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SASGO CONGRESS
31 AUGUST - 2 SEPTEMBER 2018
Spier Estate, Stellenbosch Cape Town

What is different in the South African mouth?

Neil H Wood

SEFAKO MAKGATHO HEALTH SCIENCES UNIVERSITY

aml algemeen medisch labo

University of Antwerp

University of Antwerp

SEFAKO MAKGATHO HEALTH SCIENCES UNIVERSITY

aml algemeen medisch labo

Introductory remarks

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Transmission of HPV

- Human papillomavirus is the most frequently sexually transmitted infection
- Transmission requires close contact – predominantly sexual
- Other modes of transmission include:
  - Vertical transmission
  - Practice of oral sex
  - Kissing
  - Digital (fingernails)
  - Breast tissue (Lactating or discharge)
  - Indirect pathways: Sharing baths, sharing towels, laser plumes, unsterilized instruments.

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Risk factors for oral HPV infection

- Certain sexual practices
- Number of lifetime partners
- Number of recent sex partners
- Older age
- Being male
- Current cigarette smoking

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HPV-associated oral diseases

- Manifestations of oral HPV infection:
  - Transitory (Subclinical) up to 50% of cases
  - Spontaneous regression in up to 30% of cases
  - Persistent infection

- Important to know whether infection is latent or whether virus is transcribed – mRNA

Dos Reis et al., 2009

HPV-associated oral diseases

- HPV is a known aetiologic factor for benign oral/oropharyngeal lesions:
  - Verruca Vulgaris
  - Oral Squamous Papilloma
  - Condyloma Accuminatum
  - Focal Epithelial Hyperplasia (Heck disease)

- HPV has a strong association with oropharyngeal malignancy:
  - Squamous Cell Carcinoma
  - (Some attribute 30% of oral SCC's to HPV)

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HPV-associated oral diseases

- Most prevalent type infecting oral mucosa – HPV 16 (reporting bias)

- Meta-Analysis of HPV 16 presence in Head and Neck Squamous Cell Carcinoma biopsies worldwide:
  - Oropharyngeal SCC – 31%
  - Oral SCC – 16%
  - Laryngeal SCC – 17%

- HPV 18 plays significant role in Oropharyngeal SCC development

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Global HPV prevalence in mouth and oropharynx

Global oral/oropharyngeal HPV prevalence

- Herrero R, Quint W, Hildesheim A, Gonzalez P, Struijk L, Katki HA, et al. (2013) Reduced Prevalence of Oral Human Papillomavirus (HPV) 4 Years after Bivalent HPV Vaccination in a Randomized Clinical Trial in Costa Rica. PLoS ONE 8(7): e68329.

- "Our results suggest that administration of the HPV vaccine will guard against oral infection by the HPV types responsible for the vast majority of HPV-related OPC, and open the possibility of primary prevention of these increasingly common malignancies."

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Global oral/oropharyngeal HPV prevalence

- Great variation in oral detection of HPV DNA: 0%-81%

- In population-based, case-control studies of oral cancer, the prevalence of oral HPV infection among control patients varied from 5.0% to 9.2%

- 2018 Meta-analysis:
  - Person-specific prevalence for oral HPV = 7.7%
  - Incidence: 4.38 cases/1000 per 1000 months
  - Clearance/persistence ranged from 42.1% - 80%

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South African HPV prevalence in mouth and oropharynx

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South African Literature

Authors	Year	Oral sample taken from which population	HPV types investigated
Chikandiwa et al.,	2018	181 HIV seropositive men	19xLR; 3pHR; 15xHR
Muller et al.	2016	200 MSM	24 x LR; 13 x HR
Davidson et al.	2014	125 male factory workers	19xLR; 3pHR; 15xHR
Mbulawa et al.	2014	221 heterosexual couples (442 participants)	37 HPV types
Vogt et al.	2013	34 couples	15xHR; 22 other
Paquette et al.	2013	55 OSSCa	37 HPV types
Marais et al.	2008	115 women with confirmed cervical disease	37 HPV types
Richter et al.	2008	30 women, oral scraping	19xLR; 3pHR; 15xHR
Boy et al.,	2006	59 OSCCa cases	16 and 18
Van Rensburg et al.	1996	146 OSCCa cases	6, 11, 16, 18
Van Rensburg et al.	1995	66 OSCCa cases	6, 11, 16, 18

