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HEPATITIS C OUTBREAKS IN POLAND IN 2003-2013. MEDICAL PROCEDURES AS A DOMINANT ROUTE OF HCV TRANSMISSION[1].

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ABSTRACT

BACKGROUND. According to the data from routine epidemiological surveillance in Poland, over 70% of patients diagnosed with HCV infection report exclusively medical exposure which suggests that infection was probably associated with procedures performed in health care settings. To a large extent, neither the source nor the mechanism of transmission, however, may be determined. Infections detected in an acute phase, accounting for ca 2 -3% of registered hepatitis C cases per year, better reflect the actual routes of HCV transmission. Epidemiological investigations of acute hepatitis C outbreaks allow for identifying the procedures in which the virus is transmitted.
OBJECTIVE. To identify mechanisms and breaches of safety procedures, which are most frequently associated with HCV infection, based on a review of recent hepatitis C outbreaks in health care settings in Poland.
METHODS. A systematic review of reports on acute hepatitis C cases registered in routine surveillance in 2006-2013 and literature review in PubMed and SCOPUS.
RESULTS. A total of six outbreaks were documented in which 116 cases were detected. Of them, four outbreaks were identified based on surveillance data, including one unconfirmed outbreak, and information on two outbreaks was retrieved from publications. Five of the described outbreaks were acquired in health care settings, including two outbreaks which occurred in dialysis units and one outbreak was associated with alternative medicine procedures. Probably, infections were most commonly transmitted due to mistakes of medical personnel resulting from negligence or ignorance of procedures, i.e. multiple use of disposable equipment and improper use of personal protective equipment (failure to change disposable gloves). In one case, neither breaches of procedure nor actions which could lead to HCV infection were determined.
CONCLUSIONS. A detailed epidemiological investigation should be conducted in each registered case of acute hepatitis C as detected symptomatic cases allow for identifying the outbreaks.
Epidemiological investigations of outbreaks should be improved by inclusion of molecular tests. Identification of breaches of binding procedures indicates a necessity of continuing training of personnel and enhanced control of compliance with binding recommendations, especially with regard to injection safety.

Key words: *hepatitis C, acute hepatitis C, outbreak, route of transmission, Poland*

BACKGROUND

Irrespective of a substantial progress in the treatment of chronic hepatitis C, HCV infections still constitute one of the major health problems worldwide. An estimated 130-150 million individuals are chronically infected globally and 350-500,000 die each year due to long-term sequelae of hepatitis C, i.e. cirrhosis and liver cancer (1).

Injecting equipment sharing in persons who inject drugs is considered to be the most effective route of HCV transmission as well as some medical procedures, especially hemodialysis, invasive medical procedures, and transfusions of blood or blood products in the past (2-5). Less frequently, the infections are acquired through sexual contacts, vertical transmission and non-medical procedures - tattooing, piercing, beauty treatments accompanied by skin injury or acupuncture (3, 5,

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6). In case of a number of patients, exposure/risk factor which could be associated with HCV infection cannot be established (4, 7). In particular, in the majority of chronic cases of long asymptomatic course a probable route of infection may be determined by considering an individual history of exposures throughout life.

Identification of dominant route of transmission in a given population and on a defined territory is of paramount importance for planning and undertaking hepatitis C preventive and control measures, both in terms of safety of procedures accompanied by skin injury as well as the behavior and lifestyle of people.

In the EU countries, over 75% of detected HCV cases (out of those with known route of infection, in acute, chronic and "unknown" phases considered altogether) were acquired through injection drug use and only 4% through medical procedures (8). In addition, the majority of healthcare-associated infections are linked with transfusions or invasive procedures performed in the past. Such route of transmission, however, was rarely indicated in newly diagnosed acute cases.

Documented acute hepatitis C cases can provide more reliable data on the actual routes of HCV transmission. Acute cases, however, account only for a small percentage of confirmed HCV infections registered annually due to frequent asymptomatic course - 1.7% based on the ECDC (8). In order to improve the safety of medical procedures (and safety of each hospitalization which is not associated with invasive procedures), it is necessary to determine which procedures most often lead to new HCV infections and strengthen the weak points in the existing safety standards.

The aim of this study was to identify and describe the procedures most often leading to HCV infections in Poland based on the analysis of documented outbreaks of acute hepatitis C in recent years.

