LETTER TO THE EDITOR

Hepatitis B Outbreak Among Men Who Have Sex with Men in the Autonomous Province of Vojvodina, Serbia

(Short running head: Hepatitis B Outbreak Among MSM in AP Vojvodina)

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Dear Editor:

The European Centre for Disease Prevention and Control reported that there were 2896 acute hepatitis B cases in 24 EU/EEA countries in 2013.[1] The incidence ranged from 0.1 cases per 100,000 in France and Portugal to 4.3 per 100,000 in Latvia, with a male-to-female ratio of 2.2:1 in EU/EEA countries, and transmission among men who have sex with men (MSM) reported in 9.4% of all cases of acute hepatitis B.[1] Some authors consider hepatitis B virus (HBV) infection to be endemic in the MSM population with the incidence 20 times higher in MSM than in the general population worldwide.[2] However, data on HBV prevalence among MSM are available for only four EU/EEA countries.[3] Six to ten percent of MSM infected with HBV worldwide are co-infected with HIV.[4]

In AP Vojvodina, no cases of acute hepatitis B among MSM were reported from 2000 to 2009. According to active hepatitis B surveillance data from the Institute of Public Health of Vojvodina, during this time the average yearly incidence of acute hepatitis B was 3.9 per 100,000 in the general population (Table 1).[5] As it is the responsibility of a patient with HBV to declare their potential exposures, it is possible that some MSM with HBV did not report their sexual risk behavior. Nevertheless, among MSM who were tested for HBV and did report their sexual risk behavior, none were HBV positive (neither acute nor chronic infection). Eight hundred and one cases of acute hepatitis B were reported during this period with a male/female incidence rate ratio of 1.5.

In June 2011, an agglomeration of acute hepatitis B in MSM was observed. The case definition for acute hepatitis B included onset of any sign or symptom consistent with acute viral hepatitis and either jaundice or elevated serum alanine aminotransferase (ALT) levels >100 IU/L and detection of hepatitis B surface antigen (HBsAg) in serum or absence of symptoms and detection of HBsAg in serum with a documented negative HBsAg test result within six months prior to a positive test. After retrospective analysis and active

epidemiological investigation, 30 acute hepatitis B cases in MSM were identified, with the first case identified in January 2010 retrospectively. By the end of October 2012, thirty-one other cases of acute hepatitis B among MSM had been identified. This was the first outbreak recognized in the MSM population in Serbia. According to the Serbian "Law on Protection of Population from Communicable Diseases",[6] an outbreak is defined as "an occurrence of a communicable disease unusual by the number of cases, time, place and population affected, or unusual increase in the number of patients with complications or death, as well as the occurrence of two or more interrelated cases of communicable disease that never occurred in one area or an occurrence of several cases of diseases whose cause is unknown and is accompanied by a fever condition".

Sexual behavior was assessed based on self-reporting during the anamnesis as per routine. It is possible, however, that both patients and physicians had become more open to talking about sexual behavior than they were previously due to efforts to create a clinical atmosphere more conducive to disclosure of sexual orientation. Nevertheless, in MSM-friendly testing sites no cases of acute had been identified during the previous decade. As more than half (61/118) of the acute hepatitis B infections identified in men during 2010-2012 were among MSM, we believe that these hepatitis B infections among MSM reflect an outbreak, not just an increase in disclosure.

The median age of the MSM with hepatitis B was 28, with an age range of 19-52. Students comprised 33% of all cases. Almost all of the MSM (97%) had not been vaccinated against HBV. Genotype information was available for 11 cases. All but one of the MSM were infected with an identical genotype A strain with subtype adw2. One genotype D isolate with the D3 sub-genotype was isolated. Genotype A, which was predominant in this sample of MSM in AP Vojvodina, has also been found to be predominant in the MSM population across Europe and in MSM worldwide.[2] On the contrary, genotype D is the most common

genotype in the general population in Eastern Europe and Eastern Mediterranean countries, as well as in Serbia.[7]

Several measures were introduced with the aim of controlling the outbreak among MSM in AP Vojvodina. A voluntary counselling and testing (VCT) site was established in a drop-in center for MSM in Novi Sad, where all clients were counselled about the prevention of hepatitis B and vaccination against HBV was recommended. In other existing VCT centers, counsellors were sensitized to offer HBV testing and vaccination to MSM. In addition, testing and vaccination (if negative) were recommended to the sexual partners of those who tested positive.

In a country where the MSM population is still much stigmatized, implementation of broad preventive programs is difficult. The Republic of Serbia adopted the Law on the Prohibition of Discrimination[8] in 2009 and the Strategy for Prevention and Protection Against Discrimination[9] in 2013, which state explicitly that sexual orientation is a private matter and that no one can be invited to disclose their sexual orientation, but anyone has the right to disclose their sexual orientation. Discrimination due to disclosure is prohibited and discrimination based on sexual orientation is considered as a severe case of discrimination. However, the penalties for discrimination are low (US$45-850).

