Sexually Transmitted Diseases (STDs)

NB Important Concepts: the presence of one STD does not rule out other ("STDs travel together"), don't forget blood born infections (HIV/HCV/HBV), M-to-F easier than F-to-M 2/2 difference b/t types of epithelium (male: keratinized vs. female: non-keratinized), always Tx sexual partners, "Wet Prep" looks at trich/yeast/WBC/clue cells

- Inner Inflammation specifically PID, EMM, etc
 - Pelvic Inflammatory Disease (PID) aka Salpingitis aka Tubo-Ovarian Abscess
 - Def: polymicrobial infection of fallopian tubes, NB GC/CT are specific in that they are able to open up cervicouterine barrier to allow not only themselves but other bugs to ascend GU tract
 - RFs: 90% STD w/ GC/CT and 10% iatrogenic: hysteroscopy, endometrial Bx, saline infusion sono, D&C, first 21d after insertion of IUD b/c can carry bacteria past cervico-uterine barrier
 - S/S: "chandelier sign"
 - Tx: BS abx
 - Complications: infertility (in 20% of all pts with PID), ectopic pregnancy (10x increased risk), tubo-ovarian abscess (TOA) which is walled off or tubo-ovarian complex (TOC) which is not walled off and thus more responsive to antibiotics (in 10% of all pts with PID), dyspareunia, pelvic adhesions with various GI and urinary problems
 - Endo-myo-metritis (EMM)
 - Def: polymicrobial infection of endometrium ± myometrium
 - RFs: 100% iatrogenic: CS, vaginal deliveries, D&E, D&C, IUD placement
 - S/S: "chandelier sign" (cervical motion and uterine tenderness)
 - Tx: BS abx
- Middle Inflammation specifically Cervicitis/Prostatitis, Orchitis, Urethritis, etc (DDx: cancer, allergic reaction, irritants, etc)
 Chlamydia (Chlamydia trachomatis)
 - S/S: A,B,C Serotypes = Hyperendemic Blinding Trachoma (conjunctivitis leading to eyelid fibrosis and subsequent exotropia and corneal abrasion leading to blindness, common in Middle East, India, Africa), D, E, F, G, H, I, J, K Serotypes = GU Infection (mild white discharge), L1,2,3 Serotypes = Lympho Granuloma Venereum (LGV) (first ulcer/papule then painful inguinal LAD with constitutional symptoms then Crohn's like symptoms w/ proctocolitis, rectal stricture, rectovaginal fistula, elephantitis of genitals 2/2 lymphatic obstruction)

Complications: **Reiter's Syndrome, Neonatal Infection** (2/2 to passage of fetus thru birth canal resulting in conjunctivitis and pneumonia)

- Dx: GS (obligate intracellular pathogen b/c synthesizes ATP), Cx, Amplified DNA probe (Q-tip inserted into os and rotated for 15sec), Nucleic Acid Amplification Test (NAAT) (~PCR of first void urine)
- Tx: Doxy 100mg PO BID x7d or Azithromycin 1g PO x1d (NB FQ are also effective), Tx also for Gonorrhea b/c 30% of pts will have coinfection with both G and C
- o Gonorrhea (Neisseria gonorrhoae)
 - S/S: severe yellow discharge, (NB men usually symptomatic vs. women usually asymptomatic hence complications more common)
 - Complications: PID (and its complications), Fitzhugh-Curtis Syndrome (2/2 peritoneal spread forming "violinstring" adhesions b/t liver and diaphragm), Pharyngitis (2/2 fellatio), Disseminated Gonococcal Infection (2/2
 - Dematogenous spread resulting in arthritis/endocarditis/meningitis, RFs: deficiency of terminal component (esp C8) of complement aka MAC (NB also causes disseminated meningococcemia)), Neonatal Infection (2/2 to passage of fetus thru birth canal resulting in initial infection of eye, ear, pharynx, oropharynx, anorectal mucosa followed dissemination, screening is done during early pregnancy, conjunctivitis used to be a major cause of neonatal blindness b/f Tx w/ silver nitrate, tetracycline, erythromycin)
 - Dx: GS (GNC specifically bean shaped diplococci), Cx and Amplified DNA probe (Q-tip inserted into os and rotated for 15sec), DNA Probe (most common in hospitals these days)
 - Tx: Ceftriaxone 125mg IM x1 (GU/pharyngitis), 1g IV x1 (conjunctivitis), (NB emerging FQ resistance therefore try not to use anymore), Tx also for Chlamydia b/c 30% of pts will have coinfection with both G and C
- o Enterobacteriae
- Myco/Ureaplasma
- o Crabs/ Head Lice/Body Lice aka Pediculosis (Phthirus pubis/Pediculus capitis/Pediculus corporis)
 - S/S: SEVERE pruritis w/ excoriations, red macules w/ central hemorrhagic puncti as the 1mm long gray/brown bug lives at base of pubic hair
 - Dx: fluoresces blue under Wood's lamp, scrape skin and you can visibly see lice on hair shafts
 - Tx: permethrin (Elimite), malathion (Ovide) shampoo (NB benzene hexachloride (Lindane) is no longer available b/c of neurotoxicity), treat all contacts, wash/burn all clothes, sheets, towels etc as very contagious, trim finger nails, isolate pt
- Scabies (Sarcoptes Scabiei)
 - S/S: SEVERE pruritis w/ excoriations especially at night and after hot showers, linear burrows w/ one dark end, also commonly found at finger/toe web spaces, intertriginous areas, palms/soles, etc
 - Dx: scrape skin and under microscope you will see bug
 - Tx: same as for Crabs and also PO ivermectin

- Outer Inflammation specifically Vaginitis/Balanitis, etc (DDx: Behcet's, Crohn's, coital friction, post-menopausal urogenital atrophy, allergic rxn to tampons, contraceptives, soap, etc)
 - NB normal flora includes Lactobacillus which helps to maintain vaginal pH (nl ~4, worse after menses/abx/douche/sex b/c of increase in pH)
 - Trichomonas ("Trich") (Trichomonas vaginalis)
 - RFs: sex
 - S/S: non-odorous, yellow-green, frothy, high pH, discharge + cervical inflammation aka "strawberry cervix"
 - Dx: Wet Prep w/ NS showing large (larger than a WBC), motile (3-5 flagella) protozoa, PCR, ELISA
 - Tx: Flagyl 2g PO x1 or 500mg PO BID x7d to pt and sexual partner (NB there is emerging flagyl resistance)
 - Bacterial Vaginosis ("BV") (anaerobic bacteria: Gardnerella vaginalis, Mycoplasma hominis, etc)
 - RFs: sex though not considered an STD like Trich
 - S/S: mal-odorous, white, smooth, high pH, discharge
 - Dx: Wet Prep w/ NS showing "Clue Cells" (bacteria covering vaginal epithelial cells) followed by Wet Prep w/ KOH generating the "fishy" order aka "Whiff Test"
 - Tx: (same as Trich)
 - Yeast Infection (Candida spp.)
 - RFs: recent abx/steroids use, pregnancy, DM, douche, immuno-compromised, etc
 - S/S: non-odorous, white, creamy cottage cheese, nl pH, discharge + small satellite erythematous lesions
 - Dx: Wet Prep w/ KOH showing branching hyphae, Sabouraud's Culture
 - Tx: only if pt has Sx as 15% of women have asymptomatic yeast, Monistat-7 (OTC azole) x7d vs Terazole (Rx azole) x1d Cream, Fluconazole 150mg PO x1, if recurrence then consider Fluconazole Qwk x6mo
- Outer Ulcers (DDx: Behcet's Crohn's, etc)