MATERIAL AND METHODS

A retrospective analysis of individual reports on hepatitis C registered in routine surveillance system in 2006-2013 was performed, with a particular attention paid to acute hepatitis C cases. Individual reports on hepatitis C cases are available in the epidemiological surveillance system in Poland since 2006. Cases who meet the criteria of hepatitis C definition adopted by the European Commission by means of the Decision 2002/253/EC, and since 2009 – the decision 2008/426/EC) are subject to registration (9).

Detailed information on risk factors is collected since 2009, following the modification of the report form, and was available for 2010-2012.

Hepatitis C case definition used for the purpose of surveillance: all laboratory-confirmed cases (confirmed presence of antibodies or detection of virus nucleic acid), regardless of the clinical picture (2009 case definition), in previous years (2005 case definition): cases with clinical symptoms or cases with elevated transaminase activity in the course of HCV infection confirmed by the detection of anti-HCV or HCV nucleic acid in clinical samples.

Hepatitis C case definition used did not allow for differentiating acute and chronic cases. Classification of stage was based on a diagnosis made by the reporting physician using the following criteria of acute hepatitis C:

- case with documented anti-HCV seroconversion within the last 12 months
- OR symptomatic hepatitis C case (according to the case definition used in surveillance) who present with jaundice or elevated alanine transaminase activity (ALT>350 IU/mL or ALT>10N)
- OR case with HCV RNA and undetected anti-HCV with a known exposure to HCV infection within the last 6 months

Cases with markers of hepatitis of different etiology (hepatitis A, hepatitis B, EBV, CMV), alcoholic or toxic hepatitis or a history of liver diseases were excluded.

In each case notified as acute hepatitis C, the following variables were verified:

- exposure to HCV infection within six months prior to the first detection of HCV
- link with the outbreak (according to the information provided by District Sanitary-Epidemiological Stations, DSES)
- if the case occurred in the outbreak, data from outbreak investigations were analyzed.

Regardless of the surveillance data analysis, MEDLINE/PubMed and SCOPUS databases were searched using the keywords: ((*acute hepatitis C* OR *hepatitis C* OR *HCV infection*) AND *outbreak* AND *Poland*) to identify studies describing acute hepatitis C outbreaks in Poland, with particular attention paid to the mechanism of HCV transmission.

RESULTS

According to the epidemiological surveillance data, a total of 19,328 hepatitis C cases were reported in 2006 – 2013 in Poland, including 6,690 in 2010-2012. As a result of analysis of case-based reports, a total of 577 acute hepatitis C cases were identified (155 in 2010-2012) (Tab. I).

Out of hepatitis C cases (acute and chronic altogether) registered in 2010-2012, 67-75% reported medical procedures as the most likely route of transmission while injection drug use was indicated only in 6-7.5%

Table I. Number of hepatitis C cases recorded in surveillance in 2006-2013 in Poland.

	2006	2007	2008	2009	2010	2011	2012	2013
Total number of hepatitis C cases	2949	2753	2353	1939	2179	2241	2270	2644
Number of acute hepatitis C cases	100	98	89	66	44	64	47	69
Number of hepatitis C outbreaks	1	-	-	-	-	1	-	2

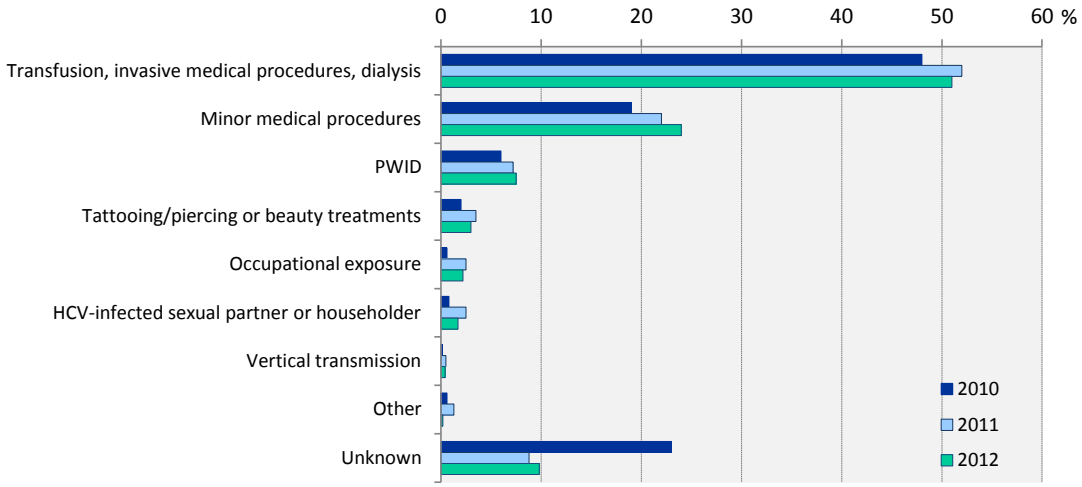

Fig 1. Hepatitis C in Poland in 2010-2012. Percentage of probable routes of transmission of HCV in the total number of cases.
Source: Case-based reports collected in routine mandatory surveillance system

of cases. Having considered only the cases with probable route of transmission specified, the percentage of infections which were probably acquired via medical procedures exceeded 80% (Fig. 1).

Based on the routine surveillance data, three outbreaks and one suspicion of outbreak were identified in 2006-2013, in which a total of 75 persons were infected. All the outbreaks occurred in health care settings, including two in dialysis units, one in the diagnostic center in the department of computed tomography and magnetic resonance imaging and one suspected outbreak, finally recognized as unconfirmed, on the hospital ward.

Having searched the PubMed and SCOPUS, a total of 28 publications were identified. Following the exclusion of duplicates and non-relevant articles, two publications describing two HCV outbreaks in Poland in 2003 were included in the analysis (10, 11). No publication describing hepatitis C outbreaks identified based on the surveillance data, i.e. 2006-2013 was found.

A total of 6 outbreaks from 2003-2013 were analyzed. Table II presents a detailed description of these outbreaks. As molecular studies confirming the link between strains isolated from patients were not performed in any of the registered outbreaks, a cluster of cases on a hospital ward, which was considered as unconfirmed, was also included.

All detected outbreaks, except for one from 2003, occurred in healthcare settings and were associated with medical procedures performed. Two outbreaks occurred in dialysis units, one was detected in the department of computed tomography (CT) and the suspected outbreak concerned patients hospitalized on hematology ward. Infections in the outbreak unrelated to healthcare settings (10), was also associated with the procedures considered to be medical i.e. intravenous infusions carried out without compliance with the safety standards in alternative medicine settings.

Acute hepatitis C was recognized in individual cases based on various criteria. In the outbreaks detected in dialysis units, diagnosis was based on anti-HCV seroconversion in patients which were regularly examined due to chronic dialysis. None of the infected dialysis patients presented perceptible symptoms of viral hepatitis. Detection of outbreaks associated with CT and "chelation therapy" resulted from linking the first symptomatic patients hospitalized on infectious diseases wards with a common exposure within the incubation period of the disease and then by active searching for cases in the remaining persons being the patients/clients at the time when the infection could occur.

Outbreak of hepatitis C in patients hospitalized on gynecological ward was confirmed in epidemiological investigation which was by means of civil court request after the infected patients brought the legal action against the hospital (11). Diagnosis of acute hepatitis

Tab. II. Characteristics of acute hepatitis C outbreaks in Poland in 2003-2013 by settings

