

World STI and HIV Congress

Melanie Bissessor



The contribution of *Mycoplasma genitalium* to the aetiology of sexually acquired infectious proctitis in men who have sex with men

Bissessor M^{1,2}, Tabrizi SN^{3,4}, Bradshaw CS^{1,5}, Fairley CK^{1,5}, Hocking JS², Garland SM³, Twin J⁴, Poljak M⁴, Peel J¹, Chen MY^{1,5}

- Melbourne Sexual Health Centre, Alfred Health, Victoria
- Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Victoria
- Department of Obstetrics and Gynaecology, University of Melbourne, Victoria,
- Department of Microbiology, Infectious Diseases, The Royal Women's Hospital, Murdoch Children's Research Institute, Queensland
- Central Clinical School, Monash University, Melbourne, Victoria



Background (1)

- Rectal infections with pathogens increase the risk for HIV acquisition¹
- Unprotected receptive anal sex confers a high risk for HIV acquisition²
- Previous studies have described the spectrum of pathogens responsible for proctitis in MSM^{3,4,5}

1. Bernstein KT et al. *Journal of Acquired Immune Deficiency Syndromes* 1999; 53(4):537-43
2. Jin F et al. *Journal of Acquired Immune Deficiency Syndromes* 1999; 53(1):144-9
3. Quinn TC. *The American Journal of Medicine* 1981; 71(3):395-40
4. Klausner J et al. *Clinical Infectious Disease* 2004; 38(2):300-2
5. Bissessor M et al. *STD* 2013; 44(10):769-70



Background (2)

- *Mycoplasma genitalium* causes urethritis in men and genital tract infection in women
- Previous studies identified *M. genitalium* in the rectum of MSM
- Prevalence rates between 1.6 % and 5.0%¹⁻⁴

1. Francis S et al. *Sexually Transmitted Diseases* 2008; 35 (9):797-800
2. Soni S et al. *Sexually Transmitted Infections* 2010; 86(1):21-4
3. Bradshaw CS et al. *Sexually Transmitted Infections* 2009; 85(6):432-5
4. Reinton N et al. *Sexual Health* 2013; 10(3):199-203



Aims

- Prospective study of MSM presenting with symptomatic proctitis
- Determine the prevalence of rectal *M. genitalium*
- Compare these between HIV positive and HIV negative men
- Compare the load of *M. genitalium* in men with symptomatic rectal infection to men with asymptomatic rectal infection



Methods (1)

- From 1st May 2012 all MSM with clinical proctitis at MSHC tested for rectal:
 - *Mycoplasma genitalium*
 - Gonorrhoea, Chlamydia, HSV
- Diagnosis of proctitis: clinical based on the presence of rectal pain and/or discharge



Methods (2)

- Between May 2012 and August 2013 measured prevalence of rectal *M. genitalium* in consecutive MSM with symptomatic proctitis
- Measured organism load in men with *M. genitalium*-associated symptomatic proctitis
- Compared this in a separate group of men with asymptomatic rectal *M. genitalium* infection



Methods (3)

- Asymptomatic sexual contacts of men with urethral *M. genitalium*
- Selected into the study from the beginning of the study period in consecutive order of presentation
- One case of asymptomatic rectal *M. genitalium* infection for each case of *M. genitalium* associated symptomatic proctitis



Methods (4)

- *Chlamydia trachomatis* using SDA
- Genotyping for LGV on chlamydia positive samples using an in-house OMP-1 DNA sequencing method
- *Neisseria gonorrhoeae* using culture
- HSV using an in-house herpes multiplex PCR



Methods (5)

- Syphilis serological testing using RPR and EIA
 - *Treponema palladium* by PCR using TaqMan real-time PCR assay
 - *M. genitalium* using qPCR targeting a 517bp region of the 16S rRNA gene¹
 - HIV by immunoassay (Murex UK)
- 1. Twin J et al. Journal of Clinical Microbiology 2011; 49(3):1140-2



Statistical analysis(1)