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- Herpes (Herpes Simplex Virus (HSV)
 - HSV 1>2 (young child acquires from oral secretions w/ subsequent latency at trigeminal ganglion, reactivation w/ stress) vs HSV 2>1 (sexually active adult acquires it via direct contact (virus dies at room temp esp when dried) with subsequent latency in sacral/lumbar root ganglion, reactivation with stress)
 - S/S: 1wk incubation, 6-24hr prodrome (itching, burning, tingling, etc) followed by ~2d of grouped vesicles that rupture forming ~10d of painful, multiple, 2mm ulcers w/ irregular borders and dirty/purulent base on vermillion border of lips aka "cold sore" or genitals, first episode is most severe w/ local LAD and systemic Sx but subsequent episodes are milder, shorter duration, and less frequent (90% recurrence rate ~4-8x/yr), complications (aseptic meningitis, temporal encephalitis, Bell's palsy, esophagitis, pneumonitis, Whitlow aka fingers, "tree like" keratitis, active lesions DURING pregnancy are not a problem b/c the fetus acquires the virus when passing through vaginal canal therefore proper management is: if mother has active lesions during pregnancy the mother is given acyclovir from 36wks until delivery at which the fetus is delivered via CS to prevent transmission) EXCEPTION: a primary infection during pregnancy (one acquired during pregnancy hence high IgM and no IgG) is MUCH MORE DANGEROUS in that it can transmitted across placenta during the primary viremic stage)
 - Dx: Tzanck Smear (Wright Stain shows multinucleated syncitia infected cells with Cowdry type B intranuclear inclusions - light purple center w/ a clear halo around it), Culture (Gold Standard), Serology, PCR
 - Tx: first episode (acyclovir 400mg PO TID x7-10d, etc), recurrence (acyclovir 400mg PO TID x5d, etc), prevention if ≥6 outbreaks/yr (acyclovir 400mg PO BID, etc) NB don't do topical b/c ineffective and r/o autoinoculation
 - NB 50% of +HSV pts have NO symptoms hence they don't think they have it and thus have the potential to pass it on b/c asymptomatic transmission aka "viral shedding" is very common
 - NB either HSV can infect either area but contracting one form confers some degree of immunity to the other **Syphilis** (*Treponema pallidum*)
 - Increasing in incidence dramatically
 - S/S: Early: Primary, Secondary, Early Latent (<1yr) vs Late: Late Latent, Tertiary (>1yr)
 - <u>Primary Syphilis</u>: + Direct Indirect, 3wk incubation
 - Hard Chancre w/ Regional LAD (at sight of inoculation, painless single 10mm ulcer w/ annular border, indurated heaped up margins and clean base), 3/4 stop here vs 1/4 develop secondary syphilis 1-2mo after primary syphilis if unTx
 - <u>Secondary Syphilis</u>: +Direct + Indirect
 - Mucocutaneous Lesions w/ Generalized LAD (rash on palms/soles hands, alopecia, mucosal lesions, broad based elevated lesions in moist areas aka Condylomata Lata), 2/3 stop here (Early Latent: infectious/<1yr vs. Late Latent: NOT infectious/>1yr) vs 1/3 develop tertiary syphilis several years after secondary syphilis heals if unTx
 - <u>Tertiary Syphilis</u>: Direct + Indirect
 - Syphilitic Aortitis (endarteritis of vaso vasorum of ascending proximal aorta resulting in ischemia to the aorta → dilation → aortic insufficiency, aneurysm, and narrowing of coronary ostia resulting in MI)
 - Neurosyphilis (lymphocytic meningitis, vasculitis (resulting in CVA such that syphilis is the primary cause of CVA in young pts), encephalitis (dementia and personality changes), "Tabes Dorsalis" (spinal post column degeneration resulting in paresthesia, abnl gait, lightening pain), "Argyll-Robertson Pupils" (small fixed pupils that do not react to direct/indirect light but do react to accommodation, also seen in DM))