	Year	Location/setting	Number of individuals infected	Number of individuals tested	Age, range and median	Sex M:F	HCV genotype	Symptomatic cases (including jaundice)	ALT (IU/l)	Source
1.	2003	Alternative medicine center (chelation therapy with unknown agent)	15	all individuals treated in the center during Jul-Aug 2003, number unknown	48-72; mean 61	12:3	1b	40%	121-2233	unk
	Known or suspected route of transmission and contributing factors: Intravenous infusions of unknown agent - unsafe injection practices									
2.	2003	Department of Gynecology, Obstetrics and Oncology	26 (22 had major gynecological surgeries)	unk	19-72	0:26	not determined[1]	not specified (few patients)	not available	unk
	Known or suspected route of transmission and contributing factors: Major gynecological procedures; breaches in sterilization procedures: using a dry air sterilizer, using expired biological tests, incorrect transportation of equipment and incorrect packaging of material, no control of packaging seals, using decommissioned sterilization equipment. Failure to comply with the basic sanitary rules and hygiene standards: washing hands, instruments and newborns in the same washbasin, medical equipment dried with hand towels, using non-sterile materials (swabs), instruments and equipment, no separation of sterile and non-sterile areas. Lack of written crucial procedures.									
3.	2006	Dialysis unit	53	112 on dialysis, 121 householders, 15 personnel members	32-88; 64	29:24	unk[1]	0%	not available	Probably one of 12 patients previously infected HCV
	Known or suspected route of transmission and contributing factors: Dialysis and/or injections from multiple vials; numerous breaches of procedures, the most important: multiple use of disposable needles, syringes and capillary tubes for ionometer, use of non-sterile minor medical equipment, lack of changing of dialyzer for each patient, use of erythropoietin in multi-dose vials for >1 patient. Lack of written crucial procedures.									
4.	2011	Dialysis unit	5	76 patients on dialysis and all medical personnel (number unk)	34-69; 64	4:1	2	0%	60-670	unk
	Detailed route of transmission was not identified. There were no breaches of procedures.									
5.	2013	Department of Hematology and Oncology	8	unk	27-73; 63	4:4	1b (in one patient, in the rest unk[1])	37%	34-539	unk
	Outbreak unconfirmed - Hepatitis C detected in patients receiving chemotherapy on the same hospital ward									
6.	2013	CT&MRI diagnostic center	9	22 out of 28 patients examined on the same day	34-75; 66	5:4	1 subtype undetermined	67%	23-2000	Probably patient HCV(+) examined on the same shift
	Known or suspected route of transmission and contributing factors: *Via* set for contrast media for CT & MRI injector - multiple use of disposable sets. Failure to change gloves between patients, lack of compliance with essential procedures at worksites.									

[1] HCV-RNA was positive in all patients in whom HCV genotype was not determined or unknown for authors

C (acute or recent hepatitis C) was made on a basis of symptoms or elevated transaminase activity and detection of HCV RNA (in all 26 infected women).

Suspicion of hepatitis C outbreak on hematology and oncology ward was made following the detection of anti-HCV in 8 patients of this ward receiving chemotherapy within a few months preceding the detection of HCV, in most cases on the same ward. As many as three patients presented with the symptoms of acute hepatitis or significantly elevated transaminase activity which allowed for the initial diagnosis of acute hepatitis C. Presence of other exposures reported in the incubation period of the disease, the lack of molecular confirmation of infection with the same strain of the virus, the absence of information on genotype in the majority of patients and detection of anti-HCV prior to the initiation of chemotherapy in one patient (a possible source of infections) however, did not allow for confirming the outbreak.

Sequencing of HCV to confirm the infection with the same strain was not performed in any of the described outbreaks. In three outbreaks, all patients were infected with the same HCV genotype (G1 or G2) and other exposures to infection within the incubation period were excluded.

The source of infection was indicated only in one outbreak (chronically infected patient). Sequencing of virus allowing for confirming a common source of infection for all infected persons in the outbreak, however, was not performed. Chronically infected patients, whose status was known previously (12 HCV positive persons in one unit, no data on the number of infected dialysis patients in the second unit), were also a probable source of infection in outbreaks reported in dialysis units. In none of these outbreaks, a common source of new infections was identified.

In case of two outbreaks, a probable mechanism of infection transmission was specified, i.e. in CT department and dialysis unit in 2006 (Tab. II). In dialysis station, however, a number of breaches were established (multiple use of disposable needles, syringes and capillary tubes for ionometer, failure to change dialyzers between patients, use of erythropoietin in multi-dose vials for more than one patient and injecting the remaining blood used to test the electrolyte back to the line, no separate stands for patients previously infected with HCV) which could lead to infection transmission between patients.

In the chelation therapy-related outbreak, intravenous infusions of an unknown agent was the only exposure identified. Neither the exact mechanism of transmission (e.g. use of multi-dose packages for several patients, multiple use of disposable equipment etc.) nor the source of infection (lack of access to the investigation report), however, could be determined.

In all outbreaks reported in healthcare settings except for one (dialysis unit, 2011), numerous breaches of standards were identified which could lead to infection transmission between patients.

DISCUSSION

All of the identified acute hepatitis C outbreaks were related to medical procedures, including the outbreak reported in alternative medicine center, in which intravenous infusions were administered without adherence to safety standards.

Results of inspections carried out in healthcare settings reported to be the places of exposure showed, to a large extent, the lack of developed procedures or lapses in existing procedures which confirms the possibility of HCV patient-patient transmission.

