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Review

Hepatitis B in Albanian refugees across Southeast Europe: from epidemiology to vaccination and prevention policy

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SUMMARY

In 1991, a serious political and socioeconomic crisis in Albania caused a massive migration of refugees to Northwestern Greece (Ioannina region) and to the Apulia region of Southern Italy. Seroepidemiological data on viral hepatitis marker distribution of among refugees indicated a high HBV infection endemicity in these Albanian refugees. More updated epidemiological information on hepatitis B marker prevalence of the young, non-vaccinated Albanian population became available through the national Greek-Albanian collaborative study on prevention of viral hepatitis and hepatocellular carcinoma (known with the acronym as the HEPAGA study). This study showed that 11.89% of the tested Albanian group was HBsAg(+) while only 21.19% of the group were immunoprotected against HBV. A critical point for all countries to reach or fail to reach the 1997 WHO targets is their social and political commitment to preventive medicine and vaccines, besides their effort to inform and educate both the general public and medical societies. In Southeastern Europe, where acute and chronic HBV infection is a major health problem, selected risk-group vaccination policy will have no impact on this infection and will not be able to control further transmission from this HBsAg(+) young, carrier pool. In addition, the increasing number of immigrants from high to intermediate or low endemicity regions such as Greece and Italy forms a new dynamic epidemiology of hepatitis B transmission. Sustaining available vaccination programmes against HBV is one of the greatest challenges for the near future. Other challenges are increasing vaccine coverage, continuous support in order to maintain a sustainable supply of vaccine and other related facilities and, finally, to successfully monitor the effectiveness of currently implemented vaccination programmes.

Key words: Hepatitis B, refugees, epidemiology, vaccination, Albania, Greece

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1. EPIDEMIOLOGY OF HBV INFECTION IN ALBANIAN REFUGEES ACROSS SOUTHEASTERN EUROPE

Viral hepatitis still remains a major health problem throughout the world, as hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) represent some of the most important agents responsible for parenterally and sexually transmitted diseases.

It is well known that hepatitis B, C and D epidemiology varies by geographical area. Low (less than 2%), intermediate (2%-8%) and high prevalence (more than 8%) areas have already been characterized for hepatitis B. High endemicity areas include large parts of Asia and Sub-Saharan Africa, but hepatitis is also highly endemic in South America. In Eastern Europe HBsAg(+) prevalence rates ranging from 1%-5% in the Czech Republic to 7%-10% in Moldova, have already been reported.

In 1991, a serious political and socioeconomic crisis in Albania, a small Eastern European country, caused a massive migration of refugees to Northwestern Greece (Ioannina region) and to the Apulia region of Southern

Italy.[1] Seroepidemiological data on viral hepatitis markers indicated a high HBV infection endemicity in this Albanian refugee population[2-6] (Table 1). Refugees from southern Albania represent a new, young, immigrant population characterized by a high incidence of hepatitis B virus markers. This HBV status probably reflects the low socioeconomic status of this population and probably poor hygienic conditions. The high incidence of HBV and HDV infections in this immigrant population will, in the near future, probably increase the HBV prevalence in the whole area of Southeastern Europe. Thus, the main problems are waiting to emerge in the near future and will have a severe impact on the economy of the whole area. Studies in Northwestern Greece and Southern Italy provide evidence for higher prevalence of HAV, HBV and HDV infection markers in unselected but well-defined population groups of refugees from southern Albania compared to age and sex control groups of Greek and Italian nationality[2,3].

Recent epidemiological information on hepatitis B prevalence among the young, non-vaccinated Albanian population results from the national Greek-Albanian collaborative study on prevention of viral hepatitis and hepatocellular carcinoma (the HEPAGA study), which will shortly be described. Participants in this programme were the Hepato-Gastroenterology Unit, 1st Division of Internal Medicine, Medical School of Ioannina, the Blood Bank, University Hospital of Ioannina, the Department of Internal Medicine, General Hospital of Filiates in Greece and the Hepato-Gastroenterology Department, University Hospital "Mother Teresa", Tirana in Albania. The aim of the study was to screen for hepatitis B virus markers (HBV) in a well-defined, young population (aged from 14 to 20 years) in the area of Tirana in Albania. This study was conducted under the auspices and grants from the Greek Ministry of Development and the Albanian Ministry of Education and Science. This bilateral collaborative study lasted for two years (2001-2002) (see acknowledgment). Serum samples were collected during the period from September 2001 to February 2002 and were examined for HBV markers using routine methods. According this study 11.89% of the examined population was HBsAg (+) and only 21.19% of them had HBV immunoprotection (Table 2). In addition, approximately 10% of this population had serological evidence of previous HBV exposure. This study emphasized that treating and vaccination programmes for HBV infection must be quickly undertaken and further supported in the Albanian population.

According to other studies, the prevalence of HBV markers in Albanian refugees was higher compared to the previously reported HBV prevalence among alcoholics and heroin addicts, or even patients from high hepatitis endemicity areas in Europe[6-10]. These studies suggest that young refugees from southern Albania seem to comprise a group with high transmission risk of hepatitis B virus infection.

The prevalence of hepatitis virus infection was evaluated in several gropus of Albanian refugees in Southern Italy[3-5,11]. The Albanians who arrived in Italy

Table 1. Prevalence (%) of hepatitis A, B, C and D markers: age and sex distribution in Albanian refugees. M=male, F=female, N=total number of refugees HAV= hepatitis A virus, HBV=hepatitis B virus, HCV= hepatitis C virus, HDV= hepatitis D virus, Ag=antigen, Ab=antibody Anti-=antibody against-.Numbers in parenthesis represent upper and lower confidence intervals(confidence level of 95%) (adapted from Dalekos G, et al. Eur J Gastroenterol Hepatol, 1995:7:553-8)

AGE	**0-9**		**10-19**		**20-29**		**30-39**		**40-49**		**OVER 50**		**TOTAL**	
SEX	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**
N	**280**	**193**	**331**	**195**	**406**	**145**	**176**	**114**	**77**	**31**	**23**	**13**	**1293**	**691**
HBsAg	0.36	0.52	1.21	2.56	0.98	2.76	1.70	1.75	6.49	3.22	0.13	0	1.31	1.88
HBcAb	3.93	5.18	9.06	23.1	19.9	12.4	29	17.5	39	45.2		15.4	15.9	15.8
HBsAb	3.57	4.66	7.55	19.5	18.7	10.3	26.7	16.7	31.2	38.7	8.7	15.4	14.2	13.7
HBeAg*	0	0	0	20	0	0	0	0	0	0	0	0	0	7.7
HBeAb	3.93	5.18	9.06	21	12.3	9.6	19.9	13.2	6.5	6.5	8.7	15.4	10.3	12.2
Anti-HGV*	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Anti-HAV	2.13 (n=47)	0 n=35	1.53 n=65	1.39 n=72	39.8 n=181	36.7 n=49	63.3 N=79	85.4 n=41	82.1 n=39	92.3 n=13	92.9 n=14	85.7 n=7	39.8 n=425	33.2 n=217
Anti-HCV	0 (n=155)	0 n=110	0.41 n=245	0.71 n=140	0.34 n=295	0.95 n=105	0.67 n=150	0.88 n=945	0 n=513	0	0	0	0.32	0.58

*In HBsAg positive individuals

Table 2. Hepatitis B screening in young, non-vaccinated adults (13-20 years) living in a well-defined area of Tirana (period 2001-2002) (*results of the national Greek-Albanian collaborative study on prevention of viral hepatitis and hepatocellular carcinoma, the HEPAGA study*).

Parameter tested	Number of samples	%
Hepatitis B virus not detected	226	54.88
HBsAg (+)	49	11.89
HBcore(+)/anti-HBs over 10 UI/ml	87	21.19
HBcore(+)/anti-HBs less than 10 UI/ml	14	3.49
Only HBcore(+)	14	3.49
HBcore(+) not enough serum for anti-HBs	8	1.97
HBsAg(-) not enough serum for Hbcore	12	3.09
TOTAL	410	100.00

were, in the vast majority, young males from low socio-economic classes, and therefore they did not represent the whole Albanian population. However, the large number of subjects from different geographic areas (mountain, rural and metropolitan areas), who were enrolled in these studies, provides important information on the prevalence of hepatitis B virus infection in Albania, even though these results remain to be re-confirmed. In future studies, although the vertical and horizontal represent the main transmission routes, an important role in the high HBV endemicity in Albania could also be attributed to the use of non-disposable needles and syringes in medical and vaccination practice. In addition, hospitalization in Albania is associated with high risk of hepatitis B infection, due to poor medical and nursing practice[11].

