used

**Complications**

• Hypoxia, aspiration, respiratory failure, cardiac arrhythmias

**Teething**

• Central incisors are first to erupt, between 5 & 8 months (usually 6m), lateral incisors at 8 months, 1st molars @ 14 months, canines at 19 month, second molars are last to erupt between 20 & 30 months (24 m)

• By age 2.5 years, children should have all primary teeth including second molars

• Secondary (permanent teeth) begin to erupt by 6-7 years

• Early or late tooth eruption may be within normal limits, though it can be an indicator of a nutritional, genetic or metabolic problem

**Turner Syndrome**

• Group of X chromosome abnormalities characterized by **females with an absent or nonfunctional X sex chromosome & is phenotypically female**

• Patients will have delay in motor skill development with normal intelligence

**Pathophysiology**

• Mosaicism (67-90%) – some cells have a combination of X chromosome (45, XO d/t missing X chromosome), some cells are normal (46, XX), cells w/ partial monosomies (X, abnormal X) or cells that have a Y chromosome (46, XY)

**Clinical Manifestations**

• **Hypogonadism:** 45, XO leads to gonadal dysgenesis (rudimentary fibrosed streaked ovaries) that can cause early ovarian failure (primary amenorrhea in 80% or early secondary amenorrhea), delayed secondary sex characteristics (absence of breasts), & infertility

• **Physical examination:** short stature, webbed neck (pterygium colli), prominent ears, low posterior headline, broad chest w/ widely spaced nipples, short 4th metacarpals, high-arched palate, nail dysplasia, congenital lymphedema in neonates, small mandible, narrow maxilla, epicanthal folds, pedal edema, cubitus valgus (forearm angled slightly away from body), impaired sensorineural hearing

• **Cardiovascular:** coarctation of the aorta (30%), mitral valve prolapse, bicuspid aortic valves, aortic dissection, HTN

• **Renal:** congenital abnormalities (horsehoe kidney), hydronephrosis

• **Endocrine:** osteoporosis, hypothyroidism, DM, dyslipidemia

• **GI:** telangiectasias (may present GI bleeding), inflammatory bowel disease, colon cancer

**Diagnosis**
• **Karyotyping** – definitive diagnosis, 45,XO mosaicism or X chromosomal abnormalities

**Management**
- Recombinant human growth hormone replacement (may increase final height)
- Estrogen/progesterone replacement to cause pubertal development
- Monitor for autoimmune hypothyroidism
- Possible: resect any intra-abdominal gonads to prevent malignancy

**PSYCHIATRY – 6%**

**Anxiety Disorders**

**Panic attack & panic disorder**
- Period of extreme anxiety that peaks within 10 minutes, typically declines within 30 minutes, and rarely lasts for longer than 1 hour.
- Panic attacks may have a definable trigger or be totally unexpected.
- Panic disorder is characterized by recurrent panic attacks that occur abruptly and are accompanied by debilitating fear of having additional attacks.

**Clinical Manifestations**
- At least 4 following symptoms of sympathetic symptom overdrive – sense of impending doom or dread (hallmark)
  - palpitations or tachycardia, sweating, trembling, dyspnea/hyperventilation, sensation of choking, chest discomfort, nausea, depersonalization (feel estranged from self and/or the external world), derealization (people, events, and surroundings appear to be changed or unreal), fear of losing control, fear of dying, light-headedness, numbness or tingling, chills, or hot flashes.
- The intense fear and physical symptoms may be accompanied by feelings of impending harm or death, fear of a heart attack or stroke, and/or fears of “going crazy.”

**Management**
- For acute management, a **short course of benzodiazepines** (alprazolam or lorazepam) is beneficial.
- With panic attacks, **one must r/o potentially life threatening conditions (heart attack, thyrotoxicosis)**
- For maintenance, **SSRIs** should be instituted as benzodiazepines are tapered. Paroxetine is beneficial, as are fluoxetine, venlafaxine, and sertraline.
- Treatment should continue for 8 to 12 months, because relapse rates are high after medication is discontinued
- **Pharmacotherapy + CBT most effective**

**Agoraphobia**
- Intense fear of anxiety about being in places or situations from which escape or obtaining help may be difficult
- Agoraphobia may occur w/ or w/out a hx of panic disorder, although 50-70% of pts with agoraphobia have coexisting panic disorder. If feared incapacitating event = panic attack, then agoraphobia is secondary to the panic disorder.
- Symptoms last @ least 6 months, cause significant social or occupational dysfunction

**Management**
- Similar to panic disorder – SSRI + CBT

**Social Anxiety Disorder**
- **MC type of phobia** – public speaking
- Disabling, persistent (@ least 6m) intense fear or social or performance situation in which the person is exposed to scrutiny of others
- Exposure to social situations almost always provokes anxiety & causes expected panic attacks

**Management**
- **Psychotherapy: initial treatment of choice** (CBT, relaxation techniques), pharmacotherapy – SSRIs, or combo
- **Situational: beta-blockers for performance anxiety & public speaking (Propranolol) 30-60min before performance**

**Specific Phobias**
- Persistent (@ least 6m) intense fear or anxiety of a specific situation (heights, flying), **object** (animals), or **place** (hospital)
- Exposure to the situation causes an immediate response, & the fear is out of proportion to any real danger
- **Everyday activities must be impaired by distress or avoidance of the situation or object**
- **Subtypes:** Animal, situational (elevator, airplane), natural environment (heights, thunder), and blood injection injury

**Management**
- **Exposure & desensitization therapy = treatment of choice**, may use short term benzos or beta blockers in some pts

**Generalized Anxiety Disorder**
- **MC in females, with onset in early 20s**
- Excessive anxiety or worry a majority of days for @ least 6 months about various aspects of life – the anxiety is usually out of proportion to the event
- Not episodic, situational or focal and the symptoms cause significant social or occupational dysfunction – not d/t medical illness or substance abuse

**Diagnosis**
- Associated with at least 3 of the following: fatigue, restlessness, difficulty concentrating, muscle tension, sleep disturbance, irritability, shakiness, and headaches

**Management**
- Antidepressants – **SSRIs first line** (Fluoxetine, Paroxetine, Escitalopram), SNRIs,
- Buspirone can be an adjunct to SSRIs (does not cause sedation & doesn’t potentiate CNS depression of alcohol
- MOA: partial serotonin receptor agonist & dopamine receptor antagonist
- CBT & psychotherapy, psychotherapy + pharmacotherapy is more effective

### Attention-deficit/hyperactivity disorder

- Neurodevelopmental disorder characterized by problems paying attention, impulsivity (difficulty controlling behaviors) & hyperactivity that is not age-appropriate
- Patients may continue to have symptoms as adults (inattentiveness > hyperactivity)
- 67% comorbidity with conduct & oppositional defiant disorders

#### 3 subcategories:
1. Predominantly inattentive
2. Predominantly hyperactivity/impulsive
3. Combined type

**Diagnostic Criteria**
- The symptoms must be developmentally inappropriate for age, have symptom onset before 12 years old & be present for at least 6 months, & must occur in at least 2 settings
- **At least 6 inattentive symptoms:**
  1. Easily distracted – misses details, frequently switches from one activity to another, forgets things, easily distracted when multiple things are happening simultaneously
  2. Has difficulty maintaining focus on one task or learning something new
  3. Misses details and may make many careless mistakes
  4. Forgets/ loses things needed to complete activities/tasks
  5. Difficulty in completing assignments
  6. Becomes bored with a task after a few minutes, unless doing something enjoyable
- &/ or **at least 6 hyperactivity/impulsivity symptoms**
  1. Fidgets & squirms in their seat.
  2. Constantly in motion.
  3. Talks nonstop or excessively.
  4. Impatience.
  5. Dashes around, touching or playing with everything in sight
  6. Has trouble sitting for long periods
  7. Difficulty doing quiet tasks
  8. Restlessness.
  9. Blurs out appropriate/inappropriate comments, shows unrestrained emotions
  10. Interrupts the conversation or the activities of others

**Management**
- Multimodal approach: behavior modification including social skills training, classroom modifications, & parent education
- **Stimulants**: first line medical treatment of choice – Methylphenidate, Amphetamine/Dextroamphetamine & Dexamfetamine
  - MOA: blocks reuptake & incr. release of NE & dopamine – Adverse: abdominal pain, insomnia, weight loss
  - In patients on these meds, monitor their growth because amphetamines can cause stunted growth*
- **Nonstimulants**: Atomoxetine (NE reuptake inhibitor) – similar to stims but less AE & addictive ability
  - Adverse: dry mouth, decreased appetite, insomnia
- **Adjunct medications**: alpha agonists (Guanfacine, Clonidine), bupropion, or venlafaxine

### Autism Spectrum Disorder

- Spectrum of developmental disorders characterized by impairment in social interaction or communication, restricted, repetitive stereotyped behaviors as well as other signs leading to impaired social functioning
- M>F 4:1, symptoms usually recognized between 12-24 months old
- Should be suspected if there is a rapid deterioration of social or language skills during first 2 years of life

**Diagnostic Criteria**
- Social interaction difficulties: significant emotion discomfort/detachment (avoiding eye contact, no response to affection)
- Impaired communication: either inability to communicate/ has ability to communicate but chooses not to in social settings – difficulties in understanding what is not explicitly stated (metaphors, joke humor)
- Restricted, repetitive, stereotyped behaviors & patterns of activities (interest in objects, rigid, inflexible thought patterns)
- Other signs: persistent failure to develop social relationships, failure to show preference to parents over other adults, unusual sensitivity to visual, auditory, or olfactory stimuli; unusual attachments to ordinary objects

**Management**
**Referral for neuropsychologic testing, behavior modification strategies & medications**

<table>
<thead>
<tr>
<th>Child abuse and neglect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to provide the basic needs of a child (supervision, food, shelter, affection, education)</td>
</tr>
<tr>
<td>MC is neglect</td>
</tr>
<tr>
<td><strong>Injury not adequately explained or inconsistent with history given</strong> – bruises/lac/soft-tissue swelling, dislocations/fractures, spiral fractures</td>
</tr>
<tr>
<td>Fractures of suspicion: @ metaphyseal plate, posterior ribs, skull, scapula, sternum, transverse long bone</td>
</tr>
<tr>
<td>Burns (doughnut-shaped, stocking-glove, symmetrically round)</td>
</tr>
<tr>
<td>Bruises or injuries with regular patterns on face, back, buttocks, thighs</td>
</tr>
<tr>
<td>Internal hemorrhages, abdominal injuries, bite marks, injury with shape of instrument used</td>
</tr>
</tbody>
</table>

**Risk factors:** poor, premature, colicky, medical condition

**Clinical Manifestations**

- Signs: malnutrition, withdrawal, poor hygiene, failure to thrive
- May also manifest with: anxiety, aggressive/violent behavior, PTSD, depression/suicide, substance abuse, poor self-esteem, dissociative disorders, paranoid ideation, failure to thrive
- Neglect: consider if minor allowed to engage in harmful behavior (ETOH consumption), child in unattended (in some states this is before age 13)

**Major Depressive Disorder (MDD) aka Unipolar Depression**

**Risk Factors**

- Family history, F>M 2:1, peak onset in 20s

**Pathophysiology**

- Alteration in neurotransmitters – serotonin, epinephrine, NE, dopamine, acetylcholine & histamine; genetic factors
- Neuroendocrine dysregulation: adrenal, thyroid, or growth hormone dysregulation
- 15% commit suicide, higher rates in those with a plan, white male 45 years+, & concurrent substance abuse
- Initial questionnaire: PHQ-2, if positive do the PHQ-9

**Diagnostic Criteria**

- @ least 2 distinct episodes of at least 5 associated symptoms (either depressive mood or anhedonia) almost every day for most days for at least 2 weeks:
  - Depressive mood, anhedonia, fatigue almost all day, insomnia/hypersomnia, feelings of guilt or worthlessness, recurring thoughts of death or suicide, psychomotor agitation/retardation (restlessness/slowness), significant weight change, decreased/increased appetite, decreased concentration or indecisiveness – not assoc. with mania!