Although the precise determination of the mechanism of transmission is not possible, collected data allow for making some hypotheses. According to the available information, the infections probably occurred most frequently due to human error resulting from the lack of adequate training of the personnel to operate specialist equipment (dialysis station, 2006) or deliberate omission of known procedures (Gyn. ward, CT). The latter may occur particularly with regard to the use of disposable equipment which does not have a visible contact with the patients' blood (e.g. contrast administration set, syringes, gloves). Only in one case (dialysis station, 2011), no breaches in existing procedures was established. Outbreaks described were associated with procedures of documented risk of HCV infection - in dialysis units, in connection with invasive surgical procedures or injections performed without compliance with safety standards (12-17).

Both registered outbreaks in healthcare settings as well as the percentage of acute cases reporting medical procedures as a route of transmission in the surveillance (over 60%) indicate that problem of healthcare-related HCV infections in Poland remains still unresolved. In the recent years, publications appear which indicate that the number of healthcare-acquired HCV infections in the European countries may be considerably higher (4, 7, 18-20) compared to the above-cited ECDC data. Having considered underestimated European data, however, Poland still stands out negatively against other EU countries. Due to the risk of HCV infection which is present even in case of minor procedures accompanied by skin or mucous injury, there is a necessity to remind of the strict compliance with the existing safety standards in all medical and non-medical settings in which procedures accompanied by skin injury are performed and to periodically verify the knowledge and compliance with the existing procedures by the personnel. In several cases, transmission was related to use of rather

complex equipment, usually by the mid-level personnel. Basic training on the risk of blood-borne infections usually focuses on the safety of injections. Thus, it may not be adequate with regard to more complex medical devices. Lack of awareness and/or competence of the personnel indicates the need for a more precise risk assessment by nosocomial infection control teams and carrying out specific trainings tailored to the procedures performed in a defined unit.

A certain limitation of the present review of outbreaks results from the difficulties to determine a clear definition of acute hepatitis C. Due to the asymptomatic course, most of acute cases remain undetected, however, the presence of symptoms and/or a significant increase of transaminase activity at the time of the first positive anti-HCV test result still do not provide a sufficient basis for diagnosis of acute hepatitis C (21). The only accepted criteria for the diagnosis of acute hepatitis C are: documented HCV seroconversion (in case of prior negative test result within the last 6-12 months) or detection HCV RNA or HCV core antigen with simultaneous lack of anti-HCV antibodies (detection of infection in the window period) (8). To meet the first of these criteria, regular anti-HCV testing should be performed. In Poland, however, it is carried out in an organized manner only in case of chronic dialysis patients. To detect infections in the window period, it is necessary to perform HCV RNA testing regardless of the anti-HCV test result (blood donors testing or, less frequently, in cases suspected of HCV infection with a known exposure). Other registered cases of acute hepatitis C, diagnosed based on clinical symptoms of acute hepatitis and/or significant ALT elevation should be considered as probable acute hepatitis C cases.

Review of hepatitis C outbreaks in Poland revealed limitations with regard to the possibility of full confirmation of link between detected cases, especially concerning molecular confirmation of genetic relatedness between isolates. Lack of molecular analysis may explain the absence of outbreaks associated with exposures different from healthcare-related ones. In case of infections associated with individual exposure e.g. injection drug use, it is very difficult to determine a common exposure or transmission between individuals. Moreover, despite the high number of acute cases registered in surveillance system, in which healthcare-related procedures were reported to be the only exposure during the incubation period of disease (62% of acute hepatitis C cases in 2010-2012, in which probable route of transmission was specified, Fig. 2), the majority of cases were classified as sporadic, not linked with other cases. Active searching for cases was carried out only if two or more acute cases with common exposure during incubation period were detected, most frequently occasionally. Therefore, it should be assumed that the actual number of outbreaks associated with medical procedures was higher, however, their detection was impossible due to failure to detect and register persons with asymptomatic HCV infection. Lack of the use of molecular methods in the surveillance applies also to the registered outbreaks. Out of six described outbreaks, virus genotype was determined only in three outbreaks (subtype was established only in one of them). Sequencing was not performed in any of them.

