Published in final edited form as:

Sex Transm Dis. 2018 March ; 45(3): 144–146. doi:10.1097/OLQ.0000000000000792.

Rapid Increases in Syphilis in Reproductive-Aged Women in Japan: A Warning for Other Countries?

Mary L. Kamb, MD, MPH*, Melanie M. Taylor, MD, MPH†, Naoko Ishikawa, MD, MSc‡

*Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD and TB

Prevention, Centers for Disease Control and Prevention, Atlanta, GA; †Department of

Reproductive Health Research, World Health Organization (WHO), Geneva, Switzerland;

‡Division of Communicable Diseases, Regional Office for the Western Pacific, World Health Organization, Manila, Philippines

In this issue of *Sexually Transmitted Diseases*, Arima et al.¹ report on a rapid and large increase in heterosexual syphilis in Japan, with an especially concerning rate of rise among young women of reproductive age. As is true in many industrialized countries, Japan has experienced a marked upsurge in syphilis over the past 2 decades, and national surveillance since 2012 has found an increasing proportion of primary and secondary (P&S)—that is, incident—syphilis cases each year demonstrated by a 4-fold increase in case rates, from 0.7 per 100,000 in 2012 to 3.6 per 100,000 in 2016. However, unlike most high-income countries where most P&S syphilis cases are in men who have sex with men (MSM), P&S cases in Japan are most frequently reported among men who self-report only having sex with women (MSW; 48.6% of cases), followed by women (23.2%) and MSM (22.2%). On the surface, this might suggest underreporting of male homosexual contact. However, the relatively modest increase in syphilis case rates among MSM, compared with the concurrent and similarly steep rises in case rates among both MSW and women beginning in 2013¹ (See Arima et al, Figs. 1A, B), suggests that heterosexual syphilis is indeed on the rise in Japan.

Every new syphilis case represents a serious infection with potential for problematic health outcomes, such as the possibility of enhanced HIV transmission or neurosyphilis that can lead to vision loss, hearing impairment, or stroke. Syphilis in reproductive-aged women is particularly troubling because of its potential to result in mother-to-child transmission during pregnancy with resultant adverse pregnancy outcomes such as stillbirth, neonatal death, prematurity, low birth weight, and congenital infections in infants.² Japan, which uses a strict, clinical case definition for congenital syphilis (that likely underreports cases), has reported a steady increase in congenital syphilis case rates since 2012 from 0.4 per 100,000 live births to 1.4 cases in 2016. The rising congenital syphilis rate is consistent with the finding that among Japanese women, P&S syphilis cases reported to national surveillance

Correspondence: Mary L. Kamb, CDC/DSTDP, 1600 Clifton Rd, NE MS E-02, Atlanta, GA 30333. mkamb@cdc.gov.

The conclusions, findings, and opinions expressed by the authors contributing to this article do not necessarily reflect the official position of the US Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the authors/affiliated institutions.

are primarily in women of reproductive age, with the overwhelming majority among 20- to 29-year-olds. The Ministry of Health, Labor and Welfare Japan recognizes this rise as a public health threat and has strengthened its prevention campaigns for syphilis screening and treatment targeting young women.

A similar pattern, although less dramatic increase, in syphilis case rates has been reported in other higher-income nations. For example, in the United States, where approximately 70% of all syphilis cases with known sex of sex partner are among MSM, P&S syphilis case rates among women have increased each year since 2012, with a doubling of incident syphilis cases between 2012 and 2016 and a concerning 35.6% increase from 2015 to 2016.³ As was observed in Japanese women, in 2016, P&S syphilis case rates in US women were highest among 20- to 24-year-olds (6.7 per 100,000 persons) and 25- to 29-year-olds (5.6 per 100,000 persons) compared with overall case rates in women of 1.9 per 100,000 persons. In comparison, using data from 36 states able to classify at least 70% of reports by sexual behavior, increases in P&S syphilis from 2015 to 2016 were lower in US men (16.4% increase in MSM, 22.2% increase in MSW) than in women. Distressingly, after many years of decline, congenital syphilis in the United States is also on the rise. Compared with the 2013 case rate of 8.4 per 100,000 live births, congenital syphilis has almost doubled in 2016 to 15.7 cases per 100,000 live births, with a 27.6% increase between 2015 and 2016.³

In Australia, using national data reported in 2006 to 2015, the overall rate of infectious syphilis diagnosis increased by 266% among 25- to 29-year-olds and 223% among 20- to 24-year-olds,⁴ with the largest increases occurring between 2014 and 2015. Although most syphilis cases are reported in MSM and rates of infectious syphilis among women remain relatively low, there has been a doubling between 2012 and 2015 from 1.3 cases to 2.5 cases per 100,000 persons among women, with the highest rates in younger age groups. Increases in congenital syphilis have also been noted in Australia, with a recent surge in cases occurring in aboriginal populations.⁵

