



## THE INCREASE OF HEPATITIS A INFECTIONS IN EUROPE AND POLAND IN 2017

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### ABSTRACT

In December 2016, the European Center for Disease Prevention and Control (ECDC) published a report concerning increase in the number of hepatitis A cases in the United Kingdom and the Netherlands in 2016 caused by two new virus serotypes previously detected in patients in Berlin. Spain, Italy and Germany also reported a regional increase incidence of HAV at that time. In addition to the increase in the number of cases, there was a disproportion between the incidence of women and men and a high percentage of patients declaring homosexual orientation. Patients were not vaccinated against Hepatitis A in the vast majority of cases. In Poland, from 1<sup>st</sup> January 2017 to 12<sup>th</sup> October 2017, there have been 1680 cases of hepatitis A, while in 2016 there have been only 27 infected. The goal of the study is to analyze the causes of rapid increase of hepatitis A morbidity rate in Poland in 2017. Until now, the main route of hepatitis A virus transmission was the faecal - oral path caused by the consumption of contaminated food and lack of hygiene. Based on data from the Voivodeship Sanitary and Epidemiological Station in Poland and the report of the European Center for Disease Prevention and Control (ECDC), the number of cases of sexual contact increased. The current situation in Europe is correlated with epidemiological data in Poland - most of infected are young men. The increasing number of incidence of HAV infection among MSM (man who have sex with man) is a matter of concern due to the difficulties in interrupting the spreading of the epidemic and the prevention of secondary infections related to the participation of infected in the production and trade of food. The hepatitis A vaccine may be use for a prophylactic purpose, protective vaccinations for homosexual men are now particularly recommended. The information campaigns also play an important role in the prevention of the spread of hepatitis A infection. We can make a thesis based on information obtained. The deterioration of the epidemiological situation in Poland could be a consequence of the increase morbidity rate in the European Union countries.

## BACKGROUND

**H**epatitis A is an acute disease. The symptoms include heartburn, nausea, flatulence, feeling of early fullness, darkening of urine as well as flu-like symptoms and jaundice. The disease mainly affects adults, because most children are asymptomatic. It usually requires hospitalization, especially for people infected with HBV or HCV. However, the number of hospitalizations decreased significantly after the introduction of the vaccine. The disease usually does not last longer than two months [1]. Following infection, the incubation period lasts on average 15-50 days [2]. The HAV is excreted in the faeces for 1-2 weeks before the onset of clinical symptoms and ~ 1 week after recovery [3]. HAV is mainly spread by faecal-oral pathway - eating food or drinking water contaminated with infected faeces. It can also spread through close contact with an infectious person (including being in the same household with an infected person), sexual contact (especially in men having sex with men - MSM) and using illegal drugs (contaminated needles from drug addicts) [1]. Risk Infections in the patient's environment range from 15-20% [3]. We observe an increase in the importance of infection through sexual contact (both anal and oral-anal) in the current year. For virus transmission, it is also enough to have oral contact with the parts of the body on which the virus is located. It is interesting to note that the way of the virus spreading depends on the degree of sanitary conditions in the countries. Poland has been considered as a country with low endemicity so far. In the 21st century, the incidence per 100,000 population ranged from 0.09 to 1.7 (mean 0.4) [3]. In 2016, there were 35 new cases of hepatitis A [4]. Over 2,205 new cases have already been observed in the period since 1st January to 31st October 2017, and the morbidity rate ranged up to 5.74 [5].

## THE DIAGNOSIS, COURSE OF THE DISEASE AND COMPLICATIONS

The diagnosis consists of a clinical picture and laboratory tests. The results of laboratory tests in symptomatic patients show an increase in serum transaminase, total and direct bilirubin and alkaline phosphatase level. Specific diagnosis is made by the detection of HAV-specific IgM antibodies in the blood. The sensitivity and specificity of this test is 95% and it distinguishes acute hepatitis A from other inflammations. The anti-HAV IgM test becomes positive within five to ten days, but usually does not detect the lower concentration that is present four to six months after an acute infection. Anti-HAV IgM can be detected in people who have recently received a vaccine against hepatitis A. In most cases, hepatitis A is self-limiting. Complications are more common in adults over 50 years old. Between 10 and 20 % of infected people have a relapse after six months of the acute illness, but disease did not progress in chronic hepatitis A. It is important to understand that the virus can be excreted via the faeces during relapse and can be transmitted at this time. Above all, it is important to stress that the patients with liver disease such as hepatitis B or C, or when HAV has more than one genotype

combined, present more severe course of disease [6, 7]. Very rarely, vasculitis, inflammation arthritis, thrombocytopenia, acute pancreatitis, aplastic or autoimmune hemolytic anemia, Guillain-Barré syndrome, acute kidney injury, pericarditis or infection can occur in patients with HAV [1].

## MATERIAL AND METHODS

The following material is an analysis of available articles describing the increase in cases of hepatitis A in Poland and Europe at the turn of 2016-2017.

The last epidemic of hepatitis A in Europe among MSM occurred between 2008-2011 [8]. In connection with the observed cyclical increasing the outbreaks of HAV in common, European research was undertaken to determine whether HAV strains causing explosions in various countries are genetically related. A study conducted by Stene-Joansen et al. showed that most strains found in European countries among the MSM group formed closely related groups belonging to the genotype 1A [9]. In December 2016, the European Center for Disease Prevention and Control (ECDC) published a report about the increasing outbreaks of hepatitis A in the Netherlands and the UK, caused by two new virus serotypes previously detected in patients in Berlin. Italy and Spain have also reported a recent increase of HAV cases in men.

We present a description of the epidemiological situation in Berlin, the Netherlands and the United Kingdom on the basis of available scientific articles.

## RESULTS

### *Berlin*

After the increase of morbidity rate of HAV in Berlin, the appropriate database was created to enable assessment of risk factors in infected and the serotype of the virus determined on the basis of sequencing. The article by Werber et al. describes the situation in Berlin since 14<sup>th</sup> November 2016 until 20<sup>th</sup> January 2017. In this time, 38 cases of hepatitis A have been reported. Of these, 37 are men and one is a woman. Sexual orientation was known in 32 cases (31 men, one woman); 30 identified themselves as MSM, one as heterosexual, while the woman declared homosexual orientation. The median age of 30 MSM cases is 31 years (range: 24-52 years). Six cases had a history of travel outside of Germany (Spain, Austria, Greece, Malta, Taiwan) during the assumed infection period, but most of patients were apparently infected in Germany (probably in Berlin). The results of sequencing and phylogenetic analysis show three distinct clusters of HAV strains correlated with MSM belonging to genotype 1A [10]. Two different HAV sequences detected in cases from Berlin were identified at the same time in MSM clusters in the Netherlands and the United Kingdom.

### *Netherlands*

In the Netherlands, hepatitis A is a notifiable disease. HAV infections have to be reported in one working day to the regional Public Health Services (PHS) by the laboratories and physicians. The PHS then collect epidemiological information on demographics,

occupation, symptoms, suspected source/country of infection, MSM contact (for males only) and consumption of specific food items. The PHS reports all information in the national surveillance system for notifiable diseases. Moreover, serum and/or stool samples of HAV cases are routinely sent and analyzed in the National Institute of Public Health and the Environment (RIVM). In the period from July 2016 to February 2017 in the Netherlands, 48 male cases of hepatitis A were reported. Of these, 17 were identified as men having sex with men (MSM). Ten of the 13 cases for which information about sequencing was available, were infected by a strain associated with EuroPride festival taking place on July 29th - August 6th in Amsterdam (the Netherlands). This strain was identical to the strain which caused epidemics among MSM in Taiwan. In comparison, in 29 male cases that fell ill after mid-2016 and did not declare to MSM, the strains which were not related to the current epidemic were found. Among 17 MSM cases, 11 came from outside the Netherlands (Argentina, Brazil, Canada, France, Italy, Lebanon, Peru, Spain (n=3), Suriname). The median age of 17 cases was 33 years (range: 26-52). Sequence information was available for 13 out of 17 cases. Studies have shown coexistence of three different hepatitis A strains. Most cases with sequence information available were infected by the strain RIVMHAV16-090. This strain was detected only once before 2010 and was absent in the Netherlands until now [11].

