VIRAL HEPATITIS

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CONTENTS

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March 24-25, 2011

Editorial

This issue of *Viral Hepatitis* focuses on topics covered at the VHPB's country meeting on the "Burden and prevention of viral hepatitis in Bulgaria", held on 24-25 March 2011, in Sofia, Bulgaria.

At this "country meeting" speakers provided an overview of surveillance for infectious diseases and reviewed the epidemiology of viral hepatitis. Participants discussed progress in prevention nearly 20 years after the introduction of universal vaccination against hepatitis B - Bulgaria was one of the first countries to introduce universal newborn vaccination against hepatitis B. The meeting also aimed to review implementation of new prevention strategies, control measures and monitoring systems, and identify the successes, the way forward and possible obstacles.

The meeting followed closely on a high-level European Union conference entitled "For a healthy future of our children – childhood immunization"(http://ecdc.europa.eu/en/activities/diseaseprogrammes/vpd/Pages/index.aspx), held three weeks earlier in Budapest, which looked at the impact of childhood immunization across the European Union and ways to improve collaboration within the Union on childhood vaccination strategies, especially to reach vulnerable under-vaccinated populations. It also reviewed cross-border issues related to childhood immunization, discussed the strategies for vaccinating mobile and hard-to-reach children.

General European themes covered by this Budapest meeting found national echoes in the VHPB meeting. Challenges to achieving full immunization coverage included inaccuracies or incompleteness in the recorded data and the fact that segments of the population were missed - groups that were culturally or religiously marginalized (in Bulgaria the main group is Roma, who also are separated by language barriers), and unregistered people. Ensuring protection for health-care professionals is another major issue. The segment of the urban affluent who reject vaccination does not (yet) seem to exist in Bulgaria. Data on vaccine coverage share the same objective, but differences are seen across the European Union in methodology, validation, availability of computerized registers, information collected, data format, ages covered and performance indicators.

The solutions proposed at the European level apply equally in Bulgaria: seroprevalence surveys, population-based surveys, and triangulation of data (for instance through information on vaccine procurement and management, and the use of vital statistics). Data handling could be harmonized at the European level by adoption of standardized reporting systems (for instance, