Vaginitis, STIs and HPV

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- The information contained in this lecture/presentation, which may include treatment modalities, diagnostic and therapeutic information, and instructions related to regulatory guidelines and current standards of practice, is FOR EDUCATIONAL PURPOSES ONLY and should not be taken as a treatment regimen, product indication, suggested treatment modality, or suggested standard of practice.
- Any treatments, therapies, or standards of practice must be fully investigated and prescribed by a licensed medical practitioner in accordance with accepted professional standards and regulations. Any regulatory or practice standard must be fully investigated by a licensed health care provider in accordance with their accepted professional practice standards.

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- Author of [redacted]
- Private practice physician in Phoenix Arizona.
- Writes the Environmental Medicine Column in the Townsend Letter.
- Formulated products for [redacted]
- Director of annual Women's Health Conference in Scottsdale AZ.
- Adjunct faculty at SCNM, teaching Gynecology and environmental medicine.
- Public speaker at physician conferences throughout the US and Canada.
- Served on several state and professional boards and committees.
- www.drmarchese.com

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Vaginitis
Why isn't the treatment working?

- Root cause not addressed
- Organism not correctly identified
- Wrong treatment applied
- Hard to treat strains
- Co-infections
- Biofilms

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Vaginitis
How did she get this?

- Tampons
- Sexual activity- Ph, sperm, condoms, lubricant, spermicides, transmission from partner
- Flora disruption
- Douching
- Estrogen- deficiency or excess
- Chemical irritants
- Medications- steroid, anti-fungal, anti-biotic, OCP
- DM, HIV

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Vaginal canal

- Normal pH: 3.8-4.5
- Normal flora: lactobacilli species
- Staph epidermidis, diphtheroids, streptococci, Gardnerella, E coli and anaerobic bacteria normally present
- Low estrogen levels- few lactobacilli; thin vaginal mucosa; minimal glycogen production; alkaline pH.
- Higher estrogen levels-thickening of vaginal epithelium; increase in glycogen; more lactobacilli; acidic pH

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Vaginitis
Identify the organism and strain

- Candida species- *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*, *C. glabrata*, and *C. krusei).*
- Trichomanas
- Gardnerella (bacterial vaginitis, BV. Anaerobe)
- Lactobacillus species- *L. crispatus* and *L. jensenii*
- Staph aureus, Group B Strep (AV)
- E.Coli (aerobic vaginitis, AV)
- Other Anaerobes; Atopobium vaginae, Mobiluncus mulieris, Prevotella bivia, Fusobacterium nucleatum, and Peptoniphilus species and Mycoplasma, Ureaplasma

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Co-infection?

CO-INFECTIONS

- AV was diagnosed with other organisms 30% of the time
  - AV and Candida albicans have been found together in 43% of patients
  - AV and Trichomonas vaginalis in 30%
  - AV and BV in 26%

[redacted] 2013 Dec;67(6):428-30

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Vaginitis as an STI

Mycoplasma and ureaplasma species

- Causes inflammatory sxs and increase in vaginal cytokines
- Both increase in number during BV infection
- Hormones have an influence on colonization, multiplication and persistence- estrogen/testosterone
- Plays a role in preterm birth and pregnancy complication
- Affects men too (urethritis, infertility)

1. [redacted]-Rahimian, N. Rev Microbiol. 2017 Mar 2.
2. [redacted] 2015 Sep;3(5):809-16

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Co-infections and other strains

Yeast:

- Non-Candida albicans Candida (NCAC) species
  - Candida glabrate, Saccharomyces cerevisiae
  - C. tropicalis, C. parapsilosis, C. dubliniensis, and C. krusei
  - Risk factors; pregnancy, HRT, OCP, uncontrolled diabetes, immunosuppression, antibiotics, glucocorticoid use and genetic predispositions.
  - Behavioral risk factors include; IUD, spermicides and condoms and some habits of hygiene, clothing and sexual practices.

Clin Rev Microbiol. 2016 Nov;42(6):905-27

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Biofilms

- Biofilm was present on 90% of the epithelial surfaces of BV vaginal biopsy specimens
- Biofilms exhibited higher tolerance to hydrogen peroxide and lactic acid
- Gardnerella biofilm formation assisted by co-infections, decreased lactobacillus, hormones, and pH changes
- Staph Aureus and E.coli can produce biofilms

Anal Exp Biol Med. 2016 Nov;162(1):75-78

J Infect Dis (2015) 212 (12): 1856-1861.

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Biofilms

- *Candida albicans* is able to adhere to biotic (epithelial cells) and abiotic (e.g. central venous and types of catheters) surfaces to form a biofilm
- A biofilm is a special phenotype of *C. albicans* that has encased fungal cells which alter susceptibility to antifungal drugs.
- *Candida albicans* biofilms have been considered to be one of the critical factors accounting for fungal resistance to drugs.