#### **Great Britain**

Since July 2016 to 24<sup>th</sup> January 2017, 37 HAV infections with two sequences in eight areas of Great Britain were reported, mostly of MSM (mean age: 35 years, range: 19-56), according to the study of K. Beebejaun et al. One of the strains (RIVM-HAV16-090) was detected in 13 cases, 12 of them were male, mean age 39 (range: 29-78), nine were identified as MSM, and 11 were traveling during the incubation period (seven of them to Spain and two to Germany). This strain is comparable to the strain that appeared in the Netherlands after the EuroPride event. The second strain (VRD\_521\_2016) occurred in 24 cases, 22 of them were male, median age 35 years (19-63 years), 19 were identified as MSM, and eight reported a trip during the incubation period (seven of them to Spain). Both strains belonged to genotype 1A. The authors also underline that epidemiological and laboratory studies suggest the migration of serotypes from several regions of Spain with secondary sexual transmission in the MSM population in the UK, as nine of the confirmed cases of MSM reported traveling to Spain during the incubation period. Spain also reported an increase in the number of HAV infections in men, but further details are not available [12].

#### **Hepatitis A epidemic in Poland**

Poland is a country belonging to areas of low endemicity. Since 2001, the morbidity rate per 100,000 population ranged between 0.09 to 1.7 (mean 0.4) [3]. In different years, 8-52% of patients were people who traveled to endemic areas, most often to Egypt. Even in 2015, the morbidity rate was 0.13 / 100,000 and in 2016 it was 0.09 / 100,000 [4, 5]. Hepatitis A occurs worldwide, endemically in the Mediterranean basin, Eastern Europe and Russia, and developing countries. In Poland, the

incidence is sporadic and group. The main source of the infection is contaminated food or food dragged from endemic areas. Attention is paid to risk factors because in 15-20% of cases an infection occurs in the patient's environment. These include: close contact with the patient (especially a shared flat), home or professional contact with children in nursery or kindergarten, journey to the country of endemic presence of HAV, seafood consumption, especially crustaceans and raw oysters, homosexuality of men, removal of municipal waste, liquids towards drains and maintenance of devices used for this purpose [3].

#### **All-European data**

From the beginning of 2017 to 1<sup>st</sup> August 2017, 14 countries, i.e. Austria, the Czech Republic, Denmark, Finland, France, Germany, Ireland, Latvia, Lithuania, the Netherlands, Poland, Portugal, Slovenia and Spain, reported 5983 cases of hepatitis A. This is more than the average annual quantity of cases reported by this group of countries to The European Surveillance System (TESSy) between 2007-2016 (2506 cases). Since 1<sup>st</sup> June 2016 to 26<sup>th</sup> June 2017, 16 EU countries (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden and the United Kingdom) have reported 1500 HAV (hepatitis A) cases with the confirmed genotype 1A, belonging to three separate clusters (based on HAV genetic sequencing), mainly among adult MSM. In addition to confirmed outbreak cases, additional 2660 cases of hepatitis A have been reported, likely or suspected to be related to this outbreak [13]. Most cases were reported in March 2017. The number of cases does not show the true extent of the outbreak, information of sequencing is only available in some countries and only in cases of hepatitis A. From January to August 2017, 19 countries (Austria, Belgium, The Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Iceland, Italy, Luxembourg, Malta, the Netherlands, Slovenia, Spain, Sweden and the United Kingdom) have reported 11212 lab-confirmed cases. The highest M/F ratio was 4.8 in April 2017. No other strains were widely distributed among MSM, except for the three epidemic strains and their close variants (VRD\_521\_2016, RIVM-HAV16-090, V16-258010) [14].