**These symptoms must cause significant distress/impairment (social/occupational) & are not d/t substance, bereavement, or medical conditions**

**Management**

- Psychotherapy (CBT, interpersonal therapy, supportive therapy)
- **SSRIs – first line medical management**, if no effect after 4 weeks switch to another SSRI
- 2nd line: SNRI, buproprion; TCA; Electroconvulsive therapy: rapid response if unresponsive to medical tx

**Subtypes of MDD**

1. Seasonal Affective Disorder: presence of depressive symptoms @ same time each year (MC in winter)
   - Management: SSRI, light therapy, Bupropion
2. Atypical depression: shares many of the typical symptoms of major depression but patients experience mood reactivity (improved mood in response to positive events), symptoms include significant weight gain, hypersomnia, heavy/leaden feelings in arms/legs, & oversensitivity to rejection
   - Management: MAO inhibitors
3. Melancholia: characterized by anhedonia, lack of mood reactivity, depression, severe weight loss, excessive guilt, psychomotor agitation or retardation & sleep disturbance (inc. REM time & reduced sleep, may lead to early morning awakening or mood worse in the AM)
4. Catatonic Depression: motor immobility, stupor & extreme withdrawal

**Persistent Depressive Disorder (Dysthymia)**

- MC in F, onset is in childhood, adolescence, or early adulthood

**Diagnostic Criteria**

- Chronic depressed mood for at least 2 years in adults (@ least 1 year in children/adolescents) that last most of the day, more days than not – in that period, the **patient is NOT syx free for 2m+ at a time**
- @ least 2 of the following must be present: insomnia/hypersomnia, fatigue, low self-esteem, ↓ appetite/overeating, hopelessness, poor concentration or indecisiveness
- May have major depressive episodes or meet MDD criteria continuously
- Must never have had a manic episode (rules out Bipolar I) or hypomanic episode (rules out cyclothymic disorder)

**Management**

- Combination treatment with psychotherapy & pharmacotherapy more efficacious than either alone
**Pharmacotherapy:** SSRIs, SNRIs, TCAs, and MAO inhibitors

**Psychotherapy:** includes interpersonal, cognitive, & insight-oriented psychotherapies

**Premenstrual Dysphoric Disorder**

**PMS:** Cluster of physical, behavioral & mood changes with cyclical occurrence during the luteal phase of cycle

**PMDD:** severe PMS w/ functional impairment where anger, irritability & internal tension are predominant

**Clinical Manifestations**

**Physical:** abd bloating & fatigue MC, breast swelling/pain, weight gain, HA, changes in BM, muscle/joint pain

**Emotional:** irritability MC, tension, depression, anxiety, hostility, libido changes, aggressiveness

**Behavioral:** food cravings, poor concentration, noise sensitivity, loss of motor senses

**Diagnosis**

Symptoms occurring 1-2 weeks before menses, relieved withing 2-4 days of menses onset + at least 7 symptom free days in follicular phase

Patient should record diary of symptoms for 2+ cycles

**Management**

Lifestyle modifications – stress reduction, exercise, NSAIDs, vitB6 & E, reduce caffeine, alcohol, cigarette & salt

1st line medical therapy for emotional symptoms with dysfunction = **SSRIs** (Fluoxetine, Sertraline)

OCPs (especially containing Drospirenone) can be used in patients who do not want to take SSRIs

No response to either treatment? GnRH agonist therapy

**Conduct Disorder**

Persistent pattern of behaviors that deviate sharply from the age-appropriate norms & violates the rights of others & animals in a patient UNDER 18 years of age

These individuals engage in physical &/or sexual violence, lack empathy for their victims & may lack remorse for committing crimes

MC in males, high incidence of ADHD & ODD, may progress to antisocial personality disorder

**Diagnostic Criteria**

Persistent pattern of violation of the rights of others or age-appropriate societal norms with @ least 3 behaviors over the last year & 1 in the last 6 months:

- **Aggression to humans or animals** – threatens, intimidates, or bullies others, uses weapons, physically cruel to animals or humans, sexual violence

- **Destruction or property** – engages in fire setting, vandalism, etc

- **Serious violate of rules** – runs away from home, stays out past curfew, engages in truancy (often before 13 y/o)

- **Deceitfulness or theft** – lies to obtain goods & favors, breaks into buildings/cars/homes, steals others’ property, & lacks remorse for actions

**Management**

Multimodal: behavioral modification, community & family involvement, parent management training (enforcing rules & setting limits)

**Prognosis**

Good prognosis: positive relationship with 1 parent, adolescent onset of symptoms, female gender, good interpersonal skills, high IQ, good academic performance

Poor prognosis: onset of symptoms prior to 10 years, low IQ, poor academic performance

**Oppositional Defiant Disorder**

Disorder in which children are generally defiant towards authority but is not associated with physical aggression, violating others’ basic rights or breaking laws (unlike Conduct disorder)

Persistent pattern of negative, angry or irritable mood, argumentative, or defiant behavior & intentional vindictiveness/spitefulness

50% associated with ADHD, may occasionally lead to conduct disorder

**Diagnostic Criteria**

Characterized by @ least 4 symptoms present @ least 6 months (w/ @ least one individual that isn’t a sibling):

- **Angry or irritable mood:** loses temper, anger or resentment, often blames others for their misbehaviours & has a negative attitude

- **Argumentative or defiant behavior:** breaks rules, often blames others for their behavior, argues with authority & deliberately annoys others

- **Vindictiveness:** spiteful at least 2x in past 6 months

**Management**

Psychotherapy – behavioral modification therapy, problem-solving skills, & conflict management training, & teaching parents child management (parenting skills, parent-child interaction therapy)

**Binge-eating Disorder**

**Diagnostic Criteria**


**Recurrent episodes of binge eating** characterized by eating within a 2-hour period more than people would in a similar period with lack of control during an overeating episode

- **Occurs @ least weekly x 3 months**
- Severe distress over binge eating, may be triggered by stress or mood changes, & patients are often obese
- Unlike bulimia nervosa, binge-eating episodes are **not associated with compensatory behaviors** (purging or restrictive behaviors) & they are not as fixated on their body shape or weight

**Management**
- Psychotherapy (CBT, interpersonal, dialectic behavior)
- Strict diet & exercise plan
- Topiramate (antiepileptic associated with weight loss)
- Stimulants: appetite suppressants (Lisdexamfetamine, Amphetamine)

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**Bulimia Nervosa**

*Eating disorder characterized by frequent binge eating combined with compensatory behaviors to prevent weight gain*

- Unlike anorexia, bulimics usually maintain a normal weight (or overweight) & their compensatory behaviors are ego-dystonic
- F>M 10:1, onset of age in late teens or early adulthood

**Physical Examination**
- Teeth pitting or enamel erosion (d/t vomiting)
- Russell’s sign: calluses on dorsum of the hand from self-induced vomiting
- Parotid gland hypertrophy

**Lab Findings**
- Hypokalemia, hypomagnesemia (may lead to cardiac arrhythmias)
- Increased amylase (salivary gland hypertrophy + vomiting), metabolic alkalosis from vomiting

**Diagnostic Criteria**
- **Recurrent episodes of binge eating** – recurrent episodes characterized by eating w/in a 2 hour period @ least weekly for x3m triggered by stress or mood changes
- **Compensatory behaviors**
  - **Purging type**: primarily engages in self-induced vomiting, diuretic, laxative or enema abuse
  - **Nonpurging type**: reduced caloric intake, dieting, fasting, excessive exercise & diet pills
- Perception of self-worth is excessively influenced by shape & body weight

**Management**
- Psychotherapy: CBT, group therapy, interpersonal therapy – combo psychotherapy & pharm more effective
- Pharmacotherapy: Fluoxetine (only FDA med for bulimia) – has been shown to reduce binge-purging cycle

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**Anorexia Nervosa**

- Failure to maintain a normal body weight, fear & preoccupation with body weight, body image, & being thin
- MC in F>M (90% F), 14-18 years old – seen in athletes & dancers, comorbidity with depression (60%)
- Highest mortality rate of all psychiatric conditions

**Clinical Manifestations**
- Exhibits behaviors targeted @ maintaining a low weight or certain body image – excess water, food related obsessions – it is ego-syntonic
- **Restrictive type**: strict, reduced caloric intake, dieting, fasting, excessive exercise & diet pills
- **Binge eating/purging type**: primarily engages in self-induced vomiting as well as diuretic, laxative or enema use

**Physical Examination**
- Emaciation, hypotension, bradycardia, skin/hair changes (lanugo), dry skin, salivary gland hypertrophy, amenorrhea, arrhythmias, osteopenia
- Russel’s sign: callouses on dorsum of the hand from self-induced vomiting
- BMI 17.5 or less OR body weight less than 85% of ideal weight

**Lab Findings**
- Hypokalemia (GI loss from laxatives/vomiting), increased BUN (dehydration), hypochloremic metabolic alkalosis, hypogonadotropic hypogonadism (low estrogen), & hypothyroidism

**Diagnostic Criteria**
- **Restriction of caloric intake** relative to requirements leading to **significantly low body weight**
- Intense morbid fear of fatness or gaining weight or persistent behaviors to prevent weight gain
- **Distorted body image** – self perception of being overweight

**Management**
- Medical Stabilization: hospitalization for under 75% expected body weight or patients who have medical complications; electrolyte imbalance may lead to arrhythmias
- Nutritional rehabilitation: MC complication is refeeding syndrome (inc. insulin leads to hypophosphatemia & cardiac complications)
- Psychotherapy: CBT, supervised meals, weight monitoring
**Pharmacotherapy:** if depressed, **SSRIs** (may also help with weight gain), atypical antidepressants (may help too)

**Suicide**

**Risk Factors**
- **Plan:** previous attempt is the strongest single predictive factor, organized plan > no plan
- Access to firearms is an increased risk
- Increases with **age, elderly white men** have highest risk in the US. **Females attempt suicide more than men but men are more successful,** Whites > blacks,
- **Psychiatric disorders:** majority who attempt/commit suicide have underlying psych disorders
- Substance abuse – increased risk
- Marital status: **alone** > never married > widowed > separated/divorced > married w/o children > married w/ child
- **Others:** (+) FHx of suicide, hx of impulsivity, chronic illness – among skilled workers, physicians are @ ↑ risk

**Management**
- Assuring the patient’s safety to prevent the patient from committing suicide, admission & psych evaluation
- Once safety is established – treatment is aimed @ diagnosing & treating any underlying mental disorder, including psychotherapy

---

**ORTHOPEDICS/RHEUMATOLOGY – 5%**

**Legg-Calve-Perthes Disease**

*Idiopathic* avascular necrosis of the femoral head in children due to ischemia of capital femoral epiphysis – usually unilateral

**Risk Factors**
- Children 4-10 years old, 4x M>F, obesity, coagulation abnormalities (Factor V Leiden)
- Decreased risk factors: lower incidence in African-Americans

**Clinical Manifestations**
- **Painless limping** for weeks (worsen w/ continued activity especially @ the end of the day)
- May have mild intermittent hip, thigh, knee or groin pain – may have an antalgic or Trendelenburg gait
- Restricted ROM (loss of abduction & internal rotation) – may have atrophy of the thigh muscles, may lag in bone age & height

**Radiographs**
- **Early:** increased density of the femoral epiphysis, widening of the cartilage space
- **Advanced:** deformity, (+) Crescent sign (microfractures with collapse of the bone)

**Management**
- **Observation:** activity restriction (non-weight bearing initially) with orthopedic follow up is initial treatment in most cases (usually self-limiting w/ revascularization within 2 years)
- May advocate for protected weight bearing during early stages until reossification is complete
- **Physical therapy or brace/cast,** NSAIDs for pain management
- **Surgical:** pelvic osteotomy may be indicated in some children >8 years of age, more advanced disease (lateral pillar B and B/C)

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**Congenital Hip Dysplasia**

**Abnormality in the shape & stability of the shape of the femoral head & acetabulum**

- Examination of the hip is performed during newborn assessment soon after birth & at every well-check visit until about 9 months of age & the child is walking independently

**Risk Factors**
- **Breech position @ delivery,** first-born children, females, positive family history

**Physical Examination**

Assessed for hip instability, asymmetry, or limited abduction:
- **Barlow maneuver:** gentle adduction without downward pressure to feel for dislocatability, resulting in a click, clunk or jerk
- **Ortolani maneuver:** abduction & elevation to feel for reducibility, resulting in a click, clunk or jerk
- Other findings may include: asymmetry & restricted hip abduction (look @ skin folds, femur length, or gait)
- In infants 3+ months, the dislocation may become relatively fixed & the Galeazzi test can be used instead
- Galéazzi’s test: check if knees are @ unequal heights when the hips & knees are flexed – the dislocated side will be lower

**Diagnosis**
- Clinical w/ confirmation with imaging
- **Ultrasound:** often used in children under 4 months of age
- AP Xray in older children (over 4 months)

**Management**
- ≤ 6 months of age: Pavlik harness
- 6 months-2 years: closed reduction in the OR (may need athrogram)

Other source (SmartyPANCE) suggests:

→ 6-15 months: hip spica cast
- Monitoring with routine hip radiographs until the child is skeletally mature may be needed (for osteonecrosis)
- **Hip dislocation assessment using Barlow & Ortolani maneuvers**
- In infants > 3 months, the dislocation may become relatively fixed & Galeazzi test can be used instead

### Juvenile (Idiopathic) Rheumatoid Arthritis

**Autoimmune mono or polyarthritis in children under 16 years old for 6+ weeks**

#### Types

1. **Systemic (Still’s disease):** daily/diurnal high fever, daily arthritis, salmon-colored pink migratory rash
   - No iridocyclitis (anterior uveitis) but associated w/ systemic symptoms (hepatosplenomegaly, lymphadenopathy),
   - 20% of all cases
2. **Pauci (oligo) articular:** under 5 joints involved, most commonly affects medium to large joints (knees, ankle)
   - **Iridocyclitis (anterior uveitis)**
   - 50% of all cases
3. **Polyarticular:** 5 or more small joints (usually symmetric)
   - **Iridocyclitis (anterior uveitis)**
   - Most similar to RA – includes morning stiffness; worst prognosis if RF (+)

#### Diagnosis

- Primarily clinical diagnosis
- Increased ESR & CRP, (+) ANA in oligoarticular, inc. ferritin
- Systemic (Still’s) usually associated with a negative RF & ANA
- (+) Rheumatoid factor in only 15%

#### Management

- **First-line therapy:** NSAIDs, glucocorticoids if no response to NSAIDs, physical therapy
- 2nd line or severe disease: Anakinra (interleukin-1 receptor inhibitor), Methotrexate, Leflunomide
- ANA (+) associated w/ increased risk of Iridocyclitis so routine eye exam every 3 months is recommended

### Malignant MSK Neoplasia

#### Osteosarcoma

- Malignant tumor of osteoblastic proliferation, **MC primary bone malignancy in children & young adults**
- 90% occur in the **metaphysis** of the long bones (distal femur MC, then proximal tibia & proximal humerus)
- **MC METs to the lung** (MCC of death)
- Gene is associated with familial retinoblastoma

#### Clinical Manifestations

- Localized bone pain (may occur after injury) and can be worse @ night, progressively worsening
- Joint swelling without systemic symptoms
- **Physical exam:** palpable soft tissue mass (may be tender to palpation)

#### Diagnosis

- Radiographs: "**hair on end**" or “**sunburst**” appearance (see photo) d/t tumor spicules of calcified bone radiating in right angles is classic (not specific)
- Other findings: mixed sclerotic & lytic lesions
- **Codman’s triangle:** ossification of raised periosteum (can be seen in Ewing sarcoma)

#### Biopsy: definitive diagnosis – malignant osteoid within the tumor & malignant sarcomatous stroma

#### Management

- Chemotherapy + surgical removal, with amputation (if neovascular) or limb-sparing resection (if not neovascular)

#### Ewing Sarcoma

- **2nd** MC primary bone malignancy in children & young adults (after osteosarcoma)
- Due to translocation between chromosomes 11 & 22
- **MC in Caucasian males 5-25 years old**
- Common sites for metastasis: bone, bone marrow, & lung (Lung is common cause of death)