- Check CSF if neuro Sx, Tx failure, VDRL/RPR >1:32, other 3° Sx, +HIV
- Gummas (nodular masses in bone, skin, and mucus membranes)
- Congenital Syphilis (refer to Peds)
- Dx: Direct via Visualization of Tissue (Dark Field Microscopy, FISH, etc showing tight rigid cork-screwed spirochete with forward/backward motion, rarely done anymore b/c time consuming) vs Indirect via Serology (Non-Treponomal and Treponomal Tests)
 - Non-Treponomal Test: Serum RPR (Rapid Plasma Reagin) vs CSF VDRL (Veneral Dz Research Lab), high sensitivity but low specificity, screening test, quantitative titer (eg 1:64), tests for syphilis antibody against non-specific cardiolipin-cholesterol-lecithin antigen (15% False +: pregnancy, increasing age, autoimmune dz, acute infections, collagen vascular diseases, drugs addiction, high Ig, leprosy, LGV, IE, zoonosis, TB, HIV, mycoplasma, chancroid)
 - Treponomal Test: Serum MHA-TP (Micro-Hemagglutination Assay for T. pallidum) vs CSF FTA-Abs (Fluorescent Treponemal Ab Absorption), low sensitivity but high specificity, confirmatory test, qualitative reactivity (eg. reactive vs non-reactive), tests for syphilis antibody against syphilis antigen
- Tx: all stages of Syphilis is PenG based it just varies in the precise regimen used, all people exposed <90d ago are Tx and those >90d are checked for serology, the problem is with pen allergic pts as there is lack of definitive studies on other drugs nevertheless there has been success w/ doxycycline and ceftriaxone but in general try to desensitize, there is no protective immunity therefore you can get syphilis several times (hence no vaccine), Jarisch-Hercheimer Reaction (F/chills/hypoTN/rash/LAD, occurring 1-6hrs after Tx, seen in >50% of pts, 2/2 to abrupt destruction of spirochetes and release of contents, supportive Tx as self-limited), assessed the response to Tx by the change in titer to ensure Tx adequacy
 - 1°, 2° Early Latent (infectious): PenG 2.4million units IM x1 or Doxy (you want a 4x decrease at 6mo and 8x at 12mo and if not then check CSF for syphilis sanctuary in CNS and if negative then just retreat b/c likely just ineffective initial Tx)
 - 2° Late Latent, Unknown (non-Infectious): PenG 2.4million units IM Qwk x3wks or Doxy (you want a 2x decrease at 6mo and 4x at 12mo)
 - 3°: PenG 2-4 million units IV Q4hrs x10-14d then PenG 2.4 million units IM Qwk x3wks (you want a 2x decrease at 6mo and 4x at 12mo)
- Chancroid (Haemophilus ducreyi) 0
 - S/S: 1wk incubation, 1wk duration, painful single/multiple 10mm (unlike herpes which are smaller these are large) ulcers w/ irregular borders and dirty/purulent base
 - Dx: Culture (only diagnostic test and very difficult to do hence actual incidence is likely higher)
 - Tx: Azithromycin 1g PO x1 or Ceftriaxone 250mg IM x1
- LGV (rare) 0
- Donavanosis (rare) 0
- Outer "Masses" Benign HPV (Warts)

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- Because most spontaneously resolve in a few years then most don't do anything b/c doesn't cause any problems
- Pt: Podofilox, Imiguimod cream, 15% Salicylic/Lactic Acid in collodion, 40% salicylic acid plaster
- MD: Cryo, Local Excision, Intralesions IFN, CO2 Laser Malignant HPV Pathogenesis



- DS-DNA virus, 90 different types
- The is a disruption of superficial epithelium w/ exposed basal cells (virus particularly affects the squamocolumnar jxn) Increase in age results in metaplasia (columnar to squamous) such that the sc jxn advances inward, the area b/t the old sc jxn and the new sc jxn is the transformation zone, this zone is important b/c that is where dysplasia occurs Increase in estrogen (OCPs, pregnancy, etc) results in the sc jxn advancing outward (called ectropion/eversion/erosion) which is important b/c you always want to test sc jxn not necessarily os
- HPV Infection: warts and SCC (skin in transplant pts vs genitals in nl pts)
- Virus infects basal keratinocytes and goes to nucleus (Low Risk Types: 6,11 do NOT incorporate into cell genome, but they do form condylomata acuminate aka venereal warts and verruca vulgaris aka common warts and verruca plantaris aka plantar warts and verruca plana aka flat warts), integration is the hallmark of malignancy, (High Risk Types: 16, 18 ("teenagers"), 30s, 45, 50s do integrate) proteins E6 and E7 secreted by high risk types inactivate tumor suppressor genes p53 and Rb resulting in cancer) THE HIGHER THE NUMBER THE MORE CANCEROUS
- As the cell moves from basal to outer layers virus begins to copy DNA and express some proteins w/in nucleus (resulting in nuclear atypia)
- As the cells reach outer skin layer virus particles form and at this point the cell is breaking down such that the new viruses are released (thus the virus is NOT cytolytic it just waits till cell dies)
- RFs: coitarche b/f 15 = 16x, ≥2 episodes of genital warts = 5x, ≥4yrs smoking = 4x, ≥3 sexual partners = 3x, h/o STDs, immunosuppression like HIV (synergism), lower socio-economic status, inadequate screening, h/o cervical cancer
- Symptoms
 - Early Symptoms (single wart to cauliflower growth, post coital bleeding, discharge, 50% + Pap smear)
 - Late Symptoms (post void bleeding, watery discharge, pelvic pain, ab/pelvic mass, uremia, cachexia, malodorous discharge)
- Prevention
 - Vaccine: Gardasil is against 16,18 (70% of cervical cancer) and 6,11 (90% of genital warts) while Cevarix is against only 16,18, 9-26yo, three series shot (0,2,6mo), duration of protection, not effective against active infection but still give b/c can be protective for other serotypes
 - Bethesda Classification System (Cytologic Classification) vs. CIN System (Histopathologic Classification)
 - 1st Check Adequacy (Satisfactory or Unsatisfactory)
 - 2nd Determine if Squamous or Glandular Abnormality (Glandular is rare representing 10% and when present go straight to colpo)
 - 3rd Determine Exact Type