Cell Physiol Biochem. 2016;40(3-4):727-742

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Vaginitis Testing

- pH litmus paper- in office
- Ph and amine swab- in office
- (Trichomonas APTIMA test (Gen-Probe or urine)
- Affirm VPIII Test – gardnerella, candida albicans, trichomonas vaginalis
- Culture- candida, staph aureus, Group B Strep, E. coli
- Gram stain- BV
- PCR- *Lactabacillus* species, *Gardnerella vaginalis*, *Atopbium vaginae*, bacterial vaginosis-associated bacteria-2 (BVAB-2), *Megasphaera-1*, *T. vaginalis*, and *Candida* species

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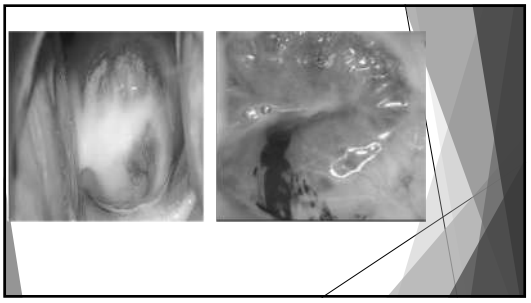

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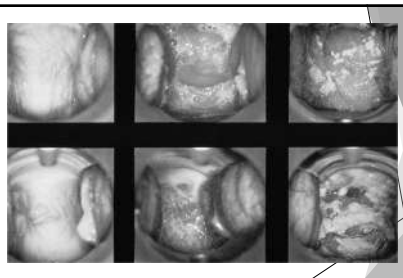

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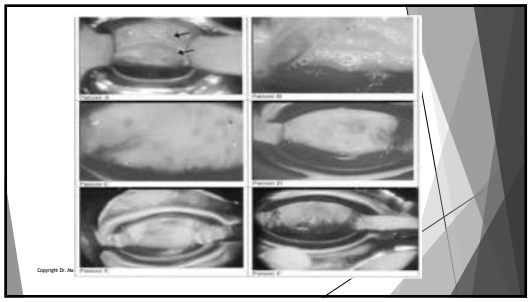

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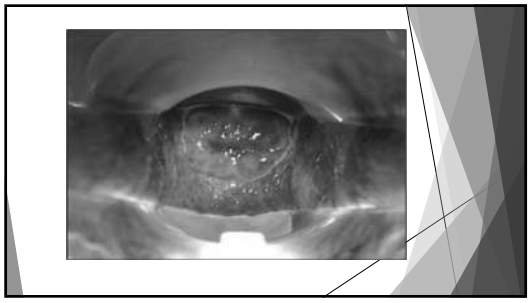

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Test Men ?

- 107 patients, PCR anal swab in MsM found
  - Gardnerella vaginalis 89%, Ureaplasma urealyticum 24.3%, Mycoplasma hominis 24.3%, Mycoplasma genitalium 9.3%, and Ureaplasma parvum 4.7%
- Urine test and urethra swabs in MsW both ureaplasma and mycoplasma found in patients with symptoms of urethritis
- These are sexually transmitted organisms

- Int J STD AIDS. 2017 Jun;28(7):708-714
- Int J STD AIDS. 2016 Sep;27(10):861-7.
- Int J Urol. 2004 Sep;11(9):750-4.

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Test Men ?

- Candida- KOH wet mount, culture
- Chronic mucocutaneous candidiasis (C. albicans)
  - *Candida* balanitis - Penile pruritus and whitish patches on the penis
- Candida Sexually transmitted?

Int J STD AIDS. 2017 Jun;28(7):708-714
Int J STD AIDS. 2016 Sep;27(10):861-7.
Int J Urol. 2004 Sep;11(9):750-4.

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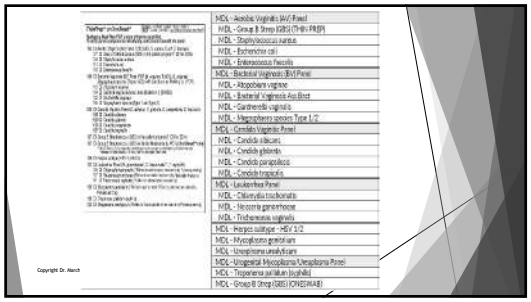

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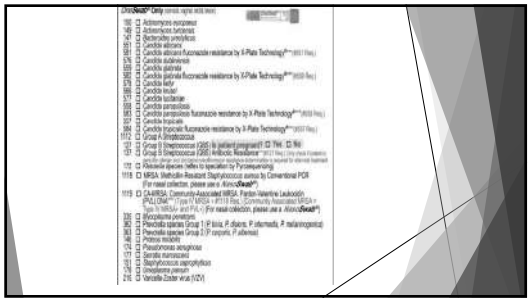

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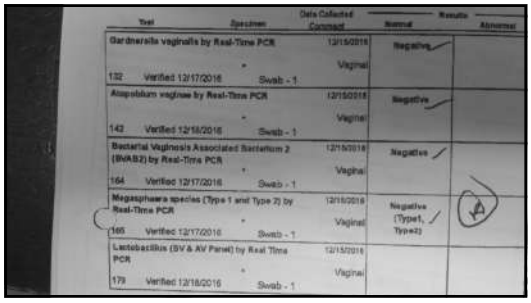

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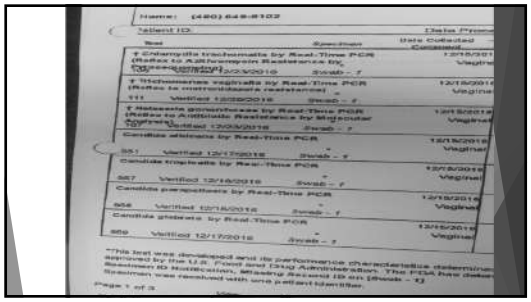