- Sample size 150 men (95% CI prevalence of 6-10%)
- Prevalence of each rectal pathogen
- Difference in prevalence between HIV positive and HIV negative men
- Chi square test to compare proportions



Statistical analysis(2)

- Log transformed rectal *M. genitalium* load
- Linear regression to determine if load differed between men with symptomatic and asymptomatic rectal infection
- Ethical approval for the study was obtained from the Alfred HREC (522/14)



Results (1)

- 154 men with proctitis
- 48 (31%) HIV positive
- 106 (69%) HIV negative
- Median age 38 years (range: 22-58 years)
- Median CD4 count : 475 cells/uL
- 81% on ART and 97% on ARV -HIV VL< 50 copies/ml
- Clinical presentation men broadly similar in both groups



Aetiology of proctitis by HIV status in MSM

Pathogens detected	HIV positive n=48	HIV negative n=106	Unadjusted Odds Ratio (95%CI) p-value
	No. (%; 95%CI)	No. (%; 95%CI)	
<i>Chlamydia trachomatis</i>	10 (21; 9-36)	20 (19; 12-26)	1.13(0.48-2.64) p=0.77
<i>Neisseria gonorrhoeae</i>	14 (29; 16-42)	24 (23;15-31)	1.41(0.65-3.04) p=0.43
HSV	9 (19; 8-30)	18 (17; 10-24)	1.20(0.47-2.73) p=0.76
HSV-1	2 (4; 0-10)	14 (13; 7-19)	0.29(0.06-1.31) p=0.09
HSV-2	7 (15; 5-25)	4 (4; 0.3-8)	4.35(1.21-5.67) p=0.02
LGV	4 (8; 0.3-16)	1 (1; 0-3)	9.5(1.03-87.83) p=0.02
Two or more pathogens	9 (19; 1-17)	8 (7; 2-12)	2.83(1.01-7.86) p=0.03

Results (3)

- 9/12 (75%) men with external anal ulceration had HSV detected:
- 5/9(56%) HIV positive
- 4/9 (44%) HIV negative
- 3 men with anal ulcers not associated with HSV were *T. pallidum* PCR positive

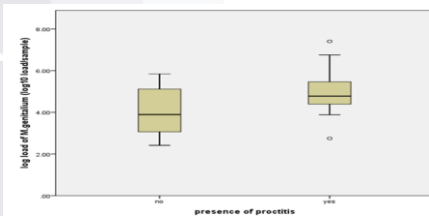


Mycoplasma genitalium associated proctitis

Pathogens detected	HIV positive n=48	HIV negative n=106	Odds Ratio (95%CI) p-value
	No. (%; 95%CI)	No. (%; 95%CI)	
<i>Mycoplasma genitalium</i>	10 (21; 9-36)	8 (8; 3-13)	3.22(1.18-8.78) p=0.02



Comparison of *M. genitalium* load



No symptoms of proctitis: median log load= 3.81 log₁₀ load/sample (IQR=3.03-5.18)

Symptoms of proctitis: median log load= 4.82 log₁₀ load/sample (IQR=4.34-5.61, p=0.023)

Among men in the asymptomatic comparison group were 4 men who were HIV positive



Discussion (1)

- First prospective cohort study of MSM with symptomatic proctitis systematically tested for rectal *M. genitalium*
- First study showing quantitative data of *M. genitalium* load in the rectum and its association with symptomatic proctitis
- Relative prevalence of pathogens seen in HIV positive men differed from that seen in HIV negative men
- Significantly higher prevalence among HIV positive men of *M. genitalium*, HSV 2, LGV and multiple pathogens



Discussion (2)

- *M. genitalium* present in 12% of MSM presenting with proctitis
- HIV positive status strongly associated with *M. genitalium* proctitis
- 21% of HIV positive men compared with 8% of HIV negative men with proctitis infected with *M. genitalium*
- Significantly higher rectal *M. genitalium* loads in men with symptomatic proctitis than men with asymptomatic rectal infection



Discussion (3)

- Other studies¹⁻⁵ examined the prevalence of rectal *M. genitalium* among MSM
- None included men specifically selected because of the presence of symptomatic proctitis

1. Francis S et al. Sexually Transmitted Diseases 2008; 35 (9):797-800.
2. Sori S et al. Sexually Transmitted Infections 2010; 86(1):21-4.
3. Bradshaw CS et al. Sexually Transmitted Infections 2009; 85(6):432-5.
4. Reinton N et al. Sexual Health 2013; 10(3):199-203.
5. Zheng et al. BMC Public Health 2014; 14:195.