#### Location

- 50% found in **diaphysis** of long bones – **femur (most common)**, pelvis, tibia, fibula are common sites

#### Clinical Manifestations
• Localized **bone pain** & swelling that may be accompanied by systemic symptoms (fever, malaise, weight loss)
• **Physical exam:** may have a palpable mass, local tenderness, or joint swelling

**Diagnosis**
- **Radiographs:** layered *periosteal reaction “onion skin” appearance* (see photo to R), lytic lesions with a “moth-eaten” appearance
- **Codman’s triangle:** ossification of raised periosteum (osteosarcoma too)
- **Labs:** increased ESR, leukocytosis
- **Histology:** sheets of monotonous small round blue cells, may have pseudo-rosettes (circle of cells with central necrosis)

**Management**
- Chemotherapy followed by limb-sparing resection when possible
- Radiation therapy when complete excision is not possible

### Benign MSK Neoplasia

#### Osteochondroma
- Cartilage-capped benign chondrogenic bony overgrowth arising on the external surface of a bone & areas of tendon insertion (proximal tibia, femur, and proximal hemurus)
- MC benign bone tumor, 10% may become chondrosarcomas
- MC between **10-20 years of age & in males**, begins in childhood & grows until skeletal maturity

**Clinical Manifestations**
- Painless, palpable mass – may develop symptoms of neurovascular compression

**Diagnosis**
- **Radiographs:** often **pedunculated** (narrow stalk) that grows away from the growth plate & involves the medullary tissue
- **Biopsy:** definitive

**Management**
- Observation if asymptomatic
- Marginal resection including cartilage cap if it becomes painful or if located in the pelvis (pelvis MC site of malignant transformation) – usually delayed until skeletal maturity

#### Osteoid Osteoma
- Benign bone tumor characterized by a small radiolucent nidus (less than 1-1.5 cm in diameter)
- Most commonly presents in second decade, M>F
- **Locations:** proximal femur MC, tibia, remainder of the femur, spine

**Pathophysiology**
- The nidus produces high levels of prostaglandins

**Clinical Manifestations**
- Progressively increasing pain worse @ night & unrelated to activity – the pain is relieved within 20-25 minutes of administration of NSAIDs
- May develop a limp, localized tenderness, & limitation of range of motion

**Diagnosis**
- **Radiographs:** small round lucency (nidus) with a sclerotic margin – CT/MRI more sensitive

**Management**
- NSAIDs w/ serial examinations or radiographs q6 months, untreated osteoid osteoma often spontaneously resolves over several years
- Surgical resection for symptomatic lesions not responsive to conservative treatment

#### Nursemaid Elbow

**Pathophysiology**
- **Radial head subluxation** – radial head is wedged into the stretched annular ligament, MC in children 2-5 y/o
- Lifting, swinging or pulling a child (longitudinal traction) while the forearm is pronated & extended

**Clinical Manifestations**
- Arm slightly flexed, forearm pronated & children refuses to use the arm (usually no swelling)
- Tenderness to palpation of the radial head (**lateral** elbow)

**Diagnosis**
- Clinical diagnosis (radiographs are normal)

**Management**
- **Closed reduction**: place pressure on the radial head w/ supination of the elbow followed by flexion of the elbow (supination-flexion technique)
  - Observe the child for normal function, if the child uses the arm after 15 minutes, no XR needed
  - If no use after 15 minutes, consider XR to r/o fracture or reattempt reduction

### Osgood-Schlatter Disease

**Apophysitis of the tibial tuberosity** (inflammation of the patellar tendon @ the insertion of the tibial tubercle) due to **overuse** (repetitive stress microtrauma) or small avulsions from repetitive knee extension & quadriceps contraction

**Pathophysiology**
- The apophysis is a muscle-tendon-bone attachment that is subject to injury from repetitive stress or an acute avulsion injury

**Risk factors**
- Most common in males, 10-15 years, during growth spurts, athletes

**Clinical Manifestations**
- **Activity-related anterior knee pain & swelling** (running, jumping, kneeling) & relieved with rest
- Prominence, swelling & tenderness to the anterior tibial tubercle

**Diagnosis**
- Imaging usually not necessary in classic presentations
- **Radiographs**: elevation, heterotopic ossification &/or bone fragmentation of the tibial tuberosity

**Management**
- **Conservative**: mainstay of treatment – RICE, NSAIDs, quadriceps stretching, knee immobilization – most syx resolve within 12-24 months
- Surgery only in refractory cases (if done, usually performed after growth plate has closed)

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### Scoliosis

**Lateral curvature of the spine**

- May be associated with kyphosis (humpback) or lordosis (sway back), more common in F, & (+) family history
- **Adolescent idiopathic**: Cobb angle 10+ degrees, age of onset at least 10 y/o, & no underlying etiology (neuromuscular, congenital)

**Screening**
- **Adams forward bend test**: most sensitive physical finding – thoracic or lumbar prominence on one side is seen w/ scoliosis
- **Scolimeter**: a 7 degree curve = abnormal
- **Forward bending sitting test**
- Assessment includes leg length, waistline asymmetry, midline skin defects, café-au-lait spots, foot deformities, & abdominal reflex asymmetry

**Diagnosis – Confirmatory**
- **Radiographs**: Cobb’s angle > 10 degrees measured on AP & lateral films
- **MRI**: not part of the initial evaluation without red flags or abnormal curve types – MRI may be indicated if rapid curve progression, left thoracic curve, abnormal reflexes, excessive kyphosis, or foot abnormalities

**Management**
- Based on skeletal maturity of the patient, severity of the deformity & curve progression
- **Observation**: Cobb angle under 25 degrees; & Risser grade 0 to 2 @ time of presentation – regular follow up to monitor progression every 6-9 months, bracing may be recommended if Cobb angle increases 5 degrees or more over a 3-6 month period

- **Bracing** may be needed to stop progression in patients with a flexible deformity & still skeletally immature: 1) if Cobb angle increases 5+ degrees over a 3-6 month period or 2) some patients with Cobb angle 30-39 degrees

- Bracing C/I if skeletally mature, little growth remaining, Cobb angle >50 degrees or <20 degrees
- **Surgical correction** may be an alternative to bracing if 40+ degrees & Risser grade 0-2 (skeletally immature)

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### Slipped Capital Femoral Epiphysis

**Displacement of the femoral head (epiphysis) from the femoral neck through the growth plate**

**Pathophysiology**
- Femoral head epiphysis slips **posterior & inferior** @ growth plate

**Risk factors**
- Children 8-16 years, **obese**, **African Americans, males** during adolescent growth spurt (due to weakness of growth plate & hormonal changes at puberty)
- If seen in children before puberty, suspect hormonal or systemic disorders (eg. hypothyroidism, hypopituitarism)

**Clinical Manifestations**
- Ipsilateral dull, achy hip, groin, thigh or knee pain with a **painful limp** worse with activity
- **Physical examination**: externally rotated leg on the affected side (limited internal rotation abduction & flexion on ROM of the hip), altered gait
- **Drehmann sign**: while in supine position, hip externally rotates and abducts w/ passive hip flexion

**Diagnosis**
XR: posterior displacement of femoral epiphysis, similar to ice cream slipping off a cone – best seen on frog-leg lateral pelvis or lateral hip view
• Widening of joint space, decrease in epiphyseal height & Steel sign – double density from superimposition of epiphysis & metaphysis

Management
• Non-weight bearing with crutches followed by internal fixation with pinning

Complications
• Avascular necrosis of the hip

ENDOCRINOLOGY – 3%

Diabetes Mellitus

Type I
• Insulin deficiency d/t pancreatic beta cell destruction – these patients often require exogenous insulin
• Onset usually under 30 y/o, 75% dx in childhood – peaks @ 4-6 years then 10-14 years
• NOT associated with obesity

Etiology
• Type 1A (Autoimmune): most common, often triggered by environmental factors (infection), increased w/ HLA DR3-DQ2 & DR4 genes
• Type 1B: non-autoimmune beta cell destruction

Clinical Manifestations
• Hyperglycemia without acidosis: MC initial presentation – polyuria, polydipsia, polyphagia
• Weight loss, lethargy
• Diabetic ketoacidosis (DKA): 2nd MC initial presentation (more common in type I); hyperglycemic hyperosmolar syndrome (more common in type II)
• Silent (asyx) incidental discovery

Type II
• Combo of insulin insensitivity (resistance) & relative impairment of insulin secretion (increased insulin levels early in the disease but may diminish with disease progression)

Risk Factors
• Likely d/t genetic & environmental factors, especially obesity (greatest risk factor) & decreased physical activity – 90% of type II diabetics are overweight
• MC 40 y/o+ with a history of impaired glucose tolerance, FHx, first degree relative, Hispanic, African-American, Pacific Islander, HTN, dyslipidemia, delivery of baby 9 lbs+, syndrome X, & insulin resistance
• CHAOS: Chronic HTN, Atherosclerosis, Obesity (central), Stroke

Clinical Manifestations
• Most asymptomatic (may be an incidental findings)
• Classic symptoms: polyphagia, polydipsia, polyuria
• Poor wound healing, increased infections, hyperglycemic hyperosmolar syndrome

Diagnosis
• Fasting Plasma Glucose Test – GOLD STANDARD:
  • Impaired tolerance (110-125), Diabetes (126+)
  • Fasting at least 8 hours on 2 occasions
• 2-Hr glucose tolerance test:
  • Impaired tolerance (140-199), Diabetes (200+)
  • 3h GTT gold standard in gestational diabetes
• Hemoglobin A1C:
  • Impaired tolerance (5.7-6.4%), Diabetes (6.5%+)
  • Indicates average blood sugar, 10-12 weeks prior to measurement
• Random glucose plasma over 200 indicates diabetes in a patient with classic syx or complications

Screening
• ADA: all adults 45+ q3 years OR any adult w/ BMI 25 kg/m2+ & 1 additional risk factor
• USPSTF: any 40-70 y/o that is overweight/obese q3y

Management of Type II DM
• Diet, exercise & lifestyle changes = initial management (Carbs 50-60%, fats 10%, protein 15-20%)
• Oral antihyperglycemic medications initiated if unable to control glucose w/ lifestyle changes – Metformin (MC – biguanide class), Sulfonylureas (Glipizide, Glyburide, Glimperide), Meglitinides (Repaglinide, Nateglinide), TZDs (Pioglitazone, Rosiglitazone[more CV Side effects]), DPP-4 inhibitors (Sitagliptin), GLP-1 agonists (Liraglutide), SGLT-2 inhibitors (-flozin)
• **Insulin** may be needed in uncontrolled with other meds

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Insulin Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-Acting</td>
<td>5-15min</td>
<td>45-75 min</td>
<td>2-4 hours</td>
<td>Given at the <strong>same time of meal</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Often used w/ intermediate or long acting insulin</td>
</tr>
<tr>
<td>Short-Acting</td>
<td>30m</td>
<td>2-4h</td>
<td>5-8h</td>
<td><strong>Given 30-60 minutes prior to meal</strong></td>
</tr>
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<td></td>
<td></td>
<td>Often used w/ intermediate or long acting insulin</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2h</td>
<td>4-12 hours</td>
<td>8-18 hours</td>
<td>Covers insulin for <strong>about half day or overnight</strong></td>
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<td></td>
<td>Often used w/ rapid or short acting insulin</td>
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<td></td>
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<td></td>
<td></td>
<td>NPH often given at bedtime</td>
</tr>
<tr>
<td>Long Acting</td>
<td>2h</td>
<td>3-9h</td>
<td>6-24 hours</td>
<td>Covers insulin for <strong>1 full day (basal insulin)</strong></td>
</tr>
<tr>
<td></td>
<td>2h</td>
<td>20-24+ h</td>
<td></td>
<td><strong>Glargine</strong> causes fewer hypoglycemia episodes than NPH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Long acting shouldn’t be mixed with other types of insulin</td>
</tr>
<tr>
<td>Pre-mixed</td>
<td></td>
<td></td>
<td></td>
<td><strong>Generally given 2x/day before mealtimes</strong></td>
</tr>
</tbody>
</table>

**Diabetes Mellitus Problems**

**Somogyi Phenomenon**
• Nocturnal hypoglycemia followed by rebound hyperglycemia

**Pathophysiology**
• Hyperglycemia occurs d/t surge in growth hormone after early AM hypoglycemia

**Management**
• Prevent hypoglycemia with any 1: **decreasing nighttime NPH dose**, move the evening NPH earlier, or give snack @ bedtime

**Dawn Phenomenon**
• Normal glucose until rise in serum glucose levels between 2-8am

**Pathophysiology**
• Results from decreased insulin activity & **nightly surge of counterregulatory hormones (during nighttime fasting)**

**Management**
• Reduce early AM hyperglycemia with any 1: increasing nighttime NPH dose, bedtime injection of NPH, avoid carb snack late, insulin pump usage early in the AM

**Insulin Waning**
• Progressive rise in glucose for bed to morning (seen when NPH evening dose is given before dinner)
• Due to ineffective dosing of NPH insulin

**Management**
• Move NPH insulin dose to bedtime or increasing evening NPH dose

**Hypoglycemia**
• Blood glucose level 70 mg/dL or less
• Complication of the management of DM – usually d/t too much insulin use, too little food, or excess exercise

**Clinical Manifestations**
• **Autonomic**: sweating, tremors, palpitations, nervousness, tachycardia, pallor, cool clammy skin
• **CNS**: HA, lightness, confusion, slurred speech, dizziness, irritability, difficulty concentrating, blurred vision, nausea, syncope

**Management of Mild to Moderate**
• 15-20g fast-acting carbohydrate, fruit juice, hard candies – recheck in 10-15 minutes

**Management of severe, unconscious, under 40 mg/dL**
• **IV bolus of D50 of IV glucagon** (SQ/IM if no IV access)
• Unknown cause? Order C-peptide, plasma insulin levels, & anti-insulin antibodies as part of the workup
• Elevated C-peptide seen in endogenous insulin production
**Diabetic Ketoacidosis**

- Consequence of **insulin deficiency & counterregulatory hormone excess**
- MC in type I DM (d/t insulin deficiency)