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LabCorp				
	Vaginal Culture - Routine Staph (only if prevalent) E. coli (only if prevalent) Yeast GBS	LC 008334	$45	Vaginal Culture - Routine - Copan Pink 
	BD Affirm System BV, Candida, Trich	LC 180026	$165	BD Affirm System 
	Nu-Swab: BV, Candida, Trich	LC 180038	$580.25	
	Nu-Swab: G/C	LC 183194	$95	Nu-Swab - Aptima Multitest Swab Kit 
	Nu-Swab: BV, Candida, Trich, +G/C	LC 180021	$325	
	Nu-Swab: Mycoplasma/ Ureaplasma	LC 180089	$295	

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Trichomonas Vaginalis

- Frothy, gray or yellow-green discharge and pruritus, but many are asymptomatic.
- The presence of cervical petechiae
- Chronic infection may be associated with minimal symptoms.
- Treatment- metronidazole 2 g orally in a single dose
  - or metronidazole 500 mg orally twice daily for 7 days
  - or Clotrimazole single 500mg tablet or cream used once PV at night
- Test and treat the male partner too
- http://www.medscape.com/viewarticle/713249_8

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Yeast treatments options

- Fluconazole 150 mg PO 1-10 days
- Clotrimazole 500mg single dose or as cream used once PV
- Miconazole 200mg suppository QD for 3 days
- Nystatin oral and/or vaginal
- Boric acid 600mg vaginally bid for 10 days
- Probiotics- oral and vaginal
- Oral Garlic, berberus/Oregon grape, caprylic acid, grapefruit seed extract

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Yeast treatment

- C. Albicans- drugs such as nystatin, low dose fluconazole, or clotrimazole is successful in more than 80% of cases
- C. Glabrata- vaginal suppositories of boric acid (600 mg, 1-2 times daily for 14 days) or flucytosine.
- Candida krusei is resistant to the triazoles, fluconazole and itraconazole

Mycoses. 2015 Mar;58 Suppl 1:1-15

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Yeast Anti-biofilm treatments

- Quercetin can sensitize the susceptibility of Fluconazole-resistant *C. albicans* isolates to fluconazole
- Quercetin Assists Fluconazole to Inhibit Biofilm Formations of Fluconazole-Resistant *Candida albicans* in *In Vitro* and *In Vivo*

ACS Chem Biol. 2010 Mar 19; 5(3): 321-332.

Mol Pharm Biochem. 2014;40(3-4):727-742

- Amphotericin B and Caspofungin- (IV/IM and many SE)
- Saponins- able to inhibit *C. albicans* biofilm formation
- Quercetin shown to be antifungal against *C. albicans* biofilm

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Bacterial Vaginitis treatment

- Test for UTI too
- Vaginal and oral probiotic
- Treat the inflammation
- Support the immune system
- Menopause vaginal atrophy
- E.coli, Group A strep, Staph Aureus, Group B strep
- *Gardnerella vaginalis*, *Atopobium vaginae*, *Mobiluncus curtisii*, *Prevotella bivia*, *Haemophilus* species, *Bacteroides* species, *Fusobacterium* species, *Peptostreptococcus* species
- Antibiotics- based on culture and sensitivity

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BV general treatment options

- Metronidazole 500 mg orally twice daily for 7 days
- Metronidazole gel 0.75% intravaginally QD for 5 days
- Clindamycin cream 2% intravaginally QD for 7 days
- Natural BV treatment research;
  - Vitamin- C
  - Tea Tree
  - Garlic
  - Lactobaccilus

- [illegible]
- [illegible]
- [illegible]
- Peterson, EE, et al., [illegible]
- Welch C, Balerk, [illegible]

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BV general naturopathic treatment options

- Tea tree suppositories- by www.teatreetherapy.com
- Probiotic vaginally- veggie caps
- V-Fresh vitamin C suppositories-by Vitanica
- Garlic capsule vaginally- veggie cap
- Menomoist for atrophy- by www.wiseways.com
- Vitamin-E suppositories for cervicitis- by www.carlsonlabs.com

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Table 1. A Comparison of Bacterial Vaginosis and Aerobic Vaginitis.

Clinical Characteristics	Bacterial Vaginosis	Aerobic Vaginitis (1)
Lactobacilli	Displaced	Displaced
Pathogen	*Gardnerella vaginalis, Atopobium vaginae, Megasphaera species, BVAB2*	*Escherichia coli*, Group B *Streptococcus*, *Staphylococcus aureus*, *Enterococcus faecalis*
Vaginal epithelial inflammation	None	Present
Elevation of pro-inflammatory cytokines (IL-1β, IL-6, IL-8)	Moderate elevation	High elevation
Immune reactive cytokine: leukocyte NE	Non reactive	Reactive
pH (Normal = 3.8 – 4.2)	1= 4.2-4.5 BV > 4.5	> 4.5; usually >6
Shed vaginal epithelial cells	Clue cells	Parabasal cells
Vaginal discharge characteristic	White, homogeneous	Yellowish
10% KOH Whiff test (fishy amine odor)	Positive	Negative
Treatment	Metronidazole * Clindamycin *	Kanamycin ovule. (5) 2% clindamycin topical. (3) Fluoroquinolones are reported to have clinical success. (3) GBS is uniformly sensitive to penicillin, ampicillin, amoxicillin, amoxicillin/ clavulanic acid. (7) *E. faecalis* is traditionally treated with ampicillin. (8)

