Understanding the terms we use: support for using 'Sexually Shared Microbiota'(SSM)

David Taylor-Robinson[1] , Patrick Horner[2,3,4] and Anna Pallecaros[5]

[1]Section of Infectious Diseases, Wright-Fleming Institute, Faculty of Medicine, Imperial College London, London, UK

[2]Population Health Sciences, University of Bristol, Bristol, UK

[3]National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Evaluation of Interventions in partnership with Public Health England, University of Bristol, Bristol, UK

[4]Unity Sexual Health, University Hospitals Bristol NHS Trust, Bristol, UK

[5]Department of Genito-urinary Medicine, Princess Grace Hospital, London, UK

There has been a rapid expansion in our understanding of the diversity and complexity of the genital tract microbiome over the past decade and our ability to detect these micro-organisms (microbiota) using sensitive and specific nucleic acid amplification tests (NAATs).[1-5] There is increasing evidence that transmission of these microbiota is the norm after unprotected sexual intercourse, with no risk of disease associated with the majority of microbiota transferred.[1, 2, 4] We would like to propose the term sexually shared microbiota (SSM) in order to avoid them being described as causing sexually transmitted infections (STIs) which is potentially stigmatizing and likely to promote the need for treatment.[3]

This article adds further to the debate [6-11] on the meaning and use of the terms "sexually transmitted infection" (STI) and "sexually transmitted disease" (STD) and considers whether they remain fit for purpose when applied to all genital- tract microbiota. Traditional STIs [12] (bacterial, viral, protozoal, and fungal) are transmitted from an individual to a recipient host mainly during sexual activity, to become attached to or to penetrate cells of the genital or other

site(s) of the host and multiply, causing an infection. This event, usually in association with a subsequent immunological reaction, may cause damage, sometimes of sufficient severity to bring about dis-ease with associated symptoms and signs. The larger the number of organisms involved (or the greater the "bacterial or viral load") the greater the chance of damage occurring and thus a risk of the host developing clinical symptoms and/or signs, with host factors also being important.[13-15] However, strictly speaking, neither infection nor disease are transmitted; it is merely the organisms that are transmitted. It follows that the terms or their abbreviations, STI and STD, are technically misnomers. However, they may be seen as short-hand for "sexual transfer of a micro-organism causing infection of, or disease of--" and have been used for decades, STI gradually creeping in after STD in recognition that many infections may remain asymptomatic,[7] although not necessarily without damage. So, avoiding these terms would seem obtuse, despite their apparent irrational meaning. It has been suggested that STI and STD may be used synonymously,[7,8] but we think differently. Although STI usage followed that of STD, the fact is that mechanistically disease follows, or may follow, infection. This caveat is emphasized by damage also being influenced by the nature of the micro-organism. Thus, for example, *Neisseria gonorrhoeae* or *Chlamydia trachomatis* are intrinsically much more likely to produce disease (some say traditional or "real" STDs) than are *Ureaplasma* spp. or *M.hominis.*[16,17] In addition, these terms are not used to describe genital human papilloma viruses (HPV) which cause cervical cancer in only a minority of those infected, presumably because of the stigma associated with these terms and that there is no effective treatment.[10, 11] Public Health England in their patient cervical screening leaflet state "HPV can be easily passed on during sexual activity between partners"[18], and WHO uses the term "sexually acquired infection".[19] Transmission of lactobacilli is unlikely to cause harm. Thus, there is clearly a spectrum of health to disease associated with sexual transmission of oral ano-genital tract microbiota. The proposal [11] to use a single term, namely "Sexually Transmissible

Infectious Disease", may find favour with a few, but it does suggest, wrongly, that all infections result in disease.

As indicated above, we will not go out of our way to avoid using STI or STD when a distinction between infection and disease is to be made, nor suggest that well-known journals do so in their titles. We know that many physicians dealing with patients refer to STIs rather than STDs, the former being marginally less emotive.[9,10] This is a practice that should continue. However, when should a genital tract micro-organism detected by NAAT be referred to as causing an STI/STD with the implication that treatment is required and when should it be considered part of the normal genital-tract microbiota? The mere presence of *Mycoplasma hominis*, *Ureaplasma urealyticum* and *Ureaplasma parvum* in the genital tract does not categorize them as pathogens. In this regard, a recent review of the literature concluded that asymptomatic carriage of these mycoplasmas is common and routine testing and treatment of asymptomatic or symptomatic men and women is not recommended as there is no evidence that more good than harm is being done.[17] Indeed, not only does it increase the risk of antimicrobial resistance[17], it is also known that antibiotic therapy may dramatically change the gut and oral microbiomes [20] and the genital-tract microbiome can't be different. It is disturbing, therefore, that an increasing number of commercial websites are offering NAAT testing for these mycoplasmas, describing them as STIs, with treatment if detected. We discuss this in more detail in our review article.[3] The idea of SSM is not new but it emphasizes that transmission of microbiota is a normal part of unprotected sexual intercourse. This terminology might be taken up more rapidly by the scientific community than by physicians and the public, although we should not underestimate their intelligence and understanding. We see SSM as a valuable additional aid in scientific discourse and also as an everyday part of our expert clinical guidance for patients and the public. It is noteworthy that the 'gut microbiome' has been

common parlance for years and that the ‘skin microbiome’ is currently a feature of television exposure. SSM may well follow.