Prevalence of HPV in SA

- South African studies:
  - Focus on targeted cohorts
  - Mostly limited number of HPV-subtype identification
  - Smaller sample sizes

  - None included children:
    - Jeftha et al., (2003) reported oral HPV prevalence of 3.6% in HIV + children vs 12.3 HIV- (2003 AADR Proceedings)

  - None included a cohort on HAART

Prevalence of HPV in SA

- Van Rensburg et al., 1995
  - 66 cases of Oral Squamous Cell Carcinoma
  - Targeted HPV 6, 11, 16 and 18

- Van Rensburg et al., 1996
  - 146 cases of Oral Squamous Cell Carcinoma
  - Targeted HPV 6, 11, 16 and 18

It could be that oral or oropharyngeal Squamous Cell Carcinoma is associated with a different type of HPV.

Prevalence of HPV in SA

- Boy et al., 2007
  - 59 patients with Oral Squamous Cell Carcinoma
  - Only investigated HPV 16 and 18
  - Results were contrasting to a meta-analysis by Miller and Johnstone (2001)

  - 7 were RT-PCR positive for HPV 16, none for HPV 18
  - All negative on *in situ* hybridiztion (ISH) for both HPV 16 and HPV 18

- By definition, the sites investigated by these three studies included the oropharynx.

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Prevalence of HPV in SA

- Richter et al., 2008
  - 30 women, HIV positive, prior to HAART
  - Oral sites *scraped*: buccal mucosa and lateral borders of the tongue

  - However: HPV types investigated –

HR: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82

P-HR: 26, 53, 66

LR: 6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 83, 84, IS39 and CP6108

Prevalence of HPV in SA

- Richter et al., 2008 continued…
  - Oral HPV types identified:

    HPV – 45, 59, 62, 72, 81, 84

  - 2/30 had multiple oral HPV types
  - 6/30 had concurrent oral/genital HPV types, but only 3 corresponded…

- Marais et al., 2008 identified oral infection with HPV in 45.5% of HIV + and 25% of HIV- women with confirmed cervical disease.
  - Most commonly identified HPV - 33, 11 and 72

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Prevalence of HPV in SA

- Paquette et al., 2013
  - HPV 16, 18, 31, 33, 35, 39, 45, 52, 58, 59 and 68
  - 37/55 Oropharyngeal Squamous Cell Carcinoma FFPE tissue specimens were HPV positive
    - HPV 16 AND 31 – 32%
    - HPV 16 – 32%
    - HPV 31 – 24%
    - HPV 16 and 18 – 8%
    - HPV 18 – 4%
  - Stark contrast to Boy et al., (2007)

Prevalence of HPV in SA

- Vogt et al., 2013
  - 34 Couples' oral and genital HPV prevalence
  - Investigated 37 types including oncogenic types:

    16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82
  - Described as 'oral' but because a gargle and rinse technique was used, the wash is representative of oral and oropharyngeal
  - 3 couples had concordant oral-genital HPV infection which supports the oral-sex transmission route.
  - Detected: HPV – 62, 72, 35, 52, 33, 58, 16, 74, 66
  - (4% oncogenic types)

Prevalence of HPV in SA

- Mbulawa et al., 2014
  - 221 Heterosexual couples – brush collection buccal
  - 6.8% of women and 13.5% of men – oral HPV positive
  - 13.5% of all participants had multiple oral HPV types
  - Most commonly identified types:

    HPV – 72, 55, 62, 61
  - Other HPV types in the mouth:

    HPV – 52, 84, 81, 11, 31, 69, 51, 81, 89, 53, 59, 42, 35, 33, 58, 16

Prevalence of HPV in SA

- Davidson et al., 2014
  - 125 Male factory workers
  - HPV types investigated:

HR: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82

P-HR: 26, 53, 66

LR: 6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 83, 84, IS39 and CP6108

  - 7 (5.6%) tested positive for oral/oropharyngeal HPV infection with one having HPV 71 and 72 co-infection
  - Two participants had a HR-HPV-type each (16 and 68)

Prevalence of HPV in SA

Only one HPV prevalence study has been done for MSM in South Africa

Müller et al. BMC Infectious Diseases (2016) 16:440
DOI 10.1186/s12879-016-1706-9