References are provided for treatment information; Fluoroquinolones, such as ciprofloxacin, ofloxacin, and levofloxacin, are contraindicated in pregnant women. Levofloxacin has improved efficacy against *Streptococci* compared to ciprofloxacin. †= Intravenous

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Ureaplasma and Mycoplasma

- Mycoplasma hominis is related to miscarriages especially in the presence of abnormal vaginal flora.
- Mycoplasma genitalium is now recognized as an STI
  - linked to cervicitis, PID in non-pregnant, and preterm birth and miscarriages in pregnant women.
- Linked to male and female infertility

- Donders GG, J Perinat Med. 2017 Jan 18.
- Lab Med Crescent Med J. 2015 Dec 26;17(12):
- Infection. 2015 Sep;3(5):809-16

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Ureaplasma and Mycoplasma

- Azithromycin 1g single dose or 250mg dose pack
- Clarithromycin 500mg BID X 10 days
- Doxycylcine 100mg BID 14 days
- Tetracycline??

- Test and treat the male partner- considered STI

- https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0012310/
- Sex Transm Infect. 2006 Aug; 82(4): 269-271.

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Case- vaginitis

- IN Nov 2017 21 year old sexually active woman presents with vaginitis sxs. She says she has had 4 yeast infx in past 6 months. Tested and treated by MD
  - Testing by wet mount 3 months ago and treated with fluconazole and then 'swab test at lab" for bacteria and yeast and she had yeast again 3 weeks ago
- 3 weeks ago with MD she tested negative for pregnancy, GC/CT/trich, normal U/A and pap smear
- Treated with fluconazole and Monistat 3 weeks prior to appt
- Current SXS of discharge and itching, no urinary sxs today
- Exam revealed mild thin white D/C. No pain, no vulvitis, urine dip/HCG neg
- Ph and amine test in office positive for bacteria-Swabs and samples collected
- Initial treated prior to test results- no wheat, no sugar, limit alcohol
- Vitamin D3 2,000iu
- V-fresh vaginal suppositories
- Oral probiotic for vaginal and urinary health

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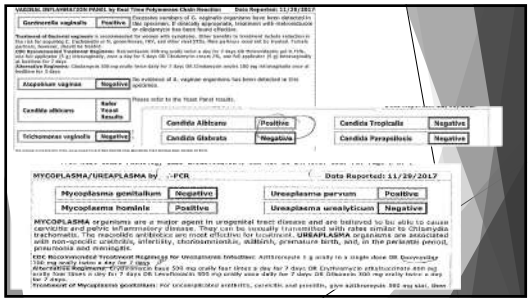

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Case- vaginitis

- Antibiotic prescription called in for Doxycycline 100mg BID for 7 days
- Stay on oral probiotic for vaginal health and add oral probiotic for GI
- She had already finished V-fresh suppositories
- Added yeast arrest suppositories before bed for 7 nights
- Last did fluconazole 5 weeks prior and 2 months prior to that round so clearly wrong antifungal.
- 3 months went by before she followed up, kept cancelling because she was 'fixed'
- Returned with itching an discharge again, has been sexually active
- She said initial treatment worked
- Exam was unremarkable- urine dip and HCG negative. No D/C and VS sense swab in office normal. Samples taken

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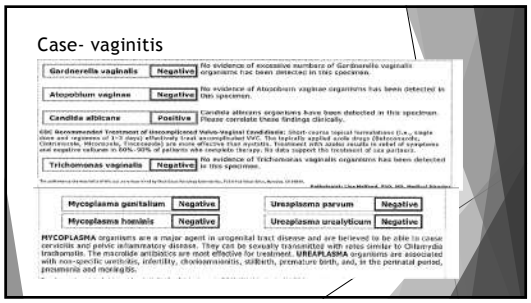
Case- vaginitis



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Case- vaginitis

- I compounded boric acid and it finally resolved
- 600mg BID for 1 week

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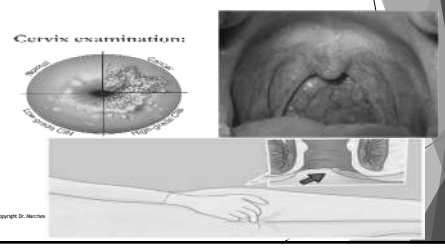
HPV



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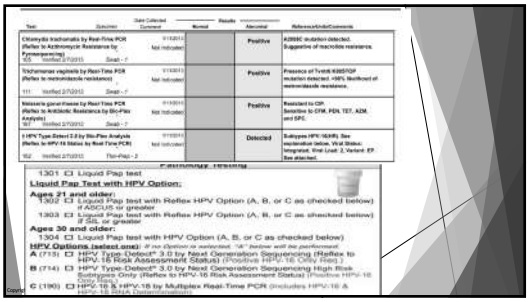