Declarations: PH was supported by the National Institute of Health Research Health Protection Research Unit (NIHR HPRU) in Evaluation of Interventions at the University of Bristol in partnership with Public Health England (PHE). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the Department of Health or Public Health England.

REFERENCES

1. Mandar R, Punab M, Borovkova N, et al. Complementary seminovaginal microbiome in couples. *Res Microbiol* 2015;166: 440-447.

2. Zozaya M, Ferris MJ, Siren JD et al. Bacterial communities in penile skin, male urethra, and vaginas of heterosexual couples with and without bacterial vaginosis. *Microbiome* 2016; 4:16.

3. Taylor-Robinson D, Horner P, Pallecaros A. Diagnosis of some genital-tract infections: part 2. Molecular tests and the new challenges. *Int J STD & AIDS* 2019. In press.

4. Unemo M, Bradshaw CS, Hocking JS, et al. Sexually transmitted infections: challenges ahead. *Lancet Infect Dis* 2017;17: e235-279.

5. Ravel J, Gajer P, Abdo Z, et al. Vaginal microbiome of reproductive-age women. *Proc Nat Acad Sci* 2011;108: Suppl. 1-4680.

6. Royer HR, Cerf C. Young women's beliefs about the terms sexually transmitted disease and sexually transmitted infection. *J Obstet Neonatal Nurs* 2009; 38: 686-692.

7. Handsfield HH. Sexually Transmitted Diseases, Infections, and Disorders: what's in a name? *Sex Transm Dis* 2015; 42:169.

8. Rietmeijer CA. You say STD**.....** *Sex Transm Dis* 2015; 42:169.

9. Lederer AM, Laing EE. What's in a name? Perceptions of the terms Sexually Transmitted Disease and Sexually Transmitted Infection among late adolescents. *Sex Transm Dis* 2017;44: 707-711.

10. Handsfield HH, Rietmeijer CA. STI Versus STD: Coda. *Sex Transm Dis* 2017; 44: 712 -713.

11. Anderson J. STD (Sexually Transmitted Disease) or STI (Sexually Transmitted Infection) : should we choose ? *Amer Sex Hlth Assoc* 2019. Available from: http://www.ashasexualhealth.org/pdfs/STDI.pdf.

12. Taylor-Robinson D, Pallecaros A, Horner P. Diagnosis of some genital-tract infections: part 1. An historical perspective. *Int J STD AIDS* 2017; 28: 1143-1149.

13. Menon S, Timms P, Allan JA, et al. Human and pathogen factors associated with *Chlamydia trachomatis*-related infertility in women. *Clin Microbiol Rev* 2015; 28: 969-985.

14. Michel CE, Sonnex C, Carne CA, et al. *Chlamydia trachomatis* load at matched anatomic sites: implications for screening strategies. *J Clin Microbiol* 2007; 45:1395-140

15. Priest D, Ong JJ, Chow EPF et al. *Neisseria gonorrhoeae* DNA bacterial load in men with symptomatic and asymptomatic gonococcal urethritis. *Sex Transm Infect* 2017; 93: 478-481.

16. Price MJ, Ades AE, Soldan K, et al. The natural history of *Chlamydia trachomatis* infection in women: a multi-parameter evidence synthesis. *Hlth Technol Assess* 2016; 20:1-250.

17. Horner P, Donders G, Cusini M, et al. Should we be testing for urogenital *Mycoplasma hominis*, *Ureaplasma parvum* and *Ureaplasma urealyticum* in men and women? – a position statement from the European STI Guidelines Editorial Board. *J Eur Acad Dermatol Venereol* 2018; 32:1845-1851.

18. Public Health England. NHS Cervical Screening Programme: Cervical screening and human papillomavirus (HPV) testing. 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/820430/HPV_primary_screening_leaflet.pdf.

19. World Health Organisation Cervical cancer information for women and girls. 2019. Available from: https://www.who.int/cancer/cervical-cancer/for-women-and-girls.

20.Shaw LP, Bassam H, Barnes CP, et al.Modelling microbiome recovery after antibiotics using a stability landscape framework. *Int Soc Microb Ecol* 2019; 13: 1845-1856.