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Sexual transmission of hepatitis C: A rare event among heterosexual couples

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Transmission of hepatitis C virus (HCV) is primarily attributed to percutaneous exposure to infected blood. Methods to prevent percutaneous transmission are well defined and clear counselling messages exist to reduce person-to-person transmission of virus (Centers for Disease Control and Prevention, 1998). While studies suggest that sexual transmission of HCV occurs infrequently, few studies thoroughly investigated sexual risk factors and potential confounding transmission modes within the household (Alter et al., 1989; Tahan et al., 2005; Vandelli et al., 2004; Piazza et al., 1997; Gordon et al., 1992; Osmond et al., 1993). These ambiguities hampered development of clear counselling messages for sexual practices among HCV-infected persons.

To obtain more quantitative information on sexual transmission risk for the most common sexual partnerships among infected persons, the HCV Partners Study studied monogamous, heterosexual couples in long-term relationships (> 36 months), without confounding exposures such as viral coinfection (HIV or HBV) or both partners having a history of injection drug use (Osmond et al., 2013). Among 500 couples and 8377 person-years of sexual contact, the HCV Partners Study found a low prevalence of HCV infection among partners, with a maximum of 1.2% (95% CI: 0.2%–2.2%) of infections potentially attributable to sexual contact. The maximal incidence of HCV infection was 7.2 per 10,000 person-years (95% CI: 1.3–13.0), and maximal risk per sexual contact was 1 per 380,000 (95% CI: 1/600,000–1/280,000). These estimates were similar to or lower than previously reported rates for both prevalences (2.0%–10.3%) (Tahan et al., 2005; Vandelli et al., 2004; Stroffolini et al., 2001) and incidence (0.0–23.3 per 10,000 person-years) (Vandelli et al., 2004; Marincovich et al., 2003; Kao et al., 2000). Overall, available data indicate that HCV transmission by sex is reassuringly low, and the HCV Partners Study provides the numerical context to counsel HCV-infected persons in monogamous partnerships.

Several study design components warrant emphasis. First, since HCV acquisition via injection drug use is common and efficient, couples with both partners having a history of injection drug use were excluded, as characterising an independent contribution of sexual activity to HCV transmission would be difficult in these couples. Additionally, the HCV

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Partners Study uniquely quantified sexual activities during the relationship, collected household risk factors for transmission and implemented a multi-step process to identify HCV concordance among infected couples. To quantify sexual risk factors, independent interviews with each partner captured the details of within couple sexual histories in self-defined intervals marked by life events that altered patterns of sex contact (pregnancy, illness, periods of absence). The frequency and type of sexual contact and protective barrier use were quantified within each interval, allowing us to calculate monthly contact rates by sexual practice throughout the relationship. For vaginal intercourse, couples reported a median of 12 contacts per month, with 83% of couples not reporting frequent condom use. After adjusting for condom use, couples reported >1 million sexual contacts (vaginal and anal), of which 35,000 were vaginal during menses and 8000 anal intercourse.

The HCV Partners Study also addressed whether specific sexual practices increased HCV transmission risk. Anal sex, with the possibility of mucosal trauma as a portal of entry for HCV, or vaginal sex during menses may present a higher likelihood of HCV transmission, although it must be acknowledged that in prior studies of populations engaged in higher risk sexual activity (e.g. HIV-uninfected men who have sex with men), no association between type of sexual activity and HCV positivity was noted (Russell et al., 2009; McMahon et al., 2007; Thomas et al., 1995; Alary et al., 2005). The HCV Partners Study assessed median contacts per month for vaginal intercourse during menses (0, range 0–10), anal intercourse (0, range 0–20) and oral sex (3, range 0–100) with these practices reported by 65%, 30% and >90% of couples, respectively. The proportion of HCV-concordant couples compared to those with one uninfected partner engaging in riskier sexual activities was numerically but not statistically higher: vaginal intercourse during menses (100% and 66%, $p = 0.55$), anal intercourse (67% and 30%, $p = 0.22$) and lack of condom use (100% and 70%, $p = 0.56$). While the number of transmission events in the HCV Partners Study may be too low to conclusively exclude an association with specific sex practices, the counter-argument, given the very low estimated overall transmission risk among monogamous couples, is that any risk for infection from engaging in specific 'high-risk' practices would also be extremely low.

While the HCV Partners Study provides much-needed reassurance for the millions living with HCV and in long-term partnerships, these results do not apply to all patient populations. Particularly, HIV-infected men who have sex with men represent a different demographic and recent publications emphasise the role of sex in HCV transmission (Rauch et al., 2005; Jin et al., 2010; Centers for Disease Control and Prevention, 2011; Witt et al., 2013; Urbanus et al., 2009; Wandeler et al., 2012). This represents a different clinical scenario with other factors (specifically, concurrent HIV infection) that are likely to be important.

Household exposures from sharing blood-contaminated objects (nail clippers, razors, toothbrushes and glass syringes for medication administration) provide a plausible alternative route for HCV transmission among partners that may be erroneously ascribed to sex contact (Stroffolini et al., 2001; Russell et al., 2009). The HCV Partners Study carefully evaluated household practices to account for potential non-sexual HCV transmission.

Although partners frequently shared personal grooming items, we found no association between sharing these items and HCV concordance among couples.

In all studies evaluating transmission events, confirming a common source of HCV infection through detailed virological analysis is essential. For sexual transmission to be plausible, partners must be infected with closely related viral quasispecies. All viraemic couples underwent HCV genotyping and concordant couples had population sequencing and phylogenetic analysis to confirm the degree of relatedness. The detailed phylogenetic analyses provide the strongest evidence to include or exclude sex as a potential transmission mode. However, among 12 HCV genotype/serotype concordant (or indeterminate) couples, 50% were HCV RNA negative. This relatively high rate of spontaneous clearance may be related to exposure at younger ages, as reported in other study populations (Kenny-Walsh, 1999; Posthouwer et al., 2006). Alternatively, one may speculate that the high rate of spontaneous clearance may be related to the mucosal route of exposure and limited HCV inocula with sexual contact. For couples with one partner clearing HCV infection, viral relatedness cannot be assessed. We addressed this limitation by calculating a maximal transmission rate assuming that antibody-positive, non-viraemic partners were infected from a common source. Thus we provided two HCV transmission rates (1) a minimum rate classifying only phylogenetically confirmed couples as transmitting HCV and (2) a maximum rate classifying all antibody-positive couples as transmitting HCV.

In conclusion, HCV transmission by sex in monogamous heterosexual couples is a rare event and data have yet to suggest risk increases with specific sexual practices. Our results provide a basis for specific counselling messages that clinicians can use with their patients, and while there are no evidence-based recommendations regarding use of condoms during vaginal intercourse or with specific sex practices such as anal sex or sex during menses, we believe that counselling messages should be individualised, including consideration of condom use to further reduce the already extremely low risk of sexual HCV transmission to zero.

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