**Etiology**
- DKA is a response to **stressful triggers:**
  - **Infection** – MCC (UTI/pneumonia)
  - Discontinuation/inadequate insulin therapy, undx diabetics, MI, CVA, pancreatitis

**Clinical Manifestations**
- Polyuria, polydipsia, nocturia, weakness, fatigue, AMS changes, N/V, chest pain, abdominal pain
- PE: Tachycardia, tachypnea, hypotension, decreased skin turgor, fruity (acetone) breath, & Kussmaul respirations (deep, continuous respirations)

**Diagnosis**
- Plasma glucose 250+ (usually not greater than 600), decreased arterial pH (under 7.3) & bicarbonate (under 22) d/t high anion gap metabolic acidosis, increased serum osmolarity, positive ketones in the urine & serum

**Management**
- SIPS: Saline, Insulin (regular), Potassium repletion, Search for underlying cause
- IV fluids: critical initial step – Isotonic 0.9% (normal saline) until hypotension & orthostasis resolves, then switch to ½ normal saline (0.45%)
- When glucose levels become 250mg/dL/ less, use D5 version of current solution (to prevent hypoglycemia from insulin)
- Regular Insulin: lowers serum glucose & switches body from catabolic → anabolic state (this reduced ketones & fatty acid production as well as decreases gluconeogenesis)
- Potassium Repletion: despite serum K+ levels, patients are always in a total body potassium deficit
  - Correction of DKA will cause hypokalemia – unless serum K+ is 5.3+, repletion of K+ is recommended
  - If serum K+ is between 3.3-5.3, IV KCl (20-30 mEq/L) is added to each liter of IV replacement fluid
  - If serum K+ is under 3.3, IV KCl (20-40 mEq/L) should be given
  - If above 5.3, delay replacement until K+ falls below 5.3, check serum K+ levels hourly
- Treatment goals: closing the anion gap in DKA determines complete management – bicarb levels more important than glucose levels in determining severity of DKA
  - Administer bicarbonate only in severe cases because it is associated with complications – overcorrection, ↑ cerebral edema

**Hyperosmolar Hyperglycemia State**

- Consequence of **insulin deficiency & counterregulatory hormone excess**
- MC in type II DM, seen in older patients associated with more severe dehydration & higher mortality compared to DKA

**Pathophysiology**
- Illness leading to reduced fluid intake (infx MC) leads to **profound dehydration**, increased osmolarity, hyperglycemia, & total body potassium deficit
- HHS is not usually associated with severe ketosis or acidosis because they make enough insulin to prevent ketogenesis

**Clinical Manifestations**
- Hyperglycemia, increased thirst, polyuria, nocturia, weakness, fatigue, confusion, N, V, & mental status changes
- PE: tachycardia, tachypnea, hypotension, decreased skin turgor (dehydration), dry mouth & increased capillary refill time

**Diagnosis**
- Increased osmolarity (320+), ↑ serum glucose (600+), absence of significant acidosis (arterial pH 7.3+ & serum bicarb 15+)

**Management**
- SIPS: Saline, Insulin (regular), Potassium repletion, Search for underlying cause

**Hypercalcemia**

- Serum total calcium greater than 10.5 mg/dL or ionized fraction of calcium greater than 5.6 mg/dL
- 99% of calcium in bone, 1% in ECF – 50% of ECF Ca2+ is ionized (active form); nL Ca2+ levels 8.5-10 mg/dL, Vitamin D **required for intestinal calcium absorption**
- Ca2+ important for: bone, blood clotting, normal cell fx, & neuromuscular transmission & is maintained within a normal range via 3 major hormones: 1) PTH 2) calcitriol 3)Calcitonin
- Hypercalcemia stimulates increased calcitonin secretion → decreased blood calcium by decreasing calcium absorption in GI tract & kidney & increasing bone mineralization (osteoblasts build)

**Etiology**
- 90& of cases d/t primary hyperparathyroidism or malignancy
- **Primary hyperparathyroidism** MCC overall (parathyroid adenoma, multiple endocrine neoplasia, Lithium therapy)
- **Malignancy** d/t PTH-related protein production
- Thiazide diuretics, hyperthyroidism, vitamin D or A intoxication, & granulomas (sarcoidosis)

**Clinical Manifestations**
- Most patients are asymptomatic
- **Stones:** nephrolithiasis (calcium oxalate & phosphate)
- **Bones:** bone pain & fractures
- **Abdominal Groans:** ileus, constipation
- **Psychic moans:** depression, anxiety, cognitive dysfunction
- Increased vascular tone (HTN), decreased DTR & weakness (hypercalcemia decreases muscle contractions)

**Diagnosis**

1. **1st step** is to repeat the measurement to verify in an asymptomatic patient (and correct calcium for albumin)
2. **Blood:** elevated PTH, elevated Calcium, decreased Phosphorous
   - Ionized serum calcium more accurate than total serum calcium
3. **Intact PTH:** once hypercalcemia is confirmed to r/o primary hyperparathyroidism
4. **PTH-related protein** often ordered if intact PTH is normal or low (to r/o malignancy)
5. **1,25 Vitamin D levels & 24h urinary Ca2+** (Ca2+ excretion usually elevated/high-normal in hyperparathyroidism & malignancy)
6. **EKG:** shortened QT interval, prolonged PR interval & QRS widening

**Management**

- **Mild (less than 12 mg/dL):**
  - No immediate tx needed, treat underlying cause & increase water intake (promotes calcium excretion)
- **Moderate (12 - 14 mg/dL):**
  - IV fluids initial management of choice if associated w/ significant symptoms (promotes excretion), IV loop diuretics (Furosemide) can be added to promote calcium excretion
  - Calcitonin and Denosumab may be helpful adjunct in malignancy-related hypercalcemia, GC in granulomatous disease

**Hyperthyroidism**

**Etiology**

- **Grave’s Disease:** iatrogenic thyrotoxicosis, thyroiditis (postpartum, deQuervain, silent, early stage), toxic multinodular goiter, toxic adenoma, TSH-secreting pituitary adenoma, Meds – amiodarone, Excess intake of T3/T4

**Clinical Manifestations**

- Calorigenic: increased metabolic rate – all processes increased, except for menstrual flow, (+) heat intolerance, weight loss
- **Skin:** Skin warm, moist, soft, fine hair, alopecia, easy bruising, – have goiter
- **CNS:** Hyperactivity: anxiety, fine tremors, nervousness, fatigue, weakness, increased sympathetic
- **GI:** Diarrhea, hyperdefecation
- **CVS:** tachycardia, palpitations, high-output heart failure, EKG changes such as PVCs

**Diagnosis**

- Low TSH, with high T3 & T4 confirms hyperparathyroidism
- With Graves’ disease only T3 is elevated & there will be (+) anti-thyrotropin antibodies
- Sometimes radioactive iodine uptake done

**Grave’s Disease**

**Pathophysiology**

- Autoimmune disease – **TSH receptor autoantibodies** target & stimulate the TSH receptor on the thyroid gland → increased thyroid hormone production, thyroid gland enlargement, & hyperthyroidism
- **Ophthalmology:** TSH-receptors autoantibodies activate retroocular fibroblasts & adipocytes, leading to orbitopathy (specific to Graves)

**Clinical Manifestations**

- **Symptoms of hyperthyroidism:** palpitations, heat intolerance, tremors, weight loss, atrial fibrillation, etc.
- **Specific to Grave’s:**
  - **Ophthalmopathy:** proptosis, exophthalmos, lid lag, diplopia, vision changes
  - **Pretibial Myxedema:** swollen red or brown patches on legs w/ non-pitting edema
  - Physical examination: diffusely enlarged nontender goiter, thyroid bruit

**Diagnosis**

- **Primary hyperthyroid profile:** decreased TSH + increased free T4 or T3
- **Hallmark:** (+) Thyroid-stimulating immunoglobulin (TSH-receptor antibodies)
- **Radioactive uptake scan:** diffuse, increased iodine uptake

**Management**

- **Radioactive iodine:** MC therapy used, ablates the thyroid within 6-18 weeks, may exacerbate ophthalmopathy initially
  - C/I in pregnant & lactating women
- **Thiouracils:** Methimazole or Propylthiouracil (Methimazole generally preferred d/t less AE, PTU preferred in 1st trimester & for thyroid storm)
- **Beta-blockers** (Propranolol or atenolol): can be used to rapidly ameliorate symptoms such as tremor, HTN, Afibb & tachy
**Ophthalmopathy:** Glucocorticoids best initial therapy (usually given before radioactive iodine in severe ophthalmopathy)

### Hypothyroidism

#### Etiology
- **Iodine deficiency (dietary) +/- Cretinism, Hashimoto's thyroiditis, thyroiditis (postpartum, deQuervain, silent, later stage), pituitary hypothyroidism, hypothalamic hypothyroidism, Riedel's thyroiditis, Meds: Lithium, Amiodarone, alpha interferon**

#### Clinical Manifestations
- **Calorigenic:** decreased metabolic rate – all processes decreased, except for menstrual flow, (+) cold intolerance, weight gain
- **Skin:** dry, thick rough skin, loss of outer 1/3 of eyebrow, goiter, nonpitting edema (myxedema)
- **CNS:** hypoactivity – fatigue, sluggishness, memory loss, depression, decreased DTR, hoarseness of voice
- **GI:** constipation, anorexia
- **CVS:** bradycardia, decrease cardiac output, pericardial effusion

#### Diagnosis
- **Primary hypothyroid profile:** increased TSH + decreased free T4 or T3

---

**Cretinism**

#### Etiology
- Lack of maternal iodine intake in developing countries
- Dysgenesis of the thyroid gland or defect in enzymes in developed countries
- May be acquired if maternal TSH-receptor blocking antibodies passed into fetal circulation via the placenta

#### Clinical Manifestations
- **Mental developmental delays, short stature**
- **Symptoms of hypothyroidism:** decreased metabolic rate, cold intolerance, dry thick rough skin, constipation, weight gain, menorrhagia, myxedema, weakness & lethargy
- **Goiter symptoms** in older children – hoarseness & dyspnea (tracheal compression)
- **Physical examination:** coarse facial features, macroglossia, umbilical hernia, hypotonia (decreased DTRs), prolonged jaundice, feeding problems & congenital malformations

#### Diagnosis
- **Primary hypothyroid profile:** increased TSH + decreased free T4 or T3

#### Management
- Levothyroxine (synthetic T4)

---

**Subclinical Hypothyroidism**

#### Hypothyroidism determined by laboratory tests (isolated increased TSH) in patients w/ little or no symptoms

- Subclinical hypothyroidism may be assoc/ w/ increased risk of CV disease, especially when serum TSH concentration is 10+

#### Diagnosis
- **Isolated increased TSH** (hypothyroid) + **normal** free T4 &/or T3 (subclinical)

#### Management
- Observation with follow up TSH
- Levothyroxine may be given if TSH 10+ to prevent CV complications

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**Hashimoto Thyroiditis**

#### Untreated congenital hypothyroidism

#### Pathophysiology
- **MCC of hypothyroidism in the US,** with an increased incidence in women 30-50 years
- **Autoimmune thyroid cell destruction** by anti-thyroid peroxidase & anti-thyroglobulin antibodies (& TSH receptor-blocking antibodies to a lesser extent)

#### Clinical Manifestations
- **Symptoms of hypothyroidism:** decreased metabolic rate, fatigue, cold intolerance, dry thick rough skin, constipation, weight gain, menorrhagia, myxedema (eyelid & facial edema), weakness & lethargy
- **Goiter symptoms** – hoarseness & dyspnea (d/t tracheal compression)
- Women may have galactorrhea (d/t increased prolactin)
- **Physical examination:** thyroid gland may be atrophic, normal or enlarged; bradycardia, decreased DTR, loss of outer 1/3 of eyebrows, myxedema

#### Diagnosis
- **Primary hypothyroid profile:** increased TSH + decreased free T4 or T3 – may be normal/subclinical in early disease
- (+) Antithyroid peroxidase &/or anti-thyroglobulin antibodies
- Radioactive uptake scan: diffuse decreased iodine uptake
• **Biopsy:** rarely done – **lymphocytic infiltration** w/ germinal centers & Hurthle cells (enlarged epithelial cells with abundant eosinophilic granular cytoplasm)

**Management**
- **Levothyroxine**

**Myxedema Coma**

*Rare, extreme form of hypothyroidism with a high mortality rate*

**Etiology**
- **MC in elderly women w/ longstanding hypothyroidism in Winter**

**Pathophysiology**
- Usually an acute precipitating factor (infx, CVA, CHF, sedative/narcotic use) in a patient with longstanding hypothyroidism, discontinuation/noncompliance w/ Levothyroxine therapy or failure to start Levothyroxine after tx for hyperthyroidism

**Clinical Manifestations**
- **Severe signs of hypothyroidism:** bradycardia, obtundation (coma), hypothermia, hypoventilation, hypotension, hypoglycemia, hyponatremia

**Diagnosis**
- **Primary hypothyroid profile:** increased TSH + decreased free T4 (free T4 & T3 may be so low that it’s undetectable), serum cortisol

**Management**
- **IV Levothyroxine (synthetic T4) + supportive** – ICU admission, passive warming, IV normal saline, IV glucocorticoids often

**Obesity**

*BI of 30 kg/m^2 or greater or body weight 20%+ over the ideal weight*

**Complications**
- Obesity assoc. w/ increased risk for coronary disease, DM II, breast & colon cancer

**Management**
- **Behavior modification:** exercise & dietary changes
- **Medical therapy:** antidepressants if underlying depression
- **Anti-obesity meds:** Orlistat (decreases GI fat digestion), Lorcaserin (serotonin agonist)
- **Surgical options:** gastric bypass, gastric sleeve, gastric banding & bariatric surgery

**Screening**
- Screen all adults & children 6 y/o+

**Short Stature – Growth Hormone Deficiency – Pituitary Dwarfism**

*Deficiency in pituitary production of growth hormone*

**Etiology**
- Congenital or acquired (tumor, infiltrative disease, bleeding into pituitary – Sheehan’s syndrome), pituitary infarction, or radiation therapy