Only six countries in Europe provided HBV-related prevalence data with respect to age distribution, however additional information needs to be obtained in order to better estimate prevalence and long-term consequences of hepatitis B carriage in Southeastern Europe.[1] In addition, attempts to estimate mortality due to hepatocellular carcinoma and cirrhosis attributable to hepatitis B infection have also been made using mathematic formula[12,13] (Table 3).

Although HBV surveillance systems vary in methods and completeness, the epidemiological pattern of disease is clear. In Western Europe, HBV prevalence rates vary from north to south. Southern countries have incidence rates of about 6 per 100,000 of population per year whereas northern countries such as Scandinavia, Ireland and the UK have much lower rates of about 1 per 100,000 of population. Central Europe has markedly higher incidence rates of about 20 per 100,000 per year.[14] Worldwide, the highest rates are found in the Central Asian Republics, where the rates reach 100 per 100,000 per year. However, mortality data on hepatocellular liver cancer diseases is not widely available. Hopefully, these data, together with data on hepatitis B prevalence in the general population of each European country may, in the near future, provide estimates of the number of deaths attributable to hepatitis B. These estimates, in correlation with other preventable causes of death, illustrate the importance of fighting hepatitis B in Europe.

2. HEPATITIS B PREVENTION POLICY IN SOUTHEAST EUROPE

Most countries have some form of selective vaccination policy, although targeted high risk groups vary markedly between countries. Only Albania, Bulgaria, France, Israel, Italy, Portugal and Spain have implemented national universal hepatitis B vaccination programmes[15]. A critical element for all countries to reach or fail to reach the 1997 WHO targets is their social and political commitment to preventive medicine and vaccines, besides the effort to inform and educate both the general public, and their medical societies.

Table 3. Preliminary mortality estimates per year of number of deaths from hepatocellular carcinoma and cirrhosis attributable to HBV infection in Europe. (adapted from C. Roure, Vaccine 1995;13:S18-S21).

European area	No. of deaths from cirrhosis attributable toHBV infection*	No. of deaths from hepatocellular carcinoma attributable to HBV	Total No. of deaths
Northwest Europe	160	40	200
Midwestern Europe	1700	450	2150
Southwestern Europe	2300	700	3000
Central & Eastern Europe	12500	6100	18600

*This formula takes into account the information from six European countries providing data as well as statistics published in the literature.

In Southeastern Europe where HBV acute and chronic infection represents a major health problem, selected risk group vaccination policy will have no impact on this infection and won't be able to control further transmission from young carrier pools. In addition, increasing numbers of immigrants from high or even intermediate endemicity regions, such as Albania, contribute to the increasing prevalence of hepatitis B in low endemicity countries, such as Greece and Italy.

Economic evaluations have shown that universal hepatitis B vaccination is relatively cost-effective in high and low-endemicity countries compared with other health care interventions, and suggest that control of hepatitis B by universal immunization is attainable[16].

While, many European countries have performed economic evaluation studies in an effort to guide decision-makers in their hepatitis B prevention policy; others have initiated sero-epidemiological surveys to generate input data for burden of disease calculations. Some countries have improved their surveillance systems and include viral hepatitis in their surveillance programmes (Table 4).

HBV infection is usually acquired early in life, as observed in countries with high HBV infection endemicity. Maternal-infant transmission, from HBsAg-positive mothers to their babies, may represent an important factor leading to HBV spread during childhood; thus HBsAg screening in pregnant women could further confirm this possibility (Tables 5, 6). Alternatively, HBV infection may be acquired from other infected family members, or from non-family members;the highest carrier rate being observed among males (Table 7).