Test	Specimen	Date Collected / Comment	Results: Normal	Results: Abnormal	Reference/Additional Comments
Chlamydia trachomatis by Real-Time PCR (Reflex to Azithromycin Resistance by Pyrosequencing)				Positive	A2059C mutation detected. Suggestive of macrolide resistance.
Trichomonas vaginalis by Real-Time PCR (Reflex to nitroimidazole resistance)				Positive	Presence of T-rich K365/TGP mutation detected. >95% likelihood of nitroimidazole resistance.
Neisseria gonorrhoeae by Real-Time PCR (Reflex to Antibiotic Resistance by Bio-Plex Analysis)				Positive	Resistant to CIP. Sensitive to CTM, PEN, TET, AZM, and SPC.
I HPV Type Detect 3.0 by Bio-Plex Analysis (Reflex to HPV 16 Status by Real-Time PCR)				Detected	Subtypes HPV-16/Alt: See explanation below. Viral Status: Integrated. Viral Load: 2. Variant: EP. See also test.

Cytology Testing

1301 ☐ Liquid Pap test

Liquid Pap Test with HPV Option:

Ages 21 and older:

1302 ☐ Liquid Pap test with Reflex HPV Option (A, B, or C as checked below) if ASCUS or greater

1303 ☐ Liquid Pap test with Reflex HPV Option (A, B, or C as checked below) if SIL or greater

Ages 30 and older:

1304 ☐ Liquid Pap test with HPV Option (A, B, or C as checked below)

HPV Options (select one): *If no Option is selected, "A" below will be performed*

A (713) ☐ HPV Type-Detect® 3.0 by Next Generation Sequencing (Reflex to HPV-16 Risk Assessment Status) (Positive HPV-16 Only Rflx)

B (714) ☐ HPV Type-Detect® 3.0 by Next Generation Sequencing High Risk Subtypes Only (Reflex to HPV-16 Risk Assessment Status) (Positive HPV-16 Only Rflx)

C (190) ☐ HPV-16 & HPV-18 by Multiplex Real-Time PCR (Includes HPV-16 & HPV-18 RNA Confirmation)

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Genotype testing

- What genotype does she/he have???
- Co-infections by multiple HPV types are likely to occur in more than 30% of HPV patients.
- Certain combinations of these co-infections may be more prone to cause cancer than others.

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		TEST	TEST CODE	PT PRICE	TESTING METHOD – COLLECTION
PAP	LabCorp	Pap alone	LC 192005	$45	Liquid Based Liquid Based - ThinPrep Vial 
		Pap w/ HPV (hr)	LC 195050	$95	
		G/C alone	LC 183616	$95	
		Pap w/ HPV (hr), G/C	LC 192146	$185	
	MDL	Pap alone	MDL	$75	
		Subtyping alone	MDL	$120	
		Pap with HPV Subtyping (Includes HPV: 1.a, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)	MDL	$170	
		Pap w/ HPV subtyping, G/C	MDL	$170+80 = $250	

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HPV positive, negative, latent, subclinical, clinical

- Latent HPV infection – They probably have HPV in very low numbers (perhaps 1 HPV) per infected cell. Not contagious
- Subclinical HPV infection - changes in the skin cells of the lower genital tract that *cannot* be seen with the "naked" eye. –Dysplasia
- Clinical HPV - warts and precancerous changes on the external genitalia-vulvar, perianal, as well as cervical and other lower genital tract cancers usually *can* be seen with the "naked" eye.

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HPV methylation

- HPV 16-positive women with lower plasma concentrations of folate were nine times more likely to be diagnosed with CIN II compared to HPV 16-negative women with higher folate
- Women with lower folate status may have hypomethylated HPV 16, and thus may be unable to keep oncogene expression at level sufficiently low to avoid progression.
- Piyathilake C.J. Cancer Prev Res (Phila). 2014 Nov; 7(11): 1128-1137.

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HPV methylation

- Higher degree of methylation of HPV 16 is associated with a lower likelihood of being diagnosed with CIN II
- Also showed that low plasma folate and B12 was linked to higher rate of HPV 16 CIN II and III.
- Methyl donor micronutrients play a role in maintaining a high degree of methylation at specific CpG sites in the HPV E6 promoter and enhancer that are associated with the likelihood of being diagnosed with higher grades of CIN.

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HPV testing

- Cervical- Pap smear in liquid based cytology, PCR swab
- Anal- Pap smear, PCR swab
- Throat/Mouth- PCR swab, pap smear
- Urine- In 213 men gargles and urine were collected, and cells were preserved in liquid-based cytology then analysis with PCR.
  - HPV detection rates were 18.8% and 22.1% in oral and urine samples

BMC Infect Dis. 2014 Jan 27;14:43.