**Clinical Manifestations**
- Children/Infancy: short stature, growth delays, **dwarfism, fasting hypoglycemia**
  - Infancy: hypoglycemia & micropenis
- Adults: mild→moderate central obesity, increased BP, **dyslipidemia**, decreased bone mass & density, decreased CO, muscle wasting, increased inflammatory markers, impaired concentration

**Diagnosis**
- Serial measurements over 2.5 standard deviations below the normal mean should prompt GH eval
- **Labs:** decreased GH, decreased insulin-like growth factor 1 & decreased insulin-like growth factor binding protein-3
- **XR of child’s hand to determine bone age** – the bone age in affected children is usually 2 years+ behind chronological age
- **Arginine & sleep stimulation test** – no change in GH release if hypopituitarism
- **CT/Brain MRI** to evaluate cause

**Management**
- Subcutaneous injections of **recombinant human growth hormone** to try & stimulate normal growth
- Surgery may be necessary to remove a pituitary adenoma if that is the cause

**HEMATOLOGY – 3%**

**Anemias**

*Hgb under 13.5 or Hct under 39% in males, Hgb under 12 or Hct under 37% in females,*

**Microcytic: Iron Deficiency Anemia**

- MCC of anemia worldwide
Etiology
- **Chronic blood loss**: MC in US – excessive menstruation, occult GI blood loss (colon ca) – parasitic hookworm MCC of blood-loss related IDA in resource-poor countries
- **Decreased absorption**: diet (MCC worldwide), Celiacs, bariatric surgery, H. pylori

Risk Factors
- **Increased metabolic requirements**: children, pregnant & lactating women
- **Cow milk ingestion in young children**: infants fed cow’s milk younger than 1 y/o, toddlers fed large volumes of cow’s milk

Pathophysiology
- Decreased RBC production d/t lack of iron & decreased iron stores (decreased ferritin) (iron is stored in ferritin primarily in bone marrow, liver & spleen)

Clinical Manifestations
- Classic symptoms of anemia: fatigue, weakness, exercise intolerance, dyspnea
- Palpitations, SOB, headaches, tinnitus
- CNS: poor concentration, apathy, irritability, poor school performance, cognitive disturbances, restless leg syndrome

Pagophagia: craving for ice (specific); Pica: appetite for non-food substances (clay, starch)

PE: koilonychia (spooning of the nails), angular cheilitis (inflammation of one/both corners of mouth), tachycardia, glossitis (smooth tongue), signs of anemia (pallor)

Diagnosis
- CBC: microcytic hypochromic anemia classic (may be normocytic, normochromic early on), ↑RDW (RBC distribution width), anisocytosis; ↓ reticulocytes – may have thrombocytosis & poikilocytosis
- Iron studies: decreased ferritin under 15 ng/mL, (pathognomonic & one of the earliest findings), ↑TIBC (transferrin), ↓ transferrin saturation under 15-20%, ↓ serum iron
- Bone marrow: absent iron stores definitive diagnosis (rarely performed)
- Peripheral smear: poikilocytosis (pencil/cigar-shaped cells)

Management
- **Iron replacement** → increased reticulocytes (within 5-10 days), correction of anemia (6-8weeks), & iron stores repletion (1-6m)
  - Ferrous sulfate 3mg/kg once or twice daily – usually given as a 325 mg dose
  - Increased absorption – take w/ vitamin C, with water or orange juice & on an empty stomach – give iron 2h before or 4h after ingestion of antacids
  - Preparations: oral (ferrous sulfate), iron-containing formulas in bottle-fed infants, iron-enriched food & red meats – parenteral

Screening
- Check hemoglobin & hematocrit @ 12 & 18 months, 12 years (in females)

-----------------------------------
**Microcytic Thalassemia**

*Unbalanced hemoglobin synthesis d/t decreased production of one globin polypeptide chain (beta or alpha)*

- After 6 months, adult Hgb = predominant hemoglobin - HgbA (adult) = (αα, ββ) – 95%
  - HgbA2 (αα, δδ) – 1.5-3%, HgbF (fetal) - (αα, γγ) - trace
- **Think thalassemia if microcytic hypochromic anemia, normal/↑ serum iron, normal/↑ ferritin OR no response to iron treatment**

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**Alpha Thalassemia**

- Decreased α-globin chain production – 4 genes determine this type
- **MC in SE Asians** 68%, Africans 30%, Mediterraneanean (5-10%)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Abnormal Alleles</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silent Carrier State</td>
<td>1/4</td>
<td>Clinically normal (usually asymptomatic)</td>
</tr>
<tr>
<td>α-thalassemia minor (trait)</td>
<td>1/4</td>
<td>Mild microcytic anemia – no treatment needed</td>
</tr>
<tr>
<td>α-thalassemia intermedia</td>
<td>3/4</td>
<td>Presents similar to β-thalassemia major</td>
</tr>
<tr>
<td>Hydrops fetalis</td>
<td>4/4</td>
<td>Assoc. w/ stillbirth or death shortly after birth</td>
</tr>
</tbody>
</table>

**Hgb electrophoresis in Alpha Thalassemia:**
- 1 & 2 gene deletion: normal Hb ratios in adults (distinguishes alpha from beta)
- 3 gene deletion: presence of HbH (beta chain tetramer) – Heinz bodies
- 4 gene deletion: presence of Hb Bart (gamma tetramer)
- DNA analysis provides definitive diagnosis

-----------------------------------
*Hemoglobin H Disease (Alpha Thalassemia Intermedia)*

A type of alpha thalassemia characterized by decreased alpha-globin chain production

Pathophysiology

- ¾ gene deletions cause decreased alpha chain production – excess beta chains form insoluble beta chain tetramers (Heinz bodies) with no O2-carrying capacity in the RBCs
- The presence of Heinz bodies in RBCs leads to destruction by the spleen (hemolytic anemia) which is characterized by moderate→severe anemia (Hgb levels of 7-10 g/dL)
Clinical Manifestations

- Patients are usually **symptomatic @ birth** – neonatal jaundice & anemia
- Symptoms of anemia & hepatosplenomegaly, pigmented gallstones
- **Increased bone marrow hematopoiesis**: frontal bossing, maxilla overgrowth

**Diagnosis**

- **Microcytosis, hemolytic anemia** (schistocytes, tear drop cells, increased reticulocytes), **target cells**, basophilic stippling, increased RBC count, decreased Hgb (7-10 g/dL)
- (+) **Heinz bodies**
- Hemolysis (increased indirect bilirubin, decreased haptoglobin)
- **Iron overload**: normal or increased serum iron
- **Hemoglobin electrophoresis**: presence of HbH (beta chain tetramer) – confirms diagnosis!

**Management**

- **Episodic blood transfusions** during periods of increased hemolysis or severe anemia (infection, pregnancy)
- Vitamin C & folate supplementation (substrates for RBC production)
- **Iron chelating agents (Deferoxamine, Deferasirox)** prevent iron overload & remove excess iron from chronic transfusions – also avoid iron supplementation
- Splenectomy in some cases (stops RBC destruction) may be needed by 2nd or 3rd decade
- **Definitive treatment in major**: bone marrow transplant

---

**Beta Thalassemia**

- Genetic hemoglobinopathy characterized by **decreased production of beta-globin chains**, leading to excess alpha chain
- **Risk factors**: MC in Mediterranean (Greek, Italian), Africans & Indians

**Clinical Manifestations**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Abnormal Alleles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta thalassemia trait (minor)</td>
<td>½</td>
</tr>
<tr>
<td>Beta thalassemia Major (Cooley’s Anemia)</td>
<td>2/2</td>
</tr>
<tr>
<td>Beta-thalassemia Intermedia</td>
<td>Mild homozygous forms</td>
</tr>
</tbody>
</table>

**Clinical Manifestations of beta thalassemia major**

- **Beta thalassemia major (Cooley’s anemia)**: both beta genes are mutated – deficient beta chain production leads to excess alpha chains that aren’t able to form tetramers which leads to ineffective erythropoiesis & shortened RBC life span
- **Symptoms often occur after 6 months of life** (when fetal hemoglobin begins to diminish)
- **Anemia**: severe, chronic anemia: pallor, irritability, dyspnea, mental delays; **hemolytic anemia**: hepatosplenomegaly, jaundice
- **Extramedullary hematopoiesis**: bony abnormalities, abnormal, delayed skeletal development, extramedullary expansion (frontal bossing, “hair on end” appearance of the skull, osteoporosis, abnormal ribs)
- **Osteoporosis**: by age 10, the haematopoietically-active red marrow is replaced by inactive yellow-marrow which leads to osteoporosis, compression fractures, cord compression, scoliosis & disc degeneration
- **Endocrine abnormalities**: (d/t iron overload) – hypogonadism, diabetes, growth failure, hypothyroidism
- Enlarged kidneys (d/t increased hematopoiesis in the kidneys)
- **Cardiac dysfunction**: heart failure (high output), arrhythmias

**Diagnosis**

- **CBC in beta thalassemia major**: peripheral smear will show **target cells**, teardrop cells, basophilic stippling, nucleated RBCs

**Management**

- **Beta thalassemia minor (trait)**: no treatment needed, genetic counseling, **moderate disease**: folate (if increased reticulocyte count), avoid oxidative stress (Sulfa drugs)
- **Beta thalassemia major**: **often requires transfusions**
- **Macrocytic: Vitamin B12 (Cobalamin) Deficiency**
- Sources of B12: natural sources mainly animal in origin (meats, eggs, dairy)
- Absorption: B12 is released by the acidity of the stomach & combines with intrinsic factor, where it is absorbed mainly in the distal ileum

**Pathophysiology**

- B12 deficiency → **abnormal synthesis of DNA**, nucleic acids & metabolism of erythroid precursors
- B12 is needed to convert homocysteine to methionine for DNA synthesis

**Etiology**

- **Decreased absorption**: pernicious anemia MCC (lack of intrinsic factor d/t parietal cells antibodies, leading to gastric atrophy), Zollinger-Ellison syndrome, Celiac disease, meds (H2 blockers & PPIs), fish tapeworm
- **Decreased intake**: vegans (lack of consumption of meat & meat products)
• Anemia symptoms similar to folate but associated with neurologic abnormalities
• **Hematologic:** fatigue, exercise intolerance, pallor
• **Epithelial:** glossitis, diarrhea, malabsorption
• **Neurologic symptoms:** symmetric paresthesia MC initial symptoms (especially involving the legs), lateral & posterior spinal cord demyelination & degeneration: ataxia, weakness, vibratory, sensory & proprioception deficits, decreased DTRs (hypotonia), (+) Babinski, seizures, psychoses

**Diagnosis**

**CBC with smear:** increased MCV + megaloblastic anemia (**hypersegmented neutrophils, macro-ovalocytes**, mild leukopenia &/or thrombocytopenia
• Decreased serum B12 levels, increased LDH, **increased homocysteine**
• **Increased methylmalonic acid** distinguishes B12 from folate deficiency

**Management**
• **Routes of administration:** oral, sublingual, nasal & IM/deep subcutaneous injection
• **Symptomatic anemia or neuro findings:** start with IM B12 – in adults, IM cyanocobalamin injection weekly until the deficiency is corrected & then once monthly – patients can be switched to oral after symptom resolution
• If pernicious anemia – patients need IM therapy monthly for life
• **Dietary deficiency:** oral B12 replacement
• **B12 has NEURO SYMPTOMS & INCREASED MMA, FOLATE IS NO NEURO & NORMAL MMA**

**Macrocytic:** Folate Deficiency

**Pathophysiology**
• Function of folate: folate required for DNA synthesis – deficiency causes abnormal synthesis of DNA, nucleic acids & metabolism of erythroid precursors

**Etiology**
• **Inadequate intake:** MCC (alcoholics, unbalanced diet)
• **Increased requirements:** pregnancy, infancy, hemolytic anemias, malignancy, psoriasis (increased skin turnover)
• **Impaired absorption:** Celiacs, inflammatory bowel disease, chronic diarrhea, anticonvulsants (phenytoin, phenobarbital, carbamazepine)
• **Impaired metabolism:** Methotrexate, Trimethoprim, Pentamidine, antiseizure meds (phenytoin, valproic, carbamazepine), ethanol
• **Loss:** dialysis

**Clinical Manifestations**
• Anemia symptoms similar to folate but associated with neurologic abnormalities
• **Hematologic:** fatigue, exercise intolerance, pallor
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• Decreased serum B12 levels, increased LDH, **increased homocysteine**
• **Increased methylmalonic acid** distinguishes B12 from folate deficiency

**Normocytic:** Anemia of Chronic Disease

**Etiology**
• Chronic inflammatory conditions: chronic infection, inflammation, autoimmune disorders, malignancy

**Pathophysiology**
• 3 main factors decrease serum iron:
  1. **Increased hepcidin:** hepcidin is an acute phase reactant that blocks the release of iron from macrophages & reduces GI absorption of iron
  2. **Increased ferritin:** ferritin is an acute phase reactant that sequesters iron into storage
  3. **Erythropoietin inhibition** via cytokines

**Diagnosis**

**CBC with smear:** milk normocytic normochromic anemia (may present with microcytic hypochromic anemia early on), Hgb usually not less than 9-10 mg/dL – decreased reticulocytes, with normal to increased RDW
• **Iron studies:** normal to increased ferritin + normal/decreased TIBC + decreased serum iron

**Management**
• Treating the underlying disease will help to correct the anemia
• Erythropoietin-alpha if renal disease or low erythropoietin levels

**Hemolytic Anemias**

• Anemia d/t increased RBC destruction when the rate of destruction exceeds the bone marrow’s ability to replace destroyed cells

  Two types:
  
  - Intrinsic (inherited disorders): sickle cell, thalassemia, G6PD deficiency, hereditary spherocytosis
  - Extrinsic (acquired disorders): autoimmune hemolytic anemia, DIC, TTP, HUS, paroxysmal nocturnal hemoglobinuria, hypersplenism