Squamous Intraepithelial Lesions	Subtypes	% that	Initial Management	Subsequent Management
(SILs)		Progress		
		to Cancer		
"Atypical Squamous Cells" (ASC)	"- of Undetermined	0.1%	If ASC-US then a reflex HPV Test	 NEGATIVE
	Significance" (ASC-US)		(Hybrid Capture Assay which uses	Colposcopy =
0	opyright 2015	- Alex	RNA probes on the Pap sample determining the presence of 12 high	PA Cold Knife Conization (CKC)
			risk serotypes) and if - HPV Test then	POSTIVE
			just repeat Q4-6mo x3 and if any abnl	Colposcopy =
			again then Colposcopy VS if + HPV	Loop
			Test then go straight to Colpo w/	Electrosurgical
			Punch Bx	Excision
	"but cannot exclude HSIL"	0.2%	Colpo w/ Punch Bx (microscope w/ a	Procedure (LEEP)
	(ASC-H)		green filter that gives a magnified	
"Low-grade Squamous		20%	view of cervix that is stained with	
Intraepithelial Lesion" (LSIL) =		(takes 7yr	acetic acid (dehydrates cells and	
CIN-I		to become	precipitates nucleic proteins which	
(Partial Thickness Dysplasia)		SCC)	are seen as white, increased white =	
"High-grade Squamous		40%	increased N/C ratio, Aceto-white	
Intraepithelial Lesion" (HSIL) =		(takes 4yr	epithelium, atypical vessels should be	
CIN-II & CIN-III		to become	biopsied)	
(Full Thickness Dysplasia w/ CIS)		SCC)		
"Squamous Cell Carcinoma" (SCC)	Large Cell Keratinizing	100%	Stage	
	Large Cell NON-Keratinizing	100%	• I = confined to cervix =	

Small Ce	II 100%	cone Bx
		II = beyond cervix but to not pelvic wall = radical butters the many (10)
		dissection (old pt) or radiation (young pt)
		III = beyond cervix and to pelvic wall = cysplatin head change i madiation
		 IV = beyond pelvis (direct (rectum/ab/bladder)
		indirect (lung/liver/bone)) = same

- Pap Smear
 - o Don't schedule during menses and wait 48hrs after intercourse and vaginal medications and use of tampons
 - o sens 80% spec 90%
 - screening (refer)
 - assess transformation zone which may be at external os (therefore use spatula 1 complete turn or broom 5 complete turns) or endocervical canal (therefore use cytobrush 1/2 turn or broom 5 complete turns), apply sample directly to slide (TraditionalSlide-Based Pap) 50% sensitive or to liquid-based medium and then to slide (ThinPrep Pap) 80% sensitive b/c less debris and clumping
 - o do GC/CT testing after HPV testing b/c you might remove dysplasia cells and cause a false negative
 - b/c Pap smear is 50% false negative must do biopsy if lesion is present and sometimes colposcopy and conization
 if you see a gross lesion that looks cancerous do NOT Pap b/c you might just pick up necrosis and thus no actual cytologic



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