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Oral/Throat

- Head and neck cancers are caused by tobacco and alcohol
- 70% of cancers of the oropharynx are linked to HPV
- Oropharyngeal cancers (back of the throat, including tongue and tonsils) are the most common among men.
- 70 percent of cases of oropharynx cancer is caused by HPV16
- 3 to 5 percent of adolescents and 5 to 10 percent of adults have an active oral HPV infection.
- https://www.mountsinai.org/patient-care/service-areas/ent/areas-of-care/head-and-neck-cancer/oral-cancer/hpv/hpv-faq

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Oral/Throat

- The odds of HPV-positive throat cancer doubled in individuals who have one-five lifetime oral sexual partner
- The risk increased five-fold in patients with six or more oral sexual partners in their lifetime
- Symptoms include hoarseness, pain or difficulty swallowing, pain while chewing, a lump in the neck, a feeling of a lump in the throat, change in voice, or non-healing sores on the neck
- https://www.mountsinai.org/patient-care/service-areas/ent/areas-of-care/head-and-neck-cancer/oral-cancer/hpv/hpv-faq

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Oral testing- cell collection

- Swab the
  - buccal gutters, bilaterally
  - both cheek mucosas
  - both peritonsillar pillars
  - tonsils and pharynx.
- Place the swab immediately into the ThinPrep fluid, breaking off the handle.

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Oral/Throat
HPV natural treatment

- Mighty Flow-lozenges, rinse, spray
- Curcumin
- Green tea
- Resveratrol
- Folic acid
- Anti viral herbs
- Vitamin- C
- Nutrients- vitamin A, vitamin E, iron, ß-carotene, and folate intake may be a factor in the improved prognosis in those with HPV-positive HNSCC.

- Nutr Cancer. 2011;63(5):734-42.

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Oral/Throat
HPV natural treatment

- Curcumin- *in vitro* studies in oral cancer cells, curcumin has shown to have a strong anti-HPV effect
- Curcumin is a potent inhibitor for the activity of host nuclear transcription factors AP-1 and NF-kB
- Curcumin suppresses transcription of the HPV16/E6 oncogene during the carcinogenic process in oral cancer cells.

- Mishra A, Kumar R, Kohaar I Curcumin modulates cellular AP-1, NF-kB, and HPV16 E6 proteins in oral cancer. *Francermedicalscience* 9, 525 (2015).

Francermedicalscience. 2015 Apr 23;9:525.

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Oral/Throat
HPV natural treatment

- TriCurin- curcumin, resveratrol and green tea. Studied in HPV16 induced Head and neck squamous cell carcinoma
- Cell viability, clonogenic survival, and tumorsphere formation were inhibited and significant apoptosis was induced by TriCurin in HPV-positive HNSCC cells
- Folic acid supplementation altered the growth rate of HPV16 oral cancer cell lines. Increases survival and modulates high risk HPV-induced phenotypes

- Oncotarget. 2016 Jul 16.
- Cancer Cell Int. 2012 Mar 23;12:10

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Oral/Throat
HPV natural treatment

- *Trametes versicolor* and *Ganoderma lucidum* (Reishi)
- 472 patients oral swabs for gingivitis.
- 61 were positive for HPV16 or 18.
  - Twenty patients were given control; 5% clearance after 2 months of treatment
  - 41 patients were given *versicolor* and Reishi; 88% clearance after 2 months of treatment.

- Donatini Bruno.. *International Journal of Medicinal Mushrooms*, 16(5):497-498 (2014)

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Anal

- HPV is responsible for 90% of anal and cervical cancers, 70% of vaginal and vulvar cancers, and 60% of penile cancers.
- Women with a history of CIN3 showed increased risk of HPV-related anal carcinomas and high grade anal intraepithelial neoplasia (AIN)
- This risk remained significantly increased, even after long-term follow-up of up to 20 years
- 54,320 women with a diagnosis of CIN2 or CIN3 were identified between 1985 and 2005
- There were statistically significant increases in anal cancers 5-9 years after CIN diagnosis

https://www.cdc.gov/cancer/hpv/statistics/
JClin Oncol. 2017 May 25:
Gynecol Oncol. 2014 Sep;134(3):523-6

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Anal

- AIN affects the peri-anal skin, perineum, or natal cleft too
- Symptoms; itching and soreness or no symptoms
- Recognizable clinical signs of pigmentation, white lesions, fissuring, etc.
- Test for HPV alone with PCR or HPV and cytology with pap
- Diagnostic punch biopsies should be carried out if there are physical signs suggestive of AIN, or persistent ulceration.
- Same cervical/Oral HPV treatment
- Anal suppositories
  - Green tea?
  - Curcumin?

Skin Therapy Lett. 2015 Jan-Feb;20(1):6-8.

57

Cervical

- Methylfolate
- Methyl B12
- Vitamin C
- Anti-viral herbal tincture- formulate
- Green tea extract
- Indole-3-carbinol
- DIM
- Medicinal mushrooms
- Curcumin

58

Beta carotene

- Epidemiological studies show retinol intake and serum retinol levels have been found to be 4.5x lower among women with cervical dysplasia who progress to cervical cancer.
- Vitamin A intake and vitamin A blood levels inversely associated with cervical cancer.
  - Marshall K. PMID: 12777161
  - Zhang X et al. PMID: 22005522

59

Ascorbic acid

- Patients with the highest dietary intakes of vitamin A, beta-carotene, and vitamin C had lower cervical cancer risks than those with the lowest intake of these nutrients.
  - Kim J et al. PMID: 20099192

60

Green Tea

- ECGC in green tea was evaluated on cervical epithelial; cells and cervical cancer cells and HPV.
- Green tea inhibited cancer cell growth, induced apoptosis, decreased gene expression, and cell cycle changes.