**Diagnosis**

- **Peripheral smear: increased reticulocytes** (immature RBCs), schistocytes (bite cells) if intravascular hemolysis
- **Haptoglobin decreased** bc it becomes depleted when it binds the free Hgb with continued RBC destruction
- **Indirect bilirubin increased** d/t increased RBC destruction, which overwhelms the liver’s ability to convert it to direct
- **Reticulocyte count increases** in response to increased RBC destruction, the immature RBCs (reticulocytes) attempt to replace the mature RBCs that are being destroyed
- **LDH increases** because it is an enzyme that is released from destroyed RBCs

To Distinguish between the hemolytic anemias

- **Sickle cell anemia:** sickled cells on peripheral smear, Hgb S on hemoglobin electrophoresis
- **Thalassemia:** see above
- **G6PD deficiency:** EPISODIC hemolytic anemia associated with sulfa drugs, fava beans, infections
- **Hereditary spherocytosis:** microspherocytes, Coombs NEGATIVE
- **Autoimmune hemolytic anemia:** microspherocytes, Coombs POSITIVE

**Bleeding Disorders**

**Pathophysiology**

- Prolonged PTT: Heparin, DIC, vWD, Hemophilia A & B, antiphospholipid antibody syndrome
- Prolonged PT: Warfarin therapy, Vitamin K deficiency, DIC

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**Hemolytic Uremic Syndrome**

**Risk Factors**

- Predominantly seen in children with a recent hx of GE

**Clinical Manifestations**

- Triad of: thrombocytopenia, hemolytic anemia & renal dysfunction

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**Factor V Leiden Mutation**

**Pathophysiology**

- MC inherited cause of hypercoagulability (thrombophilia)

**Clinical Manifestations**

- Mutated Factor V is resistant to breakdown by activated protein C leading to increased hypercoagulability
### Brain Tumors

**Epidemiology**
- 2/3 of intracranial tumors are located in the posterior fossa
- **Glioblastoma** are the MC tumors in childhood & consist of astrocytomas & ependymomas
- Medulloblastomas is a primitive neuroectodermal tumor (PNET) common only in childhood

**Clinical Manifestations**
- Present with either s/sx of increased ICP or with focal neurological signs
- Alterations in personality are often the first symptoms of a brain tumor
- Nystagmus is the classic finding in posterior fossa tumors & tumors in this area tend to result in hydrocephalus secondary to CSF outflow obstruction

### INFRATENTORIAL TUMORS:

1. **Grade I Astrocytoma**
   - MC primary childhood CNS tumor w/ best posterior fossa tumor prognosis, 5-year survival 90%+

### Protein C or S Deficiency

**Etiology**
- **Inherited**: both are autosomal-dominant inherited hypercoagulable disorders (protein C is MC)
- **Acquired**: end-stage liver disease, severe liver disease w/ synthetic dysfunction, early Warfarin administration (vitamin K antagonist)

**Pathophysiology**
- **Protein C & S** are vitamin K-dependent anticoagulant proteins produced by the liver that stimulates fibrinolysis & inactivates factors V and VIII
- **Decreased protein C or S levels lead to hypercoagulability**

**Clinical Manifestations**
- **Increased incidence of DVT & PE**, (VTE more common in Protein S), **Warfarin-induced skin necrosis (protein C)**
- Purpura fulminans in newborns – red purpuric lesions at pressure points, progresses to painful black eschars

**Diagnosis**
- Protein C and S functional assay, plasma protein C & S antigen levels
- Genetic testing not routinely performed

**Management**
- **Thrombosis**: protein C concentrate; indefinite anticoagulation
- **Warfarin-induced necrosis**: immediately discontinue warfarin, administer IV vitamin K, heparin, protein C concentrate or FFP

### Antithrombin III Deficiency

**Etiology**
- **Inherited**: autosomal-dominant
- **Acquired**: liver disease, nephrotic syndrome, DIC, chemotherapy

**Pathophysiology**
- Normally, antithrombin III inhibits coagulation by neutralizing the activity of thrombin (Factors IIA, IXA, XA)
- Decreased levels lead to increased risk of clotting

**Clinical Manifestations**
- **Increased incidence of DVT & PE**

**Diagnosis**
- Antithrombin III assays

**Management**
- **Asymptomatic**: anticoagulation only before surgical procedures
- **Thrombosis**: high-dose IV heparin followed by oral anticoagulation therapy indefinitely

### Antiphospholipid Syndrome (APS)

**Etiology**
- **Inherited**: both are autoimmune disorders
- **Acquired**: systemic lupus erythematosus (SLE), infections, pregnancy

**Pathophysiology**
- **Antiphospholipid antibodies**: interfere with the formation of normal clots

**Clinical Manifestations**
- **Thromboembolism**: increased risk of DVT, PE, stroke, aortic dissection
- **Vasculitis**: livedo reticularis, skin ulcers, arthritis
- **Recurrent miscarriages**: increased risk of miscarriage

**Diagnosis**
- **Antiphospholipid antibodies**: at least two assays positive

**Management**
- **Thrombosis**: anticoagulation with LMWH or warfarin
- **Recurrent miscarriages**: anticoagulation during pregnancy with LMWH or warfarin
• Derived from astrocytes (star-shaped glial cells of the brain & spinal cord that support the endothelial cells of the blood-brain barrier, provide nutrients for cells, maintain extracellular ion balance, & repair the brain after injury
• MC type in children: pilocytic astrocytoma (grade I) aka Juvenile Astrocytoma – typically localized, considered “most benign,” MC in children & young adults, cerebellar astrocytoma & desmoplastic infantile other grade I astrocytomas

Clinical Manifestations
• Focal deficits – most common, depends on location of lesion; MC in frontal & temporal areas of the cerebral hemisphere
  • General symptoms: headaches (may be worse in morning, may wake patients up at night, may be positional), cranial nerve deficits, AMS changes, neuro deficits, ataxia, vision changes, weakness
• Increased intracranial pressure d/t mass effect → HA, N, V, papilledema, ataxia, drowsiness, stupor
• Location of tumor determines other s/sx:
  ➔ Cerebellum: weakness, tremor, ataxia
  ➔ Visual pathway: visual loss, nystagmus, proptosis
  ➔ Spinal cord: pain, weakness, gait disturbance

Diagnosis
• Brain biopsy: pilocytic astrocytomas (grade I) generally form sacs of fluid (cysts) or may be enclosed within a cyst – although usually slow growing, may become very large – fibrillary astrocytes w/ dense cytoplasmic inclusions seen [Rosenthal fibers]
• MRI

Management
• Surgical resection – combined with radiation and chemo
2. Medulloblastoma
• MC malignant posterior fossa tumor & most prevalent brain tumor in children under 7, prognosis dependent on size & dissemination but most have 5-year survival around 70%
• Bimodal peak @ age 3-4 years & at age 8-10 years
• Tends to invade the fourth ventricle & spread along CSF pathways
• “Drop metastases” occur in medulloblastoma, seeding the spinal cord from the fourth ventricle

Clinical Manifestations
• Vomiting, HA, nausea, visual changes (double vision), and unsteady walking or clumsiness

Diagnosis
• Histologic analysis shows deeply staining nuclei w/ scant cytoplasm arranged in pseudorosettes

Management
• Surgical resection – combined with radiation and chemo
3. Craniopharyngioma
• One of the MC supratentorial brain tumors of childhood associated with short stature or other endocrine associated problems
• Slow growing and benign tumor may be confined to the sella turcica or extend through the diaphragma sellae & compress the optic nerve or rarely, obstruct CSF flow

Diagnosis
• 90% of craniopharyngiomas show calcification on CT scan;

Treatment
• Surgical resection

Pathophysiology
• Ependymal cells line the ventricles & parts of the spinal column
• MC in children (mean age is 5 years), MC seen in 4th ventricle, spinal cord & medulla – may cause cauda equina in adults, 3rd MC CNS tumor in children (after astrocytoma & medulloblastoma)

Clinical Manifestations
• Infants: increased head size, irritability, sleeplessness, vomiting – may present with developmental delay
• Older children & adults: N, V, HA
• Initial symptoms typically related to increased ICP
• Changes in mood, personality or concentration may occur as well as: seizures, balance, gait disturbance, or symptoms of spinal cord compression (back pain, loss of bladder and bowel control)

Diagnosis
• CT scan/MRI with contrast: hypointense T1, hyperintense T2, enhances with gadolinium
• Brain biopsy: perivascular pseudo rosettes (tumor cells surrounding a blood vessel)

Management
• Surgical resection → adjuvant radiation therapy, chemotherapy not as helpful as usual
• Total or near total removal: 51-80% survival; less than 90% removal: 0-26% survival

Hemophilia A (Factor VIII Deficiency)

Risk Factors
• X-linked recessive disorder almost exclusively in males (rarely in homozygous females) & can be d/t spontaneous mutation
• **MC type of hemophilia** w/ first episode occurring under 18 years
• Lack of Factor 8 affects the clotting cascade → **failure of hematoma formation**

**Clinical Manifestations**

- **Hemarthrosis (80%): delayed bleeding or swelling in weight-bearing joints** (ankles, knees, elbows), soft tissues & muscles (forehead hematoma)
- Excessive hemorrhage d/t trauma & surgery or incisional bleeding (tooth extraction)
- Epistaxis, bruising, GI or urinary tract hemorrhage & less commonly presents with purpura, petechiae (because platelet function is normal) or spontaneous hemorrhage (except in severe form)

**Diagnosis**

- CBC & coagulation studies: Prolonged aPTT – normal PT, fibrinogen & platelet levels (bleeding time)
- Mixing studies: PTT corrects with mixing studies (factor deficiency)
- Most sensitive: low Factor VIII

**Management**

- **Factor VIII infusion** first-line therapy to increase levels 25-100% (depending on severity) – can be given in response to acute bleeding episode or prophylaxis (prior to surgery or after trauma)
- Desmopressin (DDAVP): transiently increases Factor VIII & vWF release from endothelial stores – may be used prior to procedures to prevent bleeding in mild disease

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**Hemophilia B (Factor IX Deficiency) (Christmas Disease)**

**Risk Factors**

- X-linked recessive disorder almost exclusively in males (rarely in homozygous females) & can be d/t spontaneous mutation
- Clinically indistinguishable from Hemophilia A
- Lack of Factor 9 affects the clotting cascade → **failure of hematoma formation**

**Clinical Manifestations**

- **Hemarthrosis (80%): delayed bleeding or swelling in weight-bearing joints** (ankles, knees, elbows), soft tissues & muscles (forehead hematoma)
- Excessive hemorrhage d/t trauma & surgery or incisional bleeding (tooth extraction)
- Epistaxis, bruising, GI or urinary tract hemorrhage & less commonly presents with purpura, petechiae (because platelet function is normal) or spontaneous hemorrhage (except in severe form)

**Diagnosis**

- CBC & coagulation studies: Prolonged aPTT – normal PT, fibrinogen & platelet levels (bleeding time)
- Mixing studies: PTT corrects with mixing studies (factor deficiency)
- Most sensitive: low Factor IX

**Management**

- **Factor IX infusion** first-line therapy to increase levels 25-100% (depending on severity) – can be given in response to acute bleeding episode or prophylaxis (prior to surgery or after trauma)
- Desmopressin (DDAVP) IS NOT USEFUL!

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**Von Willebrand Disease**

*Autosomal dominant disorder associated with ineffective platelet adhesion d/t deficient or defective vWF*

- **MC hereditary bleeding disorder** (1% of population) – may also be acquired
- Function of Von Willebrand factor: promotes platelet adhesion by crosslinking the GP1b receptor on platelets with exposed collagen on damaged epithelium & also prevents degradation of Factor VIII

**Clinical Manifestations**

- **Mucocutaneous Bleeding:** epistaxis, bleeding gums, petechiae, purpura, bruising, menorrhagia, prolonged bleeding after minor cuts – Incisinal bleeding less common than in hemophilia

**Diagnosis**

- **Initial Labs:**
  - Coagulation studies: prolonged PTT (ASA worsens PTT & bleeding time)
  - Platelet count is usually normal (except in 2B – thrombocytopenia)
- **Screening tests:**
  - Plasma VWF antigen: decreased VWF antigen or activity 30 IU or less = diagnostic
  - Plasma VWF activity: Ristocetin cofactor activity & VWF collagen bleeding – no platelet aggregation w/ Ristocetin in VWD
  - Factor VIII activity may be decreased
- Specialized assays: helps determine type

**Management**

- **Type I:** quantitative deficiency = MC type
- **Mild to moderate bleeding:** DDAVP
Severe: VWF-containing product (factor VIII concentrates, purified VWF concentrates, recombinant VWF)

Minor procedures: Desmopressin used in type I and 2A for minor trauma, dental & minor surgical procedures

Major procedures: VWF-containing product (Human derived Factor VIII concentrates)

Type II qualitative deficiency:
- DDAVP for most, VWF or DDAVP prior to procedures

Type III (severe, absent VWF):
- VWF-containing product (human-derived factor VIII concentrates, purified VWF concentrates, recombinant VWF)

Lead Poisoning

Pathophysiology
- Lead poisons enzymes which causes cell death – it shortens the life span of RBCs & inhibits multiple enzymes needed for heme synthesis which causes an acquired sideroblastic anemia
- Risk factors: MC in children (especially under 6 years) d/t increased permeability of the blood-brain barrier as well as iron deficiency (may increase lead absorption)
- Sources: ingestion or inhalation of environmental lead (paint chips or lead dust) is the primary source of childhood lead poisoning in the US (lead was used in household paints prior to 1970s)

Clinical Manifestations
- May be asymptomatic or nonspecific symptoms
- Neurologic symptoms: ataxia, fatigue, learning disabilities, difficulty concentrating, developmental delays, hearing loss, peripheral neuropathy (foot or wrist drop)
- Encephalopathy: mental status changes, vomiting, seizures, cerebral edema, SIADH
- GI: lead colic – intermittent abdominal pain, vomiting, loss of appetite & constipation
- Anemia: pallor, shock, coma
- Renal: glycosuria, proteinuria, chronic interstitial nephritis
- Burton’s line: thin, blue-black line @ base of the gums near the teeth (seen mostly in adults)

Diagnosis
- Serum lead levels: >10 mcg/dL on venous sampling – most accurate
- Peripheral smear: microcytic hypochromic anemia w/ basophilic stippling (dots of denatured RNA seen in RBCs); ringed sideroblasts in bone marrow
- Normal/↑ serum iron, ↓ TIBC
- ↑ erythrocyte protoporphyrin, elevations can be seen in both iron deficiency & lead poisoning (worse in lead poisoning)
- Radiographs: “lead lines” – linear hyperdensities @ metaphyseal plates in children

Management
- Removal of the source of lead is the most important component of treatment
- Mild 44 mcg/dL or lower: outpatient follow up & lifestyle modification
- Moderate (45-69 mcg/dL): Succimer first-line as inpatient (oral chelation), calcium disodium edetate (EDTA) if PO not tolerated. D-penicillamine = 3rd line
- Severe (70 or higher):
  - Without encephalopathy: Succimer + EDTA
  - With encephalopathy: IM Dimercaprol followed by EDTA (IM/IV)
- *Florida requires you to have 3 tests before the age of 4 – just a fingerstick that can be done in office

Acute Lymphocytic Leukemia

Malignancy arising from immature lymphoid stem cells in the bone marrow

Pathophysiology
- Overpopulation of immature WBCs (blasts) overtake normal hematopoiesis resulting in pancytopenia

Clinical manifestations
- Nonspecific symptoms associated with pancytopenia
- Pancytopenia: fever & infections (leukopenia), bleeding d/t thrombocytopenia (petechiae, purpura) & anemia (pallor, fatigue)
- CNS symptoms: HA, stiff neck, visual changes, vomiting – METs MC to CNS & testes
- Physical examination: hepatomegaly or splenomegaly MC clinical findings – may manifest as anorexia, weight loss, abdominal distention or abdominal pain – (+) lymphadenopathy

Diagnosis
- CBC & Peripheral smear: WBC 5,000-100,000, anemia, thrombocytopenia
• **Bone marrow aspiration**: hypercellular with 20%+ blasts (definitive diagnosis)
• **Flow cytometry test**: most accurate test to distinguish Leukemia subtypes

**Management**

• **Highly responsive to combo chemotherapy** (remission 85%+)
  • Induction chemotherapy includes Anthracyclines, Vincristine, and Corticosteroids
  • Maintenance therapy includes: 6-MP + Methotrexate
• **Imatinib** used if Philadelphia chromosome (+)
• **Relapsing? Stem cell transplant**
• **CNS disease or CNS preventative**: intrathecal Methotrexate

**QUICK RECALL:** ALL = child + LAD + bone pain + bleeding + fever + >20% blasts

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**Chronic Lymphocytic Leukemia**

*Mature B Cell clonal malignancy (considered the same as small cell lymphocytic lymphoma)*

• MC form of leukemia in adults
  
  **QUICK RECALL:** CLL = middle aged patient – often asymptomatic + fatigue + LAD + splenomegaly

Diagnosis: *"smudge cells"* on peripheral smear, with mature well-differentiated lymphocytes (absolute lymphocytosis 5,000+)

Treatment: observation if asymptomatic, if symptomatic or lymphocytes 100,000+ – chemotherapy
  • Curative: allogenic stem cell transplant

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**Acute Myeloid Leukemia**

*Group of hematopoietic neoplasms characterized by clonal proliferation of myeloid precursors with decreased ability to differentiate into more mature cells*

• MC acute leukemia in adults

**Pathophysiology**

• Accumulation of leukemic blasts (immature WBCs) in the bone marrow, peripheral blood or other tissues

**Subtypes**

• **Acute promyelocytic leukemia (APL or M3)**: associated with DIC, Auer rod presence and myeloperoxidase positivity
• **Acute megakaryoblastic leukemia**: MC in children under 5 with Down Syndrome
• **Acute monocytic leukemia**: associated with infiltration of the gums (gingival hyperplasia)

**Clinical Manifestations**

• **Pancytopenia**: anemia (*general fatigue* MC presenting symptom, dyspnea, weakness), thrombocytopenia (mucocutaneous bleeding), & neutropenia (increased infections & fever)
• **Lymphadenopathy & splenomegaly**
• **CBC w/ peripheral smear**: best initial test – normocytic normochromic anemia w/ nL/decreased reticulocyte count
• **Bone marrow bx**: gold standard - >20% myeloblasts, Auer rods with APL

**Diagnosis**

• **Combination chemotherapy** (Cytarabine, Doxorubicin), can add all-trans-retinoic acid for APL/M3

• **Curative**: stem cell transplant

**QUICK RECALL:** AML = adults over 50 y/o, (+) Auer rods + >20% myeloblasts

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**Chronic Myeloid Leukemia**

*Myeloproliferative disorder of uncontrolled production of mature & maturing granulocytes with fairly normal differentiation (predominantly neutrophils but also basophils & eosinophils)*

**QUICK RECALL:** CML = WBC >100K + hyperuricemia + adults 50+, 70% asyx until a blastic crisis (presents as acute leukemia)

**Diagnosis:** (+) splenomegaly, Philadelphia chromosome (translocation on chromosome 9 & 22)

**Treatment:** Philadelphia chromosome (+) – tyrosine kinase inhibitors (Imatinib)

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**Hodgkin Lymphoma**

*Germinal/pregerminal B-cell malignancy originating in the lymphatic system*

• **Bimodal distribution**: peaks @ 20 and then again at 50
• **Risk Factors**: Epstein-Barr virus, immunosuppression, smoking

**4 Major Types**

• **Nodular Sclerosing**: MC type w/ a female predominance
• **Mixed cellularity**: associated with EBV
• **Lymphocyte rich/predominant**: MC in males, this type has the best prognosis
• **Lymphocyte depleted**: MC in males over 60, usually associated with other systemic disease – worst prognosis

**Clinical Manifestations**
• **Asymptomatic PAINLESS lymphadenopathy**: MC presentation, usually painless but ETOH ingestion may induce lymph node pain within minutes

• **Upper body lymph nodes**: neck MC site (cervical & supraclavicular), axilla, shoulder, mediastinum, & abdomen – usually rubbery in consistency, not fixed, may fluctuate in size

• **Mediastinal lymphadenopathy or mass**: 2nd MC presentation, incidental finding on CXR – mass may be large w/out local syx
  
  • If syx: retrosternal chest pain, cough/dyspnea may be experienced; Adverse prognostic factor: large mediastinal adenopathy
  
  • Fatigue, pruritus, intraabdominal disease – **hepatomegaly, splenomegaly**; cholestatic liver dz, nephrotic syndrome; ↑calcemia

• **Systemic “B” symptoms**: fever, night sweats, weight loss. Pel-Ebstein fever = **cyclical fever** that recurs @ variable intervals of several days or weeks & lasts 1-2 weeks before waning

  • Symptoms d/t cytokine release by Reed-Sternberg cells & indicates advanced disease

### Diagnosis

• **Excisional whole lymph node biopsy**: Reed-Sternberg cell pathognomonic – large cells with bi-/multilobed nuclei (“owl eye appearance”) & inclusions in the nucleoli

  • Reed Sternberg cells: derived from an abnormal germinal B cell in early stage of differentiation w/ CD15 & CD30 positivity

  • CXR to check for mediastinal adenopathy

  • Staging imaging: combined PET/CT scan of chest, thorax & abdomen

### Management

• **Early Stage disease (I or II)**: combo of chemotherapy + radiation

• **Advanced State (III or IV)**: combination chemotherapy = main treatment

  • Radiation therapy may be used for select patients as consolidation “ABVD” – Adriamycin (Doxorubicin), Bleomycin, Vinblastine, Dacarbazine. “MOPP” – Mustine, Oncovin/(Vincristine), Procarbazine, Prednisolone

  • Refractory (persistent): 2nd line high dose chemo & autologous hematopoietic cell transplant are option

  *Excellent 5 year cure rate! (60%)

### Non-Hodgkin Lymphoma

**Heterogenous group of lymphocyte neoplasms w/ proliferation in the lymph nodes & spleen**

• **50 + years old**, increased risk with immunosuppression (HIV)

### Major Types

• **Diffuse large B-cell**: MC type of NHL, fast growing & aggressive form (rapidly enlarging lymph nodes) of neck, abdomen & groin – MC in middle age and elderly

• **Follicular**: 2nd MC – small cell proliferation in follicles (circular pattern) CD20+, MC in adults and presents with painless lymphadenopathy (especially in the neck, groin, axilla) – **slow growing but hard to cure**

• **Burkitt Lymphoma**: intermediate-sized B cell proliferation, associated w/ EBV (*THIS IS NOT COMMON FOR NHL), usually presents as extranodal mass – MC seen in pediatric & adolescent & HIV patients

### Risk Factors

• Increased age, hx radiation therapy, FHx, immunosuppressed, EBV, autoimmune disorder – SLE, RA, Sjogren, Hashimoto

### Clinical Manifestations

• **Local**: painless lymphadenopathy, hepatosplenomegaly – indolent lymphomas may present w/ slow growing lymphadenopathy

• **Extranodal involvement**: common. **GI tract MC site of extranodal involvement** (skin 2nd MC, CNS also common)

• B symptoms rarer in NHL but may be present in advanced

### Diagnosis

• Lymph node &/or tissue bx: required for diagnosis & classification

• Combined CT/PET scan of chest, abdomen, and pelvis for staging

### Management

• **Low grade**: syx = no tx

  • Stage I localized disease: radiation therapy, or chemo – Chlorambucil, Fludarabine, 2-CdA; ~ use Rituximab

  • Refractory? Stem cell transplant

  • Intermediate, high grade (aggressive): chemotherapy (R-CHOP) Rituximab, Cyclophosphamide, Doxorubicin, Hydrochloride, Oncovin (Vincristine), Prednisolone

### Neutropenia – Aplastic Anemia

**Pancytopenia with bone marrow hypocellularity**

### Pathophysiology

• T cells attack hematopoietic stem cells (autoimmunity) or direct stem cell damage leads to bone marrow failure, including replacement of marrow with fat

• *Only anemia where all three cell lines are decreased

### Etiology

• Idiopathic MCC, radiation exposure

• **Infections**: seronegative viral hepatitis (non A-G), **Parvovirus B19** in patients w/ baseline hemolytic anemias (SCD, G6PD deficiency) & other viruses
• **Medications:** antibiotics (Chloramphenicol, Sulfas drugs), chemotherapy (anticipated effect), Benzene, anti-epileptics (Carbamazepine, Phenytoin), Quinine, NSAIDs, anti-thyroid medications

• B12 & Folate deficiency can cause pancytopenia

**Clinical Manifestations**

**Symptoms of pancytopenia:** easy bruising, bleeding, frequent infections & fatigue

- **Thrombocytopenia:** mucocutaneous bleeding (epistaxis, bleeding gums, petechiae, purpura, bruising, menorrhagia)
- **Anemia:** weakness, fatigue, dyspnea
- **Leukopenia:** recurrent or frequent infections, fever

**Diagnosis**

- **CBC w/ peripheral smear:** @ least 2 cytopenias – few/absent reticulocytes, thrombocytopenia, neutropenia, anemia (nucleated RBCs if marrow fibrosis is present)
- **Bone marrow biopsy:** most accurate test – hypocellular, fatty bone marrow (fat cells & fibrotic stroma replace normal marrow)
- Often a diagnosis of exclusion in the setting of bone marrow failure (PNH & myelodysplastic syndrome may present similar)

**Management**

- **Supportive management initial treatment of choice** (infx prophylaxis w/ broad-spectrum abx, PRBC transfusion for hemoglobin under 7 mg/dL, or platelets for counts under 10,000 or active bleeding)
- Severe AA in otherwise healthy patients under 50 years: Allogenic hematopoietic stem cell transplant = TOC
- **Immunosuppressive therapy:** patients over 50 years or in younger patients without matched donor: Eltrombogep, anti-thymocyte globulin (ATG) + Cyclosporine, and Prednisone
- Hematopoietic growth factor G-CSF (filgastrim) reduces the incidence of infections, but it does NOT alter the course of the disease, response to IST, or survival rate

**Neutropenia – Myelodysplasia**

*Heterogenous preleukemic disorders characterized by abnormal differentiation of cells of the myeloid cell line (hypercellular bone marrow) resulting in ineffective hematopoiesis in the bone marrow (pancytopenia)*

**Risk Factors**

- 65+ years old, radiation, chemotherapy, Benzene exposure, tobacco smoke, mercury or lead exposure

**Clinical Manifestations**

- May present as asyx pancytopenia on CBC or have *syx of pancytopenia:* easy bruising, bleeding, frequent infx & fatigue

**Diagnosis**

- **CBC w/ peripheral smear:** decreased # of one/more myeloid cell lines (platelets, neutrophils, or RBCs – may be nucleated), hypersegmented neutrophils, normocytic or macrocytic anemia
- **Bone marrow biopsy:** normal or hypercellular, 20% associated with hypocellularity; **Hallmark:** dysplastic bone marrow – increased myeloblasts but less than 20%, ringed sideroblasts, pseudo-Pelger-Huet cells (hyposegmented & hypogranulated neutrophils)

**Management**

- Goals: symptomatic improvement, improve survival & decrease progression to Acute myelogenous leukemia
- Supportive management: not all patients require management but some may need intermittent blood/platelet transfusions – erythropoietin
- Systemic: Pyrimidine analogs (5-Azacitidine, Decitabine), Lenalidomide (if 5q deletion is present)
- Allogenic stem cell transplantation only effective cure but difficult in patients over 50

**UROLOGY/RENAL – 3%**

**Cystitis**

*Ascending infection of the lower urinary tract from the urethra*

**Risk Factors**

- Women – sexual intercourse, spermicidal use (especially w diaphragm
- Pregnancy – progestosterone & estrogen causes ureter dilation & inhibition of bladder peristalsis
- Elderly & postmenopausal, DM, indwelling catheter, children – may indicate VUR
- Infants: get U/S to check for congenital abnormalities
- Complicated: **underlying condition w/ risk of therapeutic failure:** syx >7 days, pregnancy, DM, indwelling catheter, immunosuppressed, anatomic abnormality, elderly, males