An important mode of secondary HBV transmission could be obligatory vaccination campaigns because of the lack of disposable syringes and needles, as happened in Albania some years ago. In chronic anti-HBe carriers with compensated liver disease, the absence of HBeAg may be due to infection with HBV pre-Core mutants. Furthermore the presence of anti-HBe antibodies and the absence of HBeAg in serum is highly prevalent in HBV carriers in Southeastern Europe. However, this HBV serological profile does not implicate absence or low levels of viral replication and subsequent lower infectivity.

Serological data from the young, Albanian population (the HEPAGA study} clearly indicated the need for urgent measures to reduce the incidence of HBV infection, as well as to avoid the further spread of other blood-borne viruses.

In order to achieve these goals, it is mandatory that help from European countries be mainly directed towards a specific educational campaign illustrating the use of simple and inexpensive hygienic measures[17,18]. In addition, basic medical equipment (needles, syringes, surgical gloves) should be immediately supplied. Finally, in any case when sero-epidemiological studies report on a high prevalence of HBV in any European region, supportive and additional preventive programmes must be immediately supported[19].

Table 4. European Survey on hepatitis B surveillance and prevention programmes-2000. (Adapted from Van Damme P. Vaccine 2001;19: 2375-9).

Country	Active surveillance	Screening of pregnant women	Universal HBV vaccination policy	Coverage 1999	HB vaccination risk group policy
Albania	Y	N	Neonates, 1994	92.9%	N
Belgium	Y	Y	Infants, 1999, Adolescents, 1999		Y
Belarus	Y	N	Neonates, 1/5/1999 Adolescents, 1998		Limited number of groups
Bosnia and Herzegovina	Y	Selective	Infants, 1999 (+ booster)	85%	Y
Czech Republic	Y	Y	N		Y
Denmark	Y	Selective	N		Y
Form. Yog. Repub.	Y	Selective	N		Y
FYROM	Y	Y	Neonates, 1997 Adolescents, 1999		Limited
Estonia					
France	Y	Y	Infants, 1994-1995, Adolescents,		Y

Table 5. Prevalence of Hepatitis A & B markers in 500 pregnant Albanian refugees. (Adapted from Malamitsi-Puchner A. et al. Eur J Epidemiol 1996;12:297-301)

Hepatitis markers	No (+ve)	%	95% C, I,
Anti-HAV	481	96.2	94.5-97.9
Anti HAV IgM	5	1.0	0.1-1.9
Total anti-HBe	354	70.8	66.8-74.8
Anti-HBc IgM	2	0.4	0.0-1.0
HBsAg	67	13.4	10.4-16.4
Anti-HBs	255	53.0	49.0-57.0
HBsAg	6	1.2	0.3-2.1
Anti-HBe	293	58.6	54.6-62.6
Anti-HBV markers	365	73.0	69.0-77-0
Anti-HDV	2	0.4	0.0-1.0

A questionnaire on hepatitis B policy was sent to the communicable disease counterparts of the 50 ministries of health in the countries of this WHO European region. The questionnaire was sent to every country to obtain information on surveillance systems, mode of case notification, and incidence of acute hepatitis B over the past five years (i.e. 1988-1992), as well as estimates of the prevalence of hepatitis B carriage and infection in the general population and in specific age groups.[20] Information was also requested about immunization policy and screening of pregnant women. At the time of publication the questionnaire had so far been returned by 29 countries, covering about 80% of the total population of the European region of WHO.

Of the 29 responding countries, nine were using standard case definition of hepatitis B and cases were notified either by clinicians or by general practitioners. In 17 countries, there is a dual system, combining notification by physicians and laboratory confirmation. There are still many European countries including Greece, Italy and Albania with no dedicated notification system for hepatitis B (Table 8).

To summarize, four main lines of action are recenavy: the development of a modern HBV surveillance system, the need for continuous information and education of the general public and medical societies, planning towards a social commitment to preventive medicine on hepatitis across Southeast Europe and finally, urgent occupational risk assessment (high-risk groups: drug users, homosexuals, dialysis patients, household contacts, clinic attendees, etc.).

We, therefore, believe that rigorous adherence to general precautions and the initiation of universal and obligatory hepatitis B vaccination programmes will be necessary in future, both in our area (Greece) and in Albania.