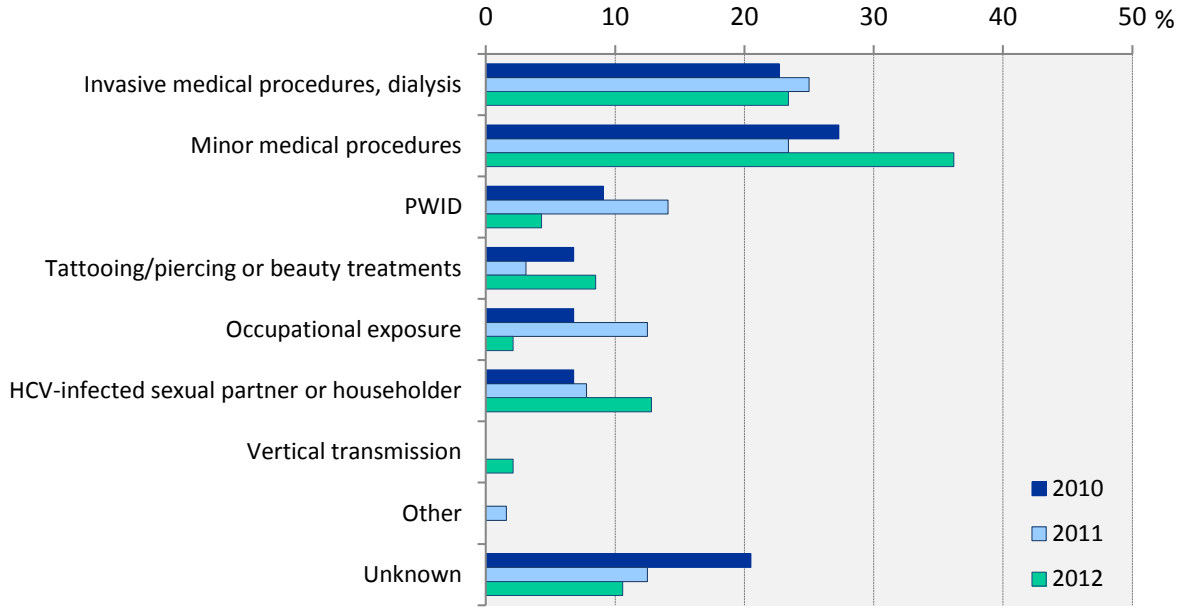

Fig 2. Acute hepatitis C in Poland in 2010-2012. Percentage of probable routes of transmission of HCV in acute hepatitis C cases.
Source: Case-based reports collected in routine mandatory surveillance system

Situation described above may result from the fact that genotyping and, possibly, viral sequencing are ordered in Poland by clinicians in patients under specialist care, and the knowledge of genotype and viral sequence does not influence the therapeutic decisions in acute hepatitis C. Knowledge of HCV sequences is an added value in the epidemiological surveillance as it allows for indicating the geographical origin of the virus, examining the virus circulation depending on the route of transmission, changes in its virulence and the time of infection (22-24). Phylogenetic analysis may assist in determining the route of transmission if it is unknown or confirming the common source of infection (25).

Analysis of surveillance data also revealed the lack of a common protocol of outbreak investigation. A common element of investigations consist in controlling the compliance with the existing procedures in healthcare settings. However, there is a lack of description of activities carried out to identify the source of infection or specify a group of people exposed.

Having indicated the limitations of the surveillance system, however, it should be noted that current hepatitis C surveillance methods allow for detecting new outbreaks, which indicates the improvement of surveillance sensitivity. Outbreaks identified on a basis of publications occurred in 2003, i.e. prior to the implementation of the case definition used in the routine surveillance in the EU countries and before introduction of a uniform epidemiological questionnaire.

CONCLUSIONS

- Detected outbreaks of acute HCV infections confirm that healthcare-related procedures accompanied by skin injury are an important source of new HCV infections in Poland.
- In the majority of cases, a detailed mechanism of transmission remains undetermined, however, in a half of detected outbreaks unsafe injections practices were indicated.
- Numerous breaches of existing procedures indicate a need to strengthen the monitoring of compliance with procedures and continuous education of personnel with regard to the current recommendations.
- Epidemiological investigations conducted in HCV outbreaks should be extended by molecular analysis of isolated viruses. There is also a need for training concerning outbreak investigation, firstly, in point source outbreak in healthcare settings.