Rectal Infection with *M. genitalium*

Authors	Population	Rectal <i>M. genitalium</i> prevalence (%95%CI)	Rectal symptoms and signs
Francis 2008	500 consecutive rectal MSM samples	27(5.4,3.6-7.7)	Not significantly associated with proctitis Associated with HIV (AOR:3.2)
Bradshaw 2009	cross sectional study 521 Australian MSM attending SOPV	8/497(1.6, 0.8-3.0)	All asymptomatic
Soni 2009	438 MSM attending STD clinic	19/412(4.6, 2.6-6.8)	Not significantly associated with proctitis Associated with HIV (AOR:7.6)
Reinton 2013	retrospective analysis of 1778 MSM rectal samples	65/1778(3.7, 2.8-4.5)	Unavailable
Zheng 2014	405 MSM attending STD clinic	22/405(5.4,3.5-7.7)	Unavailable Associated with HIV (OR:4.49)

Discussion (4)

- Higher rates of rectal *M. genitalium* among HIV positive compared to HIV negative MSM :
- 21% versus 8% (p=0.02)
- 11% versus 4% (p=0.005)¹
- 14% versus 2% (p<0.001)²
- 19% versus 5% (p=0.02)³

1. Francis S et al. Sexually Transmitted Diseases 2008; 35 (9):797-800.
2. Sori S et al. Sexually Transmitted Infections 2010; 86(1):21-4.
3. Zheng N et al. BMC Public Health 2014; 14: 195-197.



Discussion (5)

- Overall rate of rectal *M. genitalium* in our study is higher than in these previous studies
- Selected MSM with symptomatic proctitis
- Inclusion of HIV positive men, where sexual risk behaviours have contributed to higher rates of bacterial sexually transmitted infections



Discussion (6)

- In-vitro studies demonstrated that *M. genitalium* can establish long term infection in human endocervical cells¹
- Studies in females demonstrated presence of HIV susceptible cells in the mucosa of cervix with *M. genitalium* infection²
- HIV negative men with rectal mucosal inflammation severe enough to cause symptomatic proctitis and mucosal ulceration may also have increased susceptibility to HIV

1. McGowan CL et al. Infection and Immunity 2012; 80(11):3842-9
2. Maveitzenge SN et al. AIDS 2012; 26 (5):617-24



Discussion (7)

- Previous study demonstrated that symptomatic gonococcal proctitis was associated with higher loads of *N. gonorrhoeae* than seen with asymptomatic rectal gonorrhoea¹
- Organism load significantly higher in men with symptomatic rectal *M. genitalium* compared to men with asymptomatic rectal infection

1. Bissessor et al. *Journal of Clinical Microbiology* 2011; 49(12):4304-6.



Strengths and Limitations

- Conducted prospectively and consecutive MSM tested for *M. genitalium* and other rectal pathogens
- Diagnosis of proctitis was based on clinical criteria and not evaluated by rectal biopsy
- Gonorrhoea testing using culture which is less sensitive than NAAT for rectal infections^{1,2}

1. Page-Shafer KG. *Clinical Infectious Diseases* 2002; 34(2): 173-6
2. Schachter J et al. *Sexually Transmitted Diseases* 2008; 35(7): 637-42.



Conclusion

- *Mycoplasma genitalium*:
- Important rectal pathogen among MSM
- Cause of symptomatic proctitis
- Testing should be undertaken in MSM presenting proctitis



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