3. PREVENTIVE HEPATOLOGY ACROSS EUROPE: VACCINATION PROGRAMMES FOR HEPATITIS B

Sustaining the already existing vaccination programmes across European countries is one of the great challenges for the near future in Preventive Hepatology. Other challenges which still remain are increasing vaccine coverage, the maintenance of a sustainable supply of vaccine and other related facilities, and the assistance of currently implemented vaccination programmes. Hepatitis B is a major public health problem and remains an important and highly prevalent community infection, despite the availability of safe and effective vaccines for almost last 20 years.

Since hepatitis B infection is largely asymptomatic with possible long-term complications occurring after many years, it has not received the attention it deserves. The failure of the high-risk group immunization strategy and the better understanding of the burden of hepatitis B disease, have lead to a profound re-evaluation of the current vaccination strategies.

In 1993, four countries in the WHO European region implemented universal immunization programmes against hepatitis B[1,15,16]: Bulgaria, Italy, Israel and Spain. In Italy, in 1991, a law was passed establishing mandatory immunization of neonates and 12-year-old children. The latter were to be immunized only during the first 12 years of the law's application; after this period only infants continue to be vaccinated. Compliance with vaccination in infants was studied in seven Italian regions through a survey based on the cluster sampling method of the Expanded Program on Immunization (EPI). The first data in 1993 showed good coverage results: the completed immunization course ranging from 60.9% in Tuscany to 92.2% in Lombardy. In Spain, in 1991 the autonomous region of Catalonia embarked on a universal immunization programme targeted at 12-year-old children. Six other autonomous regions introduced adolescent vaccination programmes in 1992; in 1993, 10 of the 17 autonomous regions in Spain had implemented programmes of universal hepatitis B vaccination of young adolescents (12-year-olds). By November 1993, these 10 regions covered 52% of the 12-year-olds in Spain. After one year of programme implementation, the vaccination

Table 6. Prevalence of Hepatitis A & B and correlation with socioeconomic status in pregnant women form Albania (Adapted from Malamitsi-Puchner A. et al. Eur J Epidemiol 1996;12:297-301).

		Anti-HAV			Hepatitis B		
		(+) no=481	(-) n=19	*P*	n=365	(-) n=135	*P***
age (x±SD) years		25.2±4.6	23.7±5,8	0.10	25.2 ± 4,6	24.8 ± 4.7	0,38
Number persons/rooms							
(X±SD)		2,9±1,1	3.2±2,1	0,26	2.9 ± 1.1	2.9±1.2	0.79
(x±SD)		4,0±3,5	2.9±2.5	0,24	3.9±3.4	4.8±3.7	0.29
Education (x±SD) years		11.9±2,5	12.2±2.6	0.66	12,0 ± 2.4	11.8±2.7	0.32
Place of living							
South Albania		290	9		220	79	
Other		191	10	0.26	145	56	0,72
National origin							
Greece		367	12		278	101	
Albania		114	7	0.19	87	34	0,75
Vaccination with commonly used needles		481	19	1.00	365	135	1.00
Hospitalization*	YES	91	1	0.1	77	15	0.01**
	NO	389	18		287	320	
Surgery*	YES	49	1	0.41	36	14	0.87
	NO	431	18		328	121	
Abortions*	YES	3S	0	0.24	24	11	0.55
	NO	445	19		340	124	
Pregnancies*	YES	120	3	0,27	97	26	0.08
	NO	360	16		267	109	
Rersonal History of	YES	56	1	0.3	49	8	0.02**
hepatitis	NO	418	18		310	126	
History of hepatitis	YES	79	8	0.005*	59	28	0.26
In parental house	NO	381	11		289	103	
History of hepatitis	YES	40	5	0,01**	31	14	0.48
In marriage house	NO	347	9		263	93	

* In Albania, ** Statistically significant

Table 7. Countries with a selective vaccination policy for adults (adapted from C. Roure, Vaccine 1995; 13(Suppl 1):S18-S21).

Risk group	No. of countries	Percentage
Drug users	14	48
Homosexuals	9	31
Clinic attendees	2	7
Dialysis patients	19	66
Occupational groups	22	76
Household contacts	14	48

coverage varied between 73% and 96% in the participating autonomous regions. In Bulgaria, in August 1991, the Ministry of Health decided to administer HB vaccine to all new-born, through a mandatory universal HB vaccination programme. The immunization coverage increased from 71.3% in 1992 to 97% in 1998 and 1999. These coverage rates are comparable with those of infant immunizations in other countries. Israel started a universal hepatitis B immunization programme for neonates in 1989.