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REFERENCES

1. WHO, Hepatitis C Fact sheet N°164, updated April 2014. http://www.who.int/mediacentre/factsheets/fs164/en/
2. Esteban JI, Sauleda S, Quer J. The changing epidemiology of hepatitis C virus infection in Europe. J Hepatol. 2008;48:148-62.
3. Strader DB, Wright T, Thomas DL, et al. American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C. Hepatology. 2004;39:1147-71.
4. Santantonio T, Medda E, Ferrari C, et al. Risk factors and outcome among a large patient cohort with community-acquired acute hepatitis C in Italy. Clin Infect Dis 2006;43:1154–1159
5. Delarocque-Astagneau E, Pillonel J, De Valk H, et al. An incident case-control study of modes of hepatitis C virus transmission in France. Ann Epidemiol. 2007;17:755-62.
6. Ackerman Z, Ackerman E, Paltiel O. Intrafamilial transmission of hepatitis C virus: a systematic review. J Viral Hepat. 2000;7:93-103.
7. Pérez-Álvarez R, García-Samaniego J, Solá R, et al. Acute hepatitis C in Spain: a retrospective study of 131 cases. Rev Esp Enferm Dig. 2012;104:21-8.
8. European Centre for Disease Prevention and Control. Hepatitis B and C surveillance in Europe. 2012. Stockholm: ECDC; 2014.
9. Commission of the European Communities. Commission Decision of 28/IV/2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. Available at: http://ec.europa.eu/health/ph_threats/com/docs/1589_2008_en.pdf
10. Cianciara J, Jabłońska J, Horban A, et al. Epidemic outbreak of acute hepatitis C--clinical course, histology and effectiveness of therapy. Przegl Epidemiol. 2005;59:385-94. Polish.
11. Rorat M, Jurek T, Szleszkowski L, et al. Outbreak of hepatitis C among patients admitted to the Department of Gynecology, Obstetrics, and Oncology. Am J Infect Control. 2014;42:e7-e10.
12. Savey A, Simon F, Izopet J, et al. A large nosocomial outbreak of hepatitis C virus infections at a hemodialysis center. Infect Control Hosp Epidemiol. 2005;26:752-60.
13. Rao AK, Luckman E, Wise ME, et al. Outbreak of hepatitis C virus infections at an outpatient hemodialysis facility: The importance of infection control competencies. Nephrol Nurs J. 2013;40:101-10,164
14. Quer J, Esteban JI, Sánchez JM, et al. Nosocomial transmission of hepatitis C virus during contrast-enhanced computed tomography scanning. Eur J Gastroenterol Hepatol. 2008;20:73-8.
15. Pañella H, Rius C, Caylà JA; Barcelona Hepatitis C Nosocomial Research Working Group. Transmission of

hepatitis C virus during computed tomography scanning with contrast. Emerg Infect Dis. 2008;14:333-6.
16. Silini E, Locasciulli A, Santoleri L, et al. Hepatitis C virus infection in a hematology ward: evidence for nosocomial transmission and impact on hematologic disease outcome. Haematologica. 2002;87:1200-8.
17. Massari M, Petrosillo N, Ippolito G, et al. Transmission of hepatitis C virus in a gynecological surgery setting. J Clin Microbiol, 39 2001;39:2860–2863
18. Martinez-Bauer E, Forns X, Armelles M, et al. Hospital admission is a relevant source of hepatitis C virus acquisition in Spain. J Hepatol, 2008;48:20–27.
19. Gerlach JT, Diepolder HM, Zachoval R, et al. Acute hepatitis C: high rate of both spontaneous and treatment-induced viral clearance. Gastroenterology. 2003;125:80-8
20. Wiegand J, Buggisch P, Boecher W, et al; German HEP-NET Acute HCV Study Group. Early monotherapy with pegylated interferon alpha-2b for acute hepatitis C infection: the HEP-NET acute-HCV-II study. Hepatology. 2006;43:250-6.
21. Hajarizadeh B, Grebely J, Dore GJ. Case definitions for acute hepatitis C virus infection: a systematic review. J Hepatol. 2012;57:1349-60
22. Simmonds P. Genetic diversity and evolution of hepatitis C virus--15 years on. J Gen Virol. 2004;85:3173-88
23. Jackowiak P, Kuls K, Budzko L, et al. Phylogeny and molecular evolution of the hepatitis C virus. Infect Genet Evol. 2014;21:67-82.
24. Magiorkinis G, Magiorkinis E, Paraskevis D, et al. The Global Spread of Hepatitis C Virus 1a and 1b: A Phylodynamic and Phylogeographic Analysis. PLoS Med. 2009; 6(12):e1000198
25. Spada E, Abbate I, Sicurezza E, et al. Molecular epidemiology of a hepatitis C virus outbreak in a hemodialysis unit in Italy. J Med Virol. 2008;80:261-7.

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