**Etiology**

- E. Coli (#1) MCC; – Staph saprophyticus 2nd MCC in sexually active women
- Gram (-) uropathogens – Klebsiella, Proteus, Enterobacter, Pseudomonas; Enterococci in indwelling catheters

**Clinical Manifestations**

- **Irritative symptoms:** dysuria (burning), frequency & urgency
- Hematuria, suprapubic pain & tenderness may occur

**Diagnosis**

- Urinalysis: pyuria (>10 WBCs/hpf), hematuria, leukocyte esterase, nitrates, cloudy urine, bacteriuria, increased pH with Proteus
**Diagnosis**

- Women: >1,000 CFU/mL in a clean catch specimen; epithelial (squamous cells) = contamination
- Indications: complicated UTI, infants/children, elderly, males, urologic abnormalities, refractory to treatment, catheterized patients

**Management - Uncomplicated**

- **1st line**: Nitrofurantoin [Macrobid] or Bactrim or Fosfomycin [if resistance pattern < 20%]
- **2nd line**: Fluoroquinolones (use 1st-line if sulfa allergy/1st resistance patterns), Cephalosporins, or Cefpodoxime
- Increase fluid intake, void after intercourse, hot sitz bath for abdominal discomfort. **Phenazopyridine = bladder analgesic** for not more than 48 hours/dt side effects

**Management - Complicated**

- Fluoroquinolones – PO or IV, aminoglycosides x7-10 or 14 days (depending on severity)

### Enuresis

**Distinct episodes of urinary incontinence (bedwetting) while sleeping in children 5 years or older**

- **Evaluation**: complete history, PE, voiding diary & UA
- **Monosymptomatic**: enuresis in the absence of lower UTI symptoms & without bladder dysfunction, high rate of spontaneous resolution

**Primary Enuresis**

- Absence of any period of nighttime dryness – most common type, may have a family history

**Secondary Enuresis**

- Enuresis after a dry period of at least 6 months, usually d/t an unusually stressful event (birth of a sibling, divorce)

**Management**

- **Behavioral**: 1st-line therapy – motivational therapy (children 5-7 years old), education & reassurance
  - Bladder training: regular voiding schedule, deliberate voiding prior to sleeping, waking the child up to urinate intermittently, avoid caffeine-based drinks & high sugar content, restrict fluids
- **Enuresis alarm**: most effective long-term therapy, usually used if children fail to respond to behavioral therapy and before medical therapy
  - Sensor placed on the bed pad & goes off when wet – continued until minimum of 2w of consecutive dry nights
- **Desmopressin**: used in nocturnal polyuria with normal bladder functional capacity, better for short term use
  - **MOA**: Synthetic ADH which reduces urination & may cause hyponatremia - liberal use of salt to reduce incidence
- **Imipramine**: TCA used in refractory cases
  - **MOA**: stimulates ADH secretion, detrusor muscle relaxation & decreases time spent in REM sleep

### Glomerulonephritis (Nephritic Syndrome)

**Immunologic inflammation of the glomeruli → protein & RBC leakage into the urine**

**Etiology**

1. **IgA Nephropathy (Berger’s disease)**: MCC of acute glomerulonephritis, often affecting **young males** within days (24-48hours) after URI or GI infection (d/t IgA immune complexes), IgA is the first line defense in respiratory & GI secretions, so infections may cause IgA overproduction
2. **Post-infectious**: MC after **Group A streptococcus**, 10-14 day after skin (impetigo) or pharyngeal infection (may occur after any infection)
   - Classically: 2-14 year old boy with facial edema up to 3 weeks after Strep with scanty, cola-colored/dark urine (hematuria & oliguria), increase anti-streptolysin (ASO) titers, low serum complement (C3)
3. **Membranoproliferative/Mesangiocapillary**: due to SLE, viral hepatitis (HCV, HBV), hypocomplementemia, cryoglobulinemia – membranoproliferative usually presents w/ a **mixed nephritic-nephrotic picture**
4. **Rapidly progressive glomerulonephritis (RPGN)**: associated w/ poor prognosis (rapid progression to ESRD – weeks/months) – **Crescent formation on biopsy** (**crescents formed d/t fibrin & plasma protein deposition collapsing the crescent shape of Bowman’s capsule**)
   - Goodpasture’s Disease (only presents w/ RPGN): (+) anti-GBM antibodies against type IV collagen of the glomerular basement membrane in kidney & lung alveoli – presents w/ AGN + hemoysis
   - Vasculitis: characterized by lack of immune deposits & (+) ANCA antibodies
   - Microscopic Polyangiitis (vasculitis of small renal vessels): (+) P-ANCA
   - Granulomatosis w/ polyangiitis (Wegener’s): necrotizing vasculitis: (+) C-ANCA

**Clinical Manifestations**

- HHAP – Hematuria, HTN, azotemia (high levels of nitrogen-compounds in blood), & proteinuria (edema)
- **Hallmark**: Hematuria (cola or tea-colored urine), peripheral & periorbital edema, fever, abdominal or flank pain, malaise, oliguria (AKI)
- **Hypertension common**
- **UA**: Hematuria, RBC casts, dysmorphic RBCs (acanthocytes), proteinuria (usually < 3.5g), high specific gravity (>1.020 osm)
- Increased BUN and Creatinine
- **Gold standard:** Renal biopsy – not needed in most cases
  - **IgA nephropathy:** IgA mesangial deposits on immunostaining
  - **Poststreptococcal:** hypercellularity, increased monocytes/lymphocytes, immune humps of IgG, IgM, & C3
  - **Goodpasture syndrome:** linear IgG deposits in the glomerular basement membrane

### Management
- Self-limited with a good prognosis
- IgA nephropathy or proteinuria: ACE inhibitors +/- Corticosteroids
- Edema, hypervolemia, or hypertension: Loop diuretics (edema); HTN (beta-blockers, CCBs)
- Post-streptococcal AGN: Supportive +/- Abx; Lupus nephritis? Steroids or cyclophosphamide
- Rapidly progressive AGN or severe disease: Corticosteroids + Cyclophosphamide

### Nephrotic Syndrome

*Glomerular damage → increased urinary protein loss (not RBC loss like nephritic)*

#### Types
- Primary: based on kidney biopsy
  - Membranous nephropathy – non-diabetic adults
  - Minimal change disease – MCC in kids, assume this is the cause if child improves after tx w/ corticosteroids
  - Focal segmental glomerulosclerosis – obese patients, heroin, HIV + black males

#### Clinical Manifestations
- **Hallmark**: Proteinuria, hypoalbuminemia, edema, HLD*
- **Edema** = predominant feature (especially in children), may see ascites
  +/− increased BUN/Cr (varying degrees), dyspnea, transudative pleural effusion*, DVTs, frothy urine

#### Diagnosis
- UA: Proteinuria (usually 3.5g+/day), urine dipstick protein (3+/4+), fatty casts, oval fat bodies “maltese cross”**
- Biopsy: hypocellular, minimal change disease: nL on light microscopy, loss of podocytes on electron microscopy, associated w/ loss of negative glomerular basement membrane charge which further facilitates albumin loss

### Hydrocele

*Serous fluid collection within the layers of the tunica vaginalis of the scrotum*

#### Pathophysiology
- MCC of painless scrotal swelling – idiopathic MC, a reactive hydrocele can occur w/ inflammatory conditions (Orchitis, testicular tumor, epididymitis)

#### Types
- Communicating: peritoneal/abdominal fluid enters scrotum via a patent processus vaginalis that failed to close
- Non-communicating: derived from fluid from the mesothelial lining of the tunica vaginalis (no connection to peritoneum)

#### Clinical Manifestations
- Painless scrotal swelling (may increase throughout the day), may complain of dull ache or heavy sensation w/ increasing size
- Translucency (transilluminates), fluid located anterior and lateral to the testes
- Swelling worse with Valsalva if Communicating type

#### Diagnosis
- Testicular U/S – initial test of choice: used to r/o testicular tumor and other masses

#### Management
- Often resolves within the first 12 months of life in infants, self-limited in adults – usually no tx (watchful waiting)
- Surgical excision may be needed if beyond 1 year of age to reduce the risk of hernia/ hydroceles assoc. w/ comps

### Hypospadias

*Congenital anomaly of the male urethra that results in abnormal ventral placement of the urethral opening, penile curvature & abnormal foreskin development*

#### Pathophysiology
- Failure of urogenital folds to fuse during development – abnormal development of the urethral fold & ventral foreskin of the penis - the urethral opening can be within the glans, shaft, scrotum or perineum
- Proximal hypospadias is usually associated with additional genitourinary malformation

#### Clinical Manifestations
- Increased risk of UTIs, deflection of the urinary system, erectile dysfunction
- PE: ventral placement of urethra, abnL foreskin w/ incomplete closure around glans (dorsal hooded prepuce), abnL curvature (chordee)

#### Diagnosis: Clinical

#### Management
- Do NOT circumcision in the neonatal period because the foreskin may be used to repair the defect
- Elective surgical correction (arthroplasty) may include penile straightening
- Hypospadias repair usually performed in healthy full-term infants most commonly between 6 months-1 year
**Paraphimosis – UROLOGICAL EMERGENCY**

Retracted foreskin that can’t be returned to the normal position

**Pathophysiology**
- Retracted foreskin becomes trapped behind the corona of the glans & forms a tight band, constricting penile tissues which can lead to gangrene

**Etiology**
- Forceful retraction of phimotic foreskin
- Infants & young boys: usually physiologic or iatrogenic (retraction by the caretaker)
- Adolescents & adults: can occur after balanoposthitis or penile inflammation (DM), or sexual activity

**Clinical Manifestations**
- Severe penile pain & swelling of the penis
- Enlarged, painful glans w/ constricting band of foreskin behind the glans

**Diagnosis**
- Clinical

**Management**
- **Manual Reduction**: restore original position of the foreskin, reduce edema w/ cool compresses or pressure dressing then gentle pressure to restore the foreskin to normal position
- **Pharmacologic therapy**: granulated sugar, injection of hyaluronidase
- **Definitive**: Circumcision or incision (dorsal slit)

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**Phimosis – NOT AN EMERGENCY**

Inability to retract the foreskin over the glans

**Pathophysiology**
- Distal scarring of the foreskin (after trauma, inflammation, or infection)

**Clinical Manifestations**
- Foreskin in normal position that cannot be retracted

**Diagnosis**
- Clinical

**Management**
- Proper hygiene, stretching exercises
- 4-8 weeks of topical betamethasone cream BID/TID can increase foreskin retractility
- **Definitive**: Circumcision

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**Testicular Torsion**

Spermatic cord twists & cuts off blood supply

**Pathophysiology**
- Insufficient fixation of the lower pole of the testis to the tunica vaginalis (bell-clapper deformity) → increased mobility of the testicle

**Clinical Manifestations**
- **Abrupt** onset of scrotal, inguinal or lower abdominal pain (usually <6 hours), with a swollen, tender retracted testicle
- If N&V is present, suspect torsion (usually absent in epididymitis)
- (-) Prehn Sign – no pain relief w/ elevation, (-) (absent) cremasteric reflex on affected side – no elevation of the testicle after stroking the inner thigh

**Diagnosis**
- Clinical diagnosis
- **Emergency surgical exploration = definitive diagnosis**, preferred over U/S if torsion is very likely
- **Testicular doppler ultrasound – best initial imaging modality** – decreased/absent blood flow
- Radionuclide scan = gold standard – decreased uptake

**Management**
- Urgent detorsion & orchiopexy within 6 hours of pain onset – irreversible ~12 hours of ischemia
- Manual detorsion should be performed if surgical intervention is not immediately available
- Orchiectomy if not salvageable

**Complications**
- Testicular cancer
- Infertility (75% in bilateral, 50% unilateral)

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**Cryptorchidism**

Failure of one or more testes to descend by 4 months

**Pathophysiology**
- MC on right side, 10% bilateral, ~70% descend spontaneously – MC found outside the external ring (suprascrotal), inguinal canal, or in the abdomen

**Risks**
- Prematurity, low birth weight, maternal obesity/ diabetes

**Clinical Manifestations**
- Empty, small poorly rugated scrotum, may have inguinal fullness (if located inside inguinal canal)

**Diagnosis**
- PE, scrotal U/S if neither testes palpable, MRI

**Management**
- Monitor over first 6m, most descend by 3m – Still not descended? Orchiopexy as early as 4-6m & **definitely** by 2 y/o
- Detected at puberty? Orchiectomy to reduce ca risk
- hCG or GnRH – Prader-Willi Syndrome
- Testicular cancer
- Infertility (75% in bilateral, 50% unilateral)
Vesicoureteral Reflux

Retrograde passage of urine from the bladder into the upper urinary tract

Types
1. **Primary VUR**: most common type – d/t inadequate closure of or incompetent ureterovesical junction that contains a segment of the ureter within the bladder wall – low grade reflux (Grades I and II)
2. **Secondary VUR**: d/t abnormally high voiding pressure in the bladder that leads to failure of the closure of the UVJ during bladder contraction

Clinical Manifestations
- History of recurrent infection – especially cystitis or pyelonephritis in young females

Diagnosis
- **Voiding cystourethrogram** – imaging test of choice

Management
- Mild to moderate/ grades I to II: resolves spontaneously – observe or antibiotic prophylaxis to reduce the risk of recurrent UTI (Bactrim, Trimethoprim, or Nitrofurantoin)
- Grades III-IV: Surgical correction is definitive treatment

Exanthems:

**Auricular hematoma** refers to the accumulation of blood in the subperichondrial space, usually secondary to blunt trauma → edematous, fluctuant, & ecchymotic pinna with loss of normal cartilaginous landmarks
→ can occur spontaneously in babies as a result of perichondritis &/or those with bleeding diathesis. You want to do an I & D for this – hematomas of cartilage can lead to necrosis

**Physiologic functional heart murmur aka Innocent murmurs**: these are common in children & characterized by a quiet precordium with an intensity less than grade 3 in a crescendo-decrescendo pattern with a normal second heart sound in an asymptomatic child
→ **MC murmur**: pulmonary flow murmur (because of the small size of the branched pulmonary arteries d/t the lung receiving only 15% of CO during fetal development)