The carrier rate has been reduced worldwide from over 8% to less than 2% in immunized cohorts of children in high-endemicity regions. Since the introduction of routine hepatitis B vaccination in the Alaska native population in 1981-1982, the incidence of acute hepatitis

Table 8. Southeast European countries with a universal hepatitis B immunization program and vaccination program coverage rates. (Adapted from P. Van Damme, et al. Vaccine 1998; 16:S3-S6 & P. Bonanni P. Vaccine 1998; 16:S58-S60).

Country	Screening pregnant	Universal infant immunization	Schedule	Estimate coverage	Universal Adolescent immunization	Estimate coverage
Greece	YES	Started	0, 1, 6 or 2, 4, 6, 16	90%	Started 1998 11yr adolescents	Data not available
Italy	YES	Started	3, 5, 11	90%	Started 1991 12yr adolescents	80-90%
Albania	NO	Started	0, 1, 6 or 2, 4, 6, 16	Data not available	Data not available	Data not available

B has fallen by over 98% and over a period of at least 10 years no new carriers have been detected.

Ten years after implementation of a mass vaccination program in Taiwan, which started in July 1984, the average annual incidence of hepatocellular carcinoma in children (6-14 years) has dropped significantly from 0.70 per 100 000 children between 1981 and 1986 to 0.36 between 1990 and 1994.

As of mid 2000, more than 116 countries worldwide have included hepatitis B vaccine as part of their routine national infant or adolescent immunization programmes. This represents more than 30 of the 51 countries in the WHO European region. In Western Europe, Andorra, Austria, Belgium France, Germany, Greece, Italy, Luxembourg, Malta, Monaco, Portugal, San Marino, Spain, Switzerland and Turkey have their programmes in place[1]. Some other European countries, like the Netherlands, are seriously studying the same issue or are making budgetary provisions for introduction of HB into their vaccination programmes.

In central and eastern Europe and the Newly Independent States, Albania, Belarus, Bulgaria, Estonia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Poland, parts of the Russian Federation, Romania, Slovakia, Slovenia and Uzbekistan have included hepatitis B vaccination in their national immunization programmes. Armenia, the Czech Republic, FYROM, Hungary, the Russian Federation, an the Ukraine are making serious progression towards the implementation of universal HBV immunization. In Western Europe, universal HBV immunization programmes in Spain and Italy have proved to be highly efficacious. A universal infant immunization policy was initially implemented in seven countries: Albania, Bulgaria, Israel, Italy, France, Portugal and Spain; many others followed. Among the countries in the WHO European region, Uzbekistan started to implement this policy, but for financial reasons has had to suspend its program. Latvia also intends to implement universal vaccination from the beginning of 1994, provided funds are available. Recently, countries such as Romania plan to introduce the universal infant immunization strategy into their national immunization programmes.

However, any realistic attempt to eradicate HBV will require reconsideration of previous less effective vaccination strategies and international co-operation on a global scale. In this perspective, a co-ordinated effort will be required to support those countries lacking financial resources to procure the vaccine and to maintain effective vaccination programs. We should, therefore, start thinking about new ways of delivering hepatitis B vaccines to those areas that seem to need it most. Preventive Hepatology is now in view with the prospect of controlling and possibly eliminating one of the major health threats to mankind - hepatitis B.

In 2001, Italy celebrated its 10-year infant and adolescent hepatitis B immunization programme, and will be able to end the adolescent programme as the first immunized infant cohort will have reached the target age of the adolescent programme. As a consequence of this 10-year effort, direct and indirect programme and logistics costs can be substantially reduced and savings can be allocated to other healthcare purposes.

In conclusion, in certain areas of Southeastern Europe (Greece, Italy and Albania), according to all available emerging literature (Tables 9, 10) and WHO reports[1,15,16], HBV infection represents a public health priority that should be addressed by nationwide epidemiologic and vaccination programs. Finally, a surveillance system for viral hepatitis should be set up to monitor the trend of acute viral hepatitis B, cirrhosis and hepatocellular carcinoma and to evaluate the impact of such a vaccination programmes on public health.