Stable epidemiological situation in Poland was discontinued in 2017, where the number of new patients increased 70-fold compared to the previous year. According to the data of the National Institute of Public Health - National Institute of Hygiene (NIZP-PZH) in the period from 1st January to 31<sup>st</sup> October 2017, 2205 cases were registered in Poland (morbidity 5.74 / 100,000 ) [14]. So far, this year's cases are reported mainly from the following voivodeships: Wielkopolskie, Mazowieckie, Zachodniopomorskie, Slaskie, Dolnoslaskie and Kujawsko-Pomorskie. In 2017, there were 419 cases (including 11 hospitalized patients) in the Wielkopolskie voivodeship, while it was one case in 2016. In the Mazowieckie voivodeship there were a total of 615 cases of hepatitis A (morbidity 11.5 / 100,000) and a year earlier there were 6 cases (morbidity 0.1 / 100,000). In the Slaskie voivodeship 287 cases were noted (including 111 of them in Sosnowiec), whilst there were only 3 in 2016, and in the Dolnoslaskie voivodeship a total of 88 was

observed. In the Kujawsko-Pomorskie voivodeship 25 cases of hepatitis A were registered - this is more than in years 2010-2016 together. Among the registered cases, young people in age between 20 and 40 years old were predisposed, mainly men with homosexual orientation. The highest incidence is observed in large agglomerations and voivodeships bordering with Germany. It may indicate that epidemic came from Western Europe.

## DISCUSSION

The phenomenon described in this article emphasizes the interconnectedness of MSM in Europe and the need to increase the monitoring of the movement of serotypes among the European population. Most authors underline the key role that sequencing can play in detecting epidemics, as well as the value of a common European platform to share epidemiological and virological information [15]. In Poland, vaccination on hepatitis is recommended but not obligatory. The complete vaccination schedule consists of 2 doses given at least 6-12 months apart, vaccination of children is recommended at 1 year of age. One dose costs from PLN 83 up to PLN 131. The vaccine provides protection for over 45 years [16]. Unfortunately, many people refuse to vaccinate children because they do not know the disease. Non-specific prophylactic boils down to the complying with hygiene rules especially hand hygiene, avoiding risky behaviors and strict adherence to appropriate sanitary and hygienic conditions in the production and distribution of food and meal preparation.

## CONCLUSIONS

In Poland, specific diagnosis is made by the detection of HAV-specific IgM antibodies in the blood-serological tests [3]. The viral sequencing is not routinely performed due to very high cost of this study, making it impossible to determine the source of the outbreak. However, suggesting a similarity as regards to the age and sex of patients, it can be argument that the deterioration of the epidemiological situation in Poland is a consequence of the increased incidence in the European Union countries. In addition, the highest number of cases is observed in large agglomerations and voivodeships bordering with Germany, which may be indicative of the epidemic from Western Europe. The vast majority of cases were not vaccinated against hepatitis A, it shows the need for vaccination campaigns. It is worth noting that using condoms is not a protection against HAV infection. Although co-infection with HIV and HAV does not suggest any effect of HAV infection on HIV progression rate, HIV-positive patients with positive HAV infection should be carefully monitored because their HAV infection is more symptomatic and takes longer [17]. The main preventive measure in the context of current epidemics are vaccinations among MSM. It is suggested to promote vaccinations at Pride festivals this summer, where the probability of contact with people infected with the hepatitis A virus is high. However, the limited access to the hepatitis A vaccine in some countries may affect the implementation of these measures. Some countries have reported deficiencies (eg. Austria, Denmark, Italy,

Portugal, Spain and Sweden ) [14]. According to Jacobs et al., the cost-effectiveness of HAV / HBV combination vaccine in high-risk groups is higher than that of HBV alone. Therefore, campaigns for MSM should recommend combination vaccine to decrease morbidity rate of HAV [18].

## CITE THIS AS

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## ABBREVIATIONS

**ECDC** – European Center for Disease Prevention and Control

**EU** – European Union

**HAV** – hepatitis A virus

**MSM** – man who have sex with man

**PHS** – Public Health Services

**RIVM** – National Institute of Public Health and the Environment

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