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

The prevalence of human papillomavirus infections and associated risk factors in men-who-have-sex-with-men in Cape Town, South Africa

Etienne E. Müller[1*], Kevin Rebe[2,3,4], Tobias F. Chirwa[5], Helen Struthers[2,3,4], James McIntyre[2,3,6] and David A. Lewis[7,8]

South African MSM study (MeCRU)

Prevalence of oral/oropharyngeal HPV in MSM at MeCRU

Variable	Category			N 199	%
HPV status	Negative			186	93.9
	Positive			12	6.1
	Subtype 16	1(n)	8,33%		
	Unknown subtype	11(n)	91,77%		

Comparison of demographic data, seropositivity and socio-economic status to HPV

		Overall		HPV status				p-value
				Negative		Positive		
Variable	Category	n	%	n	row %	N	row %	
		199		186		12		
Race	Black	196	98,5	183	93,8	12	6,2	>0.99
	Coloured	3	1,5	3	100,0	0	0,0	
Social Economic Status(SES)	Unemployed	105	53,3	99	94,3	6	5,7	0,41
	Employed	71	36,0	65	91,5	6	8,5	
	Student	21	10,7	20	100,0	0	0,0	
	Unknown	2						
HIV status	positive	133	66,8	123	92,5	10	7,5	0,34
	negative	66	33,2	63	96,9	2	3,1	

Table 2: Association of sexual behaviour and HPV status

Variable	Category	Overall		HPV status				p-value
				Negative		Positive		
		n	%	n	row %	N	row %	
		199		186		12		
Current sex practices	Anal sex	138	69,4	*	*	*	*	
	Oral sex	57	28,6	49	86,0	8	14,0	0,0057
	Rimming	19	9,6	17	89,5	2	10,5	0,32
	Vaginal sex	1	0,5	*	*	*	*	
Number of partners in past 6 months	0	9	4,7	7	77,8	2	22,2	0,051
	1	53	27,7	52	98,1	1	1,9	
	2	39	20,4	35	89,7	4	10,3	
	3 or more	90	47,1	85	95,5	4	4,5	
	Unknown	8						
Sex practices ever done with a male partner	Oral receptive	161	80,9	149	92,5	12	7,5	0,13
	Oral insertive	121	60,8	108	90,0	12	10,0	0,0038
	Rimming bottom	92	46,2	86	93,5	6	6,5	0,80
	Rimming top	39	19,6	35	89,7	4	10,3	0,26
	Anal bottom	15	7,5	*	*	*	*	
	Anal top	5	2,5	*	*	*	*	

Association with sexual behaviour and HIV status

				HIV status				p-value
				Positive		Negative		
		Number	%	Number	%	Number	%	
				133	66,8	66	33,2	
Current Sex Practise								
	Oral sex	57	28,6	37	64,9	20	35,1	0,74
	Rimming	19	9,6	18	94,7	1	5,3	0,0046
Number of partners in past 6 months								
	0	9	4,7	5	55,6	4	44,4	0,58
	1	53	27,7	35	66,0	18	34,0	
	2	39	20,4	23	59,0	16	41,0	
	3 or more	90	47,1	63	70,0	27	30,0	

HPV prevalence in mouth and oropharynx – Two sites at SMU

Oral/Oropharyngeal HPV prevalence at SMU

Two populations:

- HIV-management clinic (DGMAH)
- SMU Dental hospital

Oral/Oropharyngeal HPV prevalence at SMU

SITE	Participants	Notes
HIV Management Clinic	2 x males	No tonsil 1 x HPV 16 1 x HPV 67
Dental Hospital	2 x males	No Tonsil 1 x HPV 35 1 x HPV 53

Oral/Oropharyngeal HPV prevalence at SMU

SITE	Participants	HPV prevalence
HIV Management Clinic	n=72	2.8%
Dental Hospital	n=150	1.3%
MeCRU (MSM)	N=199	6.1%

Consistent with current available data from similar SA cohorts

Concluding remarks

•Oral/Oropharyngeal HPV prevalence appears to be at the lower end of the global reported spectrum.

•Study design diversity precludes the collating of data to perform a meta-analysis of South African studies

•Current results could support the proposal for vaccination of boys

Thank you