- Int J Gynecol Cancer. 2010 ;20(4):617-624

61

I3C / DIM

- Estrogen is another well-known factor in the development of CIN.
- I3C and DIM have been shown to alter estrogen metabolism pathways and suppress viral oncogene expression.

- Sepkovic DW et al. PMID: 21383027
- Ashrafian Levon et al. PMCID: PMC4685602

62

Indole-3-carbinol

- 30 patients with CIN II-III
- 17 took I-3-C 400mg for 12 weeks (13 placebo group)
- 8 of the 17 had complete regression
- I-3-C up-regulates tumor suppressor gene PTEN which is MOA for inhibiting development of cervical cancer.

- Gynecol Oncol 2000. Aug 78(2) 123-129
- Mol Med 2005 Jan-Dec 11(1-12):59-63

63

Cervical

Vaginal suppositories

- Green tea- compounded 150mg
- Protocols vary by cytology and HPV strain and colposcopy results

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Escharotics

- Colposcopy must be satisfactory (transformation zone seen)
- ECC negative
- No glandular or endometrial cells present

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Escharotic

- ZnCl solution: 90grams ZnCl/60ml sterile water: ½ ounce
- Sanguinaria tincture: 1ounce
- Bromelian powder: 500mg caps, 3 caps
- Calendula succus: 2 ounce
- Plastic pipette: 10 of them
- Scopettes: lots
- Green tea suppositories: 12 count

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Escharotic treatment

- Insert a well lubricated speculum
- Blot cervix clean with scopette
- "Puff" bromelain powder with pipette onto cervix and inside endocervical canal
- Leave on for 15 minutes with the heat of a lamp
- Remove powder with water and wipe extra pooled solution away

67

Con't

- Mix ZnCl and Sanguinaria together- ¼ tsp ZnCl to ¾ tsp Sanguinaria
- Apply mixture to cervix and endocervical canal. Leave for 1 minute
- Wash cervix and endocervical canal with water
- Wipe extra pooled solution away with scopette and apply calendula succus
- Insert 1 green tea suppository the next night

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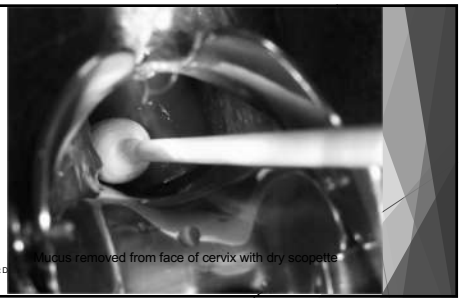
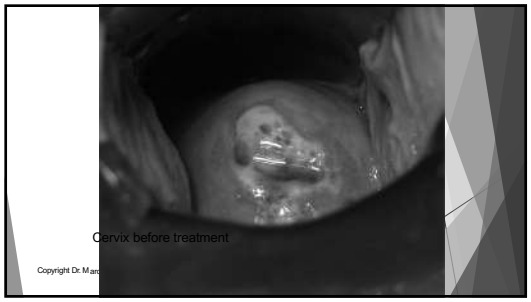


Mucus removed from face of cervix with dry scopette

69


Cervix before treatment
Copyright Dr. Marc

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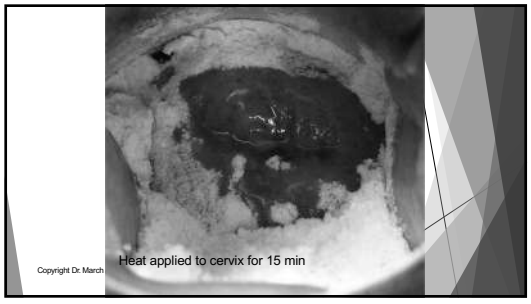
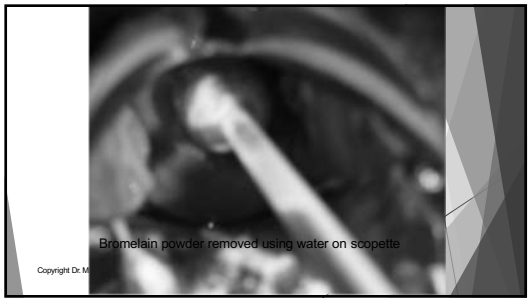
Bromelain powder applied to cervix with pipette
Copyright Dr. Marc

