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Kiss Around and Find Out: Kissing as a Risk Factor for Pharyngeal Gonorrhea

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What do we know about the role of kissing in gonorrhea transmission? Evidence suggests that gonorrhea transmission via kissing is possible, but we do not know if it is a relatively rare event or if it is one of the main drivers of gonorrhea transmission.^{1–3} In this issue, Charleson and colleagues⁴ provide a systematic review of studies of kissing as a risk factor for pharyngeal gonorrhea and chlamydia. This important systematic review serves to summarize and highlight some of the available evidence of kissing as a possible route of gonorrhea and chlamydia transmission. The authors of the review are at the forefront of this field of investigation, and many were co-authors on 4^{5–8} of the 6 studies included in the review.

Of the 6 studies in the review, 5 studies^{5–9} focused on pharyngeal gonorrhea and one focused on pharyngeal chlamydia.¹⁰ All 5 studies of gonorrhea found that self-reported kissing was significantly associated with pharyngeal gonorrhea, and this significant association remained after adjusting for cofounders in 2 of the studies. Notably, in the 2 studies^{5,8} in which kissing remained an independent risk factor for pharyngeal gonorrhea after controlling for other types of sexual behavior, there was evidence of a “dose-dependent” relationship with an increasing risk of pharyngeal gonorrhea with an increasing number of kissing partners.

However, these 2 studies^{5,8} had 2 important limitations that were not highlighted in the Charleson review. First, these 2 studies examined the association between prevalence of pharyngeal infection and reported sexual behaviors in the past 3 months. The 3-month exposure period was based on the thought that pharyngeal gonorrhea was an infection of relatively short duration, consistent with available data at the time the studies were conducted. However, a recent study by Barbee and colleagues¹¹ found the median duration of untreated pharyngeal gonorrhea is 4 months, thus the exposure period of 3 months

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might be too short to capture all relevant sexual behavior. In fact, the one study of pharyngeal gonorrhea in the Charleson review that used a 6-month exposure period found that wet kissing was not significantly associated with gonorrhea in the multivariate model.⁹ Therefore, the etiologic period of exposure in many of the studies reviewed may not align with current knowledge on the average duration of pharyngeal infection. Second, although both studies^{5,8} controlled for potential confounding factors, neither controlled for the total number of sexual partners, which could be an important marker of gonorrhea prevalence in an individual's sexual network. Gonorrhea prevalence in the sex partners of a study participant is likely positively correlated with the participant's total number of sex partners, because of assortative mixing patterns (eg, people with multiple recent sex partners tend to partner with others who also have multiple recent sex partners).^{12,13} Further, because most people kiss their sex partners, a person's number of kissing partners is highly correlated with a person's total number of sex partners.⁶ It is therefore quite possible that a cross-sectional study would find that the number of kissing partners is highly correlated with pharyngeal gonorrhea prevalence, even if gonorrhea were not transmitted through kissing, simply because those who have lots of kissing partners might have partners with higher gonorrhea prevalence than those who do not have lots of kissing partners.

Despite the important addition of the Charleson review to the body of evidence on kissing and pharyngeal gonorrhea, there are 2 key metrics that we still do not know about kissing and pharyngeal gonorrhea: What is the per-act transmission probability of gonorrhea through kissing? And how much does kissing contribute to population-level gonorrhea?

The first question is difficult to answer through classic epidemiologic studies since kissing is very common and often occurs in sexual encounters involving vaginal or anal sex¹⁴ in which the per-act probability of gonorrhea transmission is likely high. Empirical studies that attempted to measure the per-act transmission probability of gonorrhea are limited.¹⁵ To our knowledge, the few studies that have been conducted focused on the risk of transmission through penile-vaginal sex, and none have attempted to estimate the per-act transmission risk of gonorrhea through anal sex, oral sex, or other sexual behaviors. Hooper and colleagues¹⁶ estimated the per-act risk of gonorrhea transmission based on 3 factors: the incidence of urethral gonorrhea in military men on Naval ships returning from shore leave, the prevalence of vaginal gonorrhea in women working in brothels where the men had visited, and the men's reported numbers of sex acts while on shore leave; Holmes and colleagues¹⁷ had used a similar approach in another group of Naval men. Platt and colleagues¹⁸ estimated the per-act risk of gonorrhea transmission from men to women based on the infection status of 26 women who had recent sex with a man with gonorrhea, in which the woman was unlikely to have been the one to introduce the infection to the partnership.

However, these types of studies have important limitations. For example, the Hooper study and the Holmes study assumed no other sexual partners beyond female sex workers and none of the studies accounted for other potential modes of transmission, such as oral sex or anal sex, which are likely to also be performed during a sexual encounter. Attempting to replicate this study design for kissing, without the complications of other routes of transmission, would require finding a population at risk for gonorrhea that reports no sexual

activity but does report kissing, which is likely a small population. Short of a strictly conducted experiment following pharyngeal *Neisseria gonorrhoeae* (NG) challenge, in which participants are directly observed kissing to see if gonorrhea transmission occurs, we find it difficult to determine how we could reliably estimate the precise per-act probability of gonorrhea transmission through kissing.

Perhaps a much more practical, but less robust, study design would be to isolate cases in which kissing was the only risk factor, coupled with contact tracing to identify the partner. For example, Cornelisse and colleagues¹⁹ described a sexual network of 7 people (4 women, 2 men, 1 nonbinary) who were linked primarily through sexual encounters that occurred at a music festival. Six of the 7 people had pharyngeal gonorrhea in the absence of urogenital gonorrhea, including 1 woman who reported kissing as her only possible route of exposure, and none of the men had urogenital infection.¹⁹ This type of study design could potentially provide data to inform assessments about the likelihood of transmission through kissing.

The second question—how much does kissing contribute to population-level gonorrhea?—is difficult to address without knowing the per-act probability of transmission through kissing.³ The currently available evidence is not sufficient to conclude—or to rule out—that kissing is a common route of gonorrhea transmission and a major contributor to community gonorrhea morbidity.^{1,2} A frequent, logical argument against kissing as a main driver of population-level gonorrhea is that we typically do not see pharyngeal gonorrhea in populations where kissing is much more common relative to sexual activities (ie, oral, vaginal, anal), such as among high school students. However, youth who only kiss would likely not be considered to be sexually active, and thus would not receive gonorrhea screening. Studies are needed to determine whether and to what extent pharyngeal gonorrhea exists among kissing-only youth. McLaughlin and colleagues²⁰ reported that pharyngeal gonorrhea is common (~30% prevalence) among heterosexual men and women who have been exposed to NG and suggested that studies are needed of the prevalence of pharyngeal gonorrhea among heterosexual men and women more generally, not just among those exposed to NG.

The good news is that the worldwide sexually transmitted disease (STD) research community has an abundance of talented researchers with expertise in epidemiology, microbiology, statistics, mathematical modeling, and other relevant fields. We are confident that, together, this research community can plan and conduct studies to obtain reliable estimates of the risks of gonorrhea transmission via kissing and via all other possible routes of transmission. Such estimates are vital not only to inform mathematical models of STDs but also in conveying accurate health information to the public.

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