Are the rises in syphilis case rates in Japan, and to a lesser extent other countries, a herald of increasing heterosexual and congenital syphilis around the world? There is some cause for concern: Public health focus on syphilis has waned in some countries, perhaps due to the misperception that this “old disease” is no longer a source of significant morbidity. Funding for control of sexually transmitted diseases overall has dwindled globally, leading programs to cut budgets for surveillance and, importantly, clinical services that were once provided free-of-charge as a means of protecting the public health. Syphilitic infections, particularly during pregnancy, remain a persistent cause of preventable death and disability in all regions of the world. The World Health Organization estimated that during 2012 about 1 million maternal syphilis infections globally caused 350,000 adverse pregnancy outcomes of which more than 200,000 were perinatal and neonatal deaths.⁶ Today, very few low- or middle-income countries, where syphilis burden is highest, are able to support any population-based syphilis surveillance program, let alone the type of case-based surveillance that has allowed Japan, the United States, and Australia to monitor their epidemics. In addition, current global shortages in benzathine penicillin, the single most effective drug against syphilis and the only known effective treatment of syphilis in pregnancy, have led to use of less effective treatment regimens in many countries.⁷ Among high-income countries with syphilis

epidemics among MSM, transmission to women through male bisexual activity is a factor needing further study as a potential contributor to congenital syphilis.⁸

The World Health Organization is now embarking on the second decade of its global effort to eliminate mother-to-child transmission of syphilis (congenital syphilis).⁹ Although sexually transmitted syphilis is difficult to control, congenital syphilis is eminently preventable using simple and affordable interventions: early testing and case detection before and during pregnancy and prompt treatment for syphilis-infected pregnant women (and their partners) with benzathine penicillin. Syphilis screening in pregnancy is among the most highly cost-effective public health interventions in existence, even in countries with relatively low prevalence among women.¹⁰ The global initiative to eliminate mother-to-child transmission of syphilis is based on a framework of access to quality, proven-effective maternal, newborn, and child health services, including universal screening for syphilis early in pregnancy and timely treatment, if found to be infected.¹¹ The global effort calls for national maternal, newborn, and child health programs to achieve established targets in access to early prenatal care, universal syphilis testing during pregnancy, and prompt treatment of syphilis cases. Even in the face of community syphilis prevalence of 1% (a moderately high rate), congenital syphilis elimination can be achieved with prenatal care coverage greater than 95%, prenatal syphilis screening coverage greater than 95%, prompt treatment for all syphilis seropositive pregnant women with intramuscular benzathine penicillin early in pregnancy, and close follow-up of syphilis-exposed infants. World Health Organization guidance recognizes that quality prenatal services involve many interventions that are proven effective in reducing perinatal and infant mortality^{12–14} and that prenatal services are an ideal platform for integration of these interventions. Linking elimination of mother-to-child transmission of syphilis and HIV has been a successful approach, and 9 countries have been validated as having achieved the dual-elimination targets.¹⁵ There are also new initiatives on triple elimination to link other diseases such as hepatitis B.¹⁶

Increases of syphilis among women of child-bearing age in Japan and other countries support continued public health vigilance to prevent perinatal morbidity and mortality caused by syphilis in pregnancy. Early detection of syphilis in pregnant women can be achieved through access to basic prenatal services that include syphilis screening, ideally in the first trimester, and with repeat screening in the third trimester and at delivery among women at high risk and within communities with high syphilis prevalence. Partner testing and treatment is important to reduce syphilis-associated health outcomes in infected persons and prevent congenital syphilis in future pregnancies, and may also prevent transmission from heterosexual or bisexual male partners of pregnant women. In addition, primary preventive efforts to detect and treat syphilitic infections in women before they become pregnant can reduce congenital syphilis. It is important for sexually transmitted disease public health programs to stay closely connected to their partners in maternal, newborn, and child health services both to ensure appropriate syphilis screening and treatment are included in basic prenatal care and to ensure congenital syphilis cases (including stillbirths) are detected, counted, and studied so that future infections can be prevented.

On World AIDs Day 2017, WHO released revised guidance and tools to support country-level validation of elimination of mother-to-child transmission of HIV and syphilis.^{17,18}

Both WHO and the Centers for Disease Control and Prevention have web-based educational, clinical, and surveillance tools on prevention of congenital syphilis and sexually transmitted infection prevention in reproductive-aged women that can support public health and clinical professionals whether at national, community, or clinical level.^{15,17–19}

The global public health community is conceptually aware that increasing syphilitic infections among MSM may spread to women through bisexual men, resulting in maternal and congenital syphilis. Expanded access to syphilis testing and treatment for these key populations as well as for women of reproductive age (in addition to pregnant women) may be needed to address this potential bridging phenomenon.

REFERENCES

1. Takahashi T, Arima Y, Yamagishi T, et al. Rapid increase in reports of syphilis associated with men who have sex with women and women who have sex with men, Japan, 2012–2016. *Sexually Transm Dis* 2018; 45:139–143.
2. Gomez GB, Kamb ML, Newman LM, et al. Untreated maternal syphilis and adverse outcomes of pregnancy: A systematic review and meta-analysis. *Bull World Health Organ* 2013; 91:217–226. [PubMed: 23476094]
3. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2016. Atlanta: U.S. Department of Health and Human Services, 2017.
4. Annual Surveillance Report of HIV, Viral Hepatitis, STIs 2016. The Kirby Institute P 135–40. Available at: <https://kirby.unsw.edu.au/report/annual-surveillance-report-hiv-viral-hepatitis-stis-2016>.
5. Syphilis Outbreak in NT ‘Massive’ Doctors Urge Awareness in Remote Communities. 2 2017 Available at: <http://www.abc.net.au/news/2017-02-28/syphilis-outbreak-in-remote-nt-massive,-doctors-urge-awareness/8310338>.
6. Wijesooriya NS, Roach RW, Kamb ML, et al. Global burden of maternal and congenital syphilis in 2008 and 2012: a health systems modelling study. *Lancet Global Health* 2016; 4:e525–e533. [PubMed: 27443780]
7. Nurse-Findlay S, Taylor MM, Savage M, et al. Shortages of benzathine penicillin for prevention of mother-to-child transmission of syphilis: An evaluation from multi-country surveys and stakeholder interviews. *PLoS Med* 2017; 14:e1002473. [PubMed: 29281619]
8. Tao J, Ruan Y, Yin L, Vermund SH, et al. Sex with women among men who have sex with men in China: Prevalence and sexual practices. *AIDS Patient Care STDS* 2013; 27:524–528. [PubMed: 23931683]
9. World Health Organization. Global health sector strategy on sexually transmitted infections, 2016–2021. 2007 Available at: <http://www.who.int/reproductivehealth/publications/rtis/ghss-stis/en/>. Accessed January 25, 2018.
10. Kahn JG, Jiwani A, Gomez GB, et al. The cost and cost-effectiveness of scaling up screening and treatment of syphilis in pregnancy: A model. *PLoS One* 2014; 9:e87510. [PubMed: 24489931]
11. World Health Organization. The Global Elimination of Congenital Syphilis: Rationale and Strategy for Action. 2007 Available at: <http://www.who.int/reproductivehealth/publications/rtis/9789241595858/en/>.
12. World Health Organization. Recommendations on Antenatal Care for a Positive Pregnancy Experience. 2016 Available at: http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/.
13. Victora CG. Commentary: LiST: Using epidemiology to guide child survival policymaking and programming. *Int J Epidemiol* 2010; 39(Suppl 1):i1–i2. [PubMed: 20348111]
14. Blencowe H, Cousens S, Kamb M, et al. Lives Saved Tool supplement detection and treatment of syphilis in pregnancy to reduce syphilis-related stillbirths and neonatal mortality. *BMC Public Health* 2011; 11(Suppl 3):s9.

15. World Health Organization. Prevention of Mother-to-Child-Transmission of Syphilis (Congenital Syphilis). Available at: <http://www.who.int/reproductivehealth/congenital-syphilis/en/>.
16. Asia Pacific Regional Framework for Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis 2018–2030. 2017 WPRO website. Available at: <http://www.wpro.who.int/hiv/topics/emtct/en/>.
17. World Health Organization. Validation for the Elimination of Mother-To-Child Transmission of HIV and/or Syphilis. Available at: <http://www.who.int/reproductivehealth/congenital-syphilis/WHO-validation-EMTCT/en/>.
18. World Health Organization. Criteria and Processes for Validation: Elimination of Mother-To Child Transmission of HIV and Syphilis, 2nd ed Atlanta, GA: WHO, 2017.
19. U.S. Centers for Disease Control and Prevention. CDC Call to Action: Let's Work Together to Stem the Tide of Rising Syphilis in the United States. 4 2017 Available at: <https://www.cdc.gov/std/syphilis/SyphilisCalltoActionApril2017.pdf>.