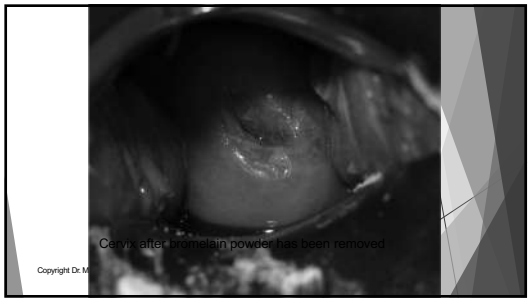
71


Heat applied to cervix for 15 min
Copyright Dr. March

72


Bromelain powder removed using water on scopette
Copyright Dr. M

73


Cervix after bromelain powder has been removed
Copyright Dr. M

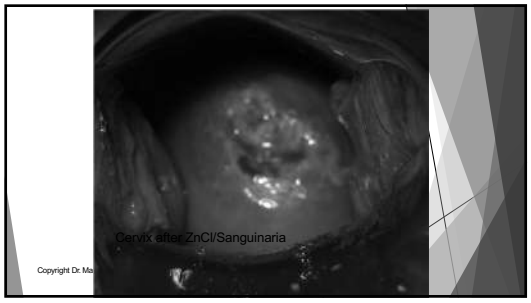
74


Cervix with ZnCl/Sanguinaria - leave for 1 min
Copyright Dr. Marchese

75


ZnCl sanguinaria removed with water
Copyright Dr. March

76


Cervix after ZnCl/Sanguinaria
Copyright Dr. Ma

77


suppositories inserted against cervix the night after
Copyright

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Cervical dysplasia case

- In 2017 a 37 y/o with ASCUS, hr HPV detected, no genotype
- First abnormal pap smear, married, monogamous 5 years
- Referred for colposcopy
- Then referred to me for escharotics
- She has MS and did a round of prednisone 6 months prior to pap smear
- DM II which is not controlled

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GYNECOLOGIC TESTING

Pap ThinPrep
Source:
Vagina, Cervix, Endocervix
Last Menstrual Period:
03/13/2017
Clinician Provided Information:
Pap Diagnosis:
Epithelial Cell Abnormality: Atypical squamous cells of undetermined significance (ASC-US)
Specimen Adequacy:
Satisfactory for evaluation.
Endocervical/transformation zone component present.
Accession #:
Cytotechnologist:
Pathologist:

Electronically signed by Mutammad Jameel Arshad M.D.
Verified 04/17/17

Report Statement:
The ThinPrep Pap Test has been evaluated with the assistance of the ThinPrep Imaging System.

HPV mRNA — Detected / Not Detected

The analytic performance characteristics of this HPV assay for vaginal specimens have been determined by Aptima Quest Diagnostics. This assay is not intended for medico-legal uses.
Methodology: nucleic acid amplification.

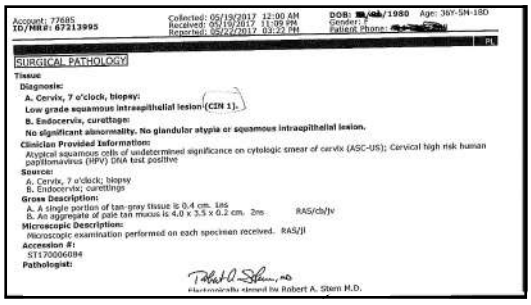
Chlamydia trachomatis/N. gonorrhoeae, ThinPrep Vial*
Source: Vagina, Cervix, Endocervix

Chlamydia trachomatis	Negative	Negative
N. gonorrhoeae	Negative	Negative

*Chlamydia trachomatis/N.

Chlamydia trachomatis and N. gonorrhoeae: Organism viability cannot be inferred since target rRNA will be detected in the absence of the organism. A test cannot be used to

80



Account: 77685
ID/MR#: 67213995
Collected: 05/19/2017 12:00 AM
Received: 05/19/2017 11:09 PM
Reported: 05/22/2017 03:22 PM
DOB: [redacted]/1980 Age: 36Y-5M-18D
Gender: F
Patient Phone: [redacted]

SURGICAL PATHOLOGY

Tissue
Diagnosis:
A. Cervix, 7 o'clock, biopsy:
Low grade squamous intraepithelial lesion (CIN 1).
B. Endocervix, curettage:
No significant abnormality. No glandular atypia or squamous intraepithelial lesion.
Clinician Provided Information:
Atypical squamous cells of undetermined significance on cytologic smear of cervix (ASC-US); Cervical high risk human papillomavirus (HPV) DNA test positive
Source:
A. Cervix, 7 o'clock; biopsy
B. Endocervix; curettings
Gross Description:
A. A single portion of tan-gray tissue is 0.4 cm. tas
B. An aggregate of pale tan mucus is 4.0 x 3.5 x 0.2 cm. 2ns RAS/cb/jv
Microscopic Description:
Microscopic examination performed on each specimen received. RAS/jl
Accession #:
ST170006094
Pathologist:

Electronically signed by Robert A. Stein M.D.

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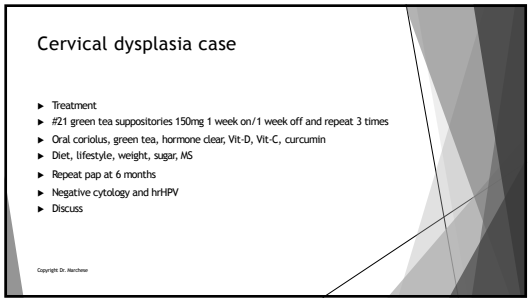
Cervical dysplasia case
Treatment
#21 green tea suppositories 150mg 1 week on/1 week off and repeat 3 times
Oral coriolus, green tea, hormone clear, Vit-D, Vit-C, curcumin
Diet, lifestyle, weight, sugar, MS
Repeat pap at 6 months
Negative cytology and hrHPV
Discuss
Copyright Dr. Marchese

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