A law on patients' rights[10] from 2013 states that "a patient has the right to the confidentiality of all personal information that he has communicated to the competent healthcare professional or healthcare associate, including those related to his state of health and potential diagnostic and therapeutic procedures, as well as the right to protection of his privacy during the conduct of diagnostic testing and treatment in whole" and it prohibits healthcare workers from informing other people about the patients' personal information. However, the LGBT population in Serbia remains highly stigmatized with almost half of the population considering homosexuality to be an illness and 80% reporting that they would not accept an

LGBT person in their family.[11] Some of the factors that contribute to existing stereotypes and prejudices about LGBT populations and promote heterosexuality only as desirable are churches, conservative nationalistic political parties, right-wing movements, and some public institutions (health institutions, police, etc).[12]

Advocacy is needed to reduce the risk of hepatitis B in the MSM population. This advocacy should be directed toward the general population as well as physicians and decision makers in order to reduce stigmatization of the MSM population, and to provide information about vaccination, as well as the risks, consequences, and prevention of sexually transmitted infections (STIs). MSM-friendly confidential and anonymous health services should be promoted with the aim of increasing HBV screening and vaccination in MSM. Routine hepatitis B immunization for children (newborns and 12 years old) in Serbia was introduced in 2005 and so it didn't cover the population affected by the outbreak. According to the 2006 Bylaw on Immunization and Chemoprophylaxis[13] some other populations are also covered by hepatitis B vaccination, such as people with hemophilia, patients on hemodialysis, and people who inject drugs, but not MSM. We recommend that hepatitis B vaccination for MSM is included in immunization programs and campaigns in Serbia.

Effective harm reduction strategies for reducing transmission of hepatitis B and other STIs exist including immunization, counseling, testing, and early diagnosis and treatment. Failure of MSM to disclose their risk behaviors could delay diagnosis and treatment and, therefore, increase transmission. The promotion of VCT services, based on MSM-friendly health services that provide a safe environment in which to disclose same-sex behavior, has resulted in MSM being diagnosed and referred for treatment earlier compared to other HIV cases.[14] Following the HIV example, health services, particularly in those countries where MSM are highly stigmatized, should be supported in developing MSM-friendly services conducive to

disclosure. Such services would greatly increase the effectiveness of efforts to identify, treat, and decrease the transmission of hepatitis B and other STIs.

Authors Disclosure Statement

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References

1. European Centre for Disease Prevention and Control: Hepatitis B surveillance in Europe – 2013. Stockholm: ECDC, 2015.

2. Urbanus AT, van Houdt R, van de Laar TJ, Coutinho RA: Viral hepatitis among men who have sex with men, epidemiology and public health consequences. Euro Surveill 2009;14(47):pii:19421.

3. European Centre for Disease Prevention and Control: Systematic review on hepatitis B and C prevalence in the EU/EEA. Stockholm: ECDC, 2016.

4. Sherman M: Strategies for managing coinfection with hepatitis B virus and HIV. Cleve Clin J Med 2009;76 Suppl 3:S30-S33.

5. Duric P, Ilic S: Sexually transmitted infections. In: Communicable diseases in AP Vojvodina 2010. Novi Sad: Institute of Public Health of Vojvodina, 2011. Available from: http://izjzv.org.rs/publikacije/ZarazneBolesti/ZB_2010.pdf

6. Republic of Serbia: Law on Protection of Population from Communicable Diseases. Official Gazette of the Republic of Serbia, 2004;125. Available at: http://www.zdravlje.gov.rs/tmpmz-admin/downloads/zakoni1/zakon_zastita_od_zaraznih_bolesti.pdf7. Lazarevic I, Cupic M, Delic D, et al.: Prevalence of hepatitis B virus MHR mutations and their correlation with genotypes and antiviral therapy in chronically infected patients in Serbia. J Med Virol 2010;82:1160–1167.

8. Republic of Serbia: Law on the Prohibition of Discrimination. Official Gazette of the Republic of Serbia, 2009; no. 22. Available at: http://www.paragraf.rs/propisi/zakon_o_zabrani_diskriminacije.html9. Republic of Serbia: Strategy for Prevention and Protection of Discrimination. Official Gazette of the Republic of Serbia. 2013; no. 60. Available at: http://www.ljudskaprava.gov.rs/sites/default/files/dokument_file/strategija_jul_2013.pdf10. Republic of Serbia: Law on Patients' Rights. Official Gazette of the Republic of Serbia. 2013; no. 45. Available at: http://izjzv.org.rs/publikacije/ZarazneBolesti/ZB_2010.pdf http://www.zdravlje.gov.rs/downloads/2013/Jun/Jul2013ZakonOPravimaPacijenata.pdf11. Commissioner for Protection of Equality by the Center for Free Elections and Democracy (CeSID): Report on public opinion survey: "Citizens' attitudes on discrimination in Serbia". Belgrade: CeSID, 2012.

12. Safe Pulse of Youth: Across homophobia. Belgrade: Safe Pulse of Youth, 2014. Available at: http://korak-hapi-step.eu/wp-content/uploads/2014/12/Prekoputa-homofobije_Analiza-%C5%BEivotnog-iskustva-LGBT-osoba-u-Srbiji-i-preporuke-za-smanjenje-diskriminacije.pdf13. Republic of Serbia: Bylaw on Immunization and Chemoprophylaxis. Official Gazette of the Republic of Serbia. 2006;11. Available at: http://www.podaci.net/_z1/2133917/P-inzlek03v0611.html

14. Duric P, Ilic S, Turkulov V, et al.: Epidemiology of HIV infection in the men who have sex with men (MSM) population of Autonomous Province (AP) Vojvodina, Serbia. J Ecol Health 2013;17:81-86.