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REFERENCES

1. Roure C. Overview of epidemiology and disease burden of hepatitis B in the European region. Vaccine 1995; 13(Suppl. 1):S18-S21.
2. Dalekos GN, Zervou E, Karabini F, Tsianos EV. Prevalence of viral markers among refugees from southern Albania: increased incidence of infection with hepatitis A, B and D viruses. Eur J Gastroenterol Hepatol 1995; 7:553-558.
3. Chironna M, Germinario C, Lopalco PL, Quarto M, Barbuti S. HBV, HCV and HDV infections in Albanian refugees in Southern Italy. Epidemiol Infect 2000; 125:163-167.
4. Da Villa G, Nuri B, Ghisetti V, et al. Epidemiology of hepatitis B and delta virus infection in Albania: an approach to universal vaccination. Res Virol 1995; 146:245-248.
5. Santantonio T, Lo Caputo S, Germinario C, et al. Prevalence of hepatitis virus infections in Albanian refugees. Eur J Epidemiol 1993; 9:537-540.
6. Papaevangelou C, Kyriakidou A, Vissoulis L, Trichopoulos D: Seroepidemiological study of HBV infections in Athens, Greece. J Hyg Camb 1976; 76:229-234.
7. Kelen CD, Green CB, Purcell RH, et al. Hepatitis B and hepatitis C in emergency department patients. N EngI J Med 1992, 326:1399-1404.
8. Mendenhall CL, Seeff L, Diehl AM, et al. Antibodies to hepatitis B virus and hepatitis C virus in alcoholic hepatitis and cirrhosis: their prevalence and clinical relevance. Hepatology 1991; 14:581-589.
9. Hadziyannis SJ, Hatzakis A, Papaioannou C, Anastassakos C, Vassiliadis E. Endemic hepatitis delta virus infection in a Greek community. In The Hepatitis Delta Virus and its Infection. Edited by Rizzetto M, Cerin JL, Purcell RH. New York: Alan R. Liss 1987:181-202.
10. Tassopoulos NC, Kyriakis P, Saggana E, Limotirakis F, Papaioannou C, Hadziyannis S. Impact of socioeconomic changes on the prevalence of HBV infection in an endemic area. J Hepatol 1987; 5(suppl 1):209.
11. Kondili LA, Tosti ME, Szklo M, et al. The relationships of chronic hepatitis and cirrhosis to alcohol intake, hepatitis B and C, and delta virus infection: a case-control study in Albania. Epidemiol Infect 1998; 121:391-395.
12. Nalpas B, Driss F, Pol S, el at. Association between HCV and HBV infection in hepato-cellular carcinoma and alcoholic liver disease. J Hepatol 1991; 12:70-74.
13. Beasley RP: Hepatitis B virus. The major etiology of hepato-cellular carcinoma. Cancer 1988; 61:1942-1956.
14. Van Damme P, Verwimp G.From Cannes 1993 to the present. Vaccine 1998; 16(Suppl):S3-S6.
15. Bonanni P. Report on Working Group 1: Albania, Andorra, Canada, France, Italy, Moldova, Portugal, Poland, Romania and Spain.Vaccine 1998; 16(Suppl):S58-S60.
16. Van Damme P. Hepatitis B: vaccination programmes in Europe-an update. Vaccine 2001; 19:2375-2379.
17. Smith A, O'Flanagan D, Igoe D, et al. Outcome of medical screening of Kosovan refugees in Ireland: 1999. Commun Dis Public Health 2000; 3:291-294.
18. Adhami JE, Angoni R. Hepatitis E virus infection in Albania. Sante 2001; 11:13-15.
19. Maynard JE. Hepatitis B vaccine: strategies for utilization. In Hepatitis B vaccine. Edited by Maupas P, Quesry P. Amsterdam: Elsevier/North Holland, Biomedical Press; 1981:13-19.
20. Malamitsi-Puchner A, Papacharitonos S, Sotos D, et al. Prevalence study of different hepatitis markers among pregnant Albanian refugees in Greece. Eur J Epidemiol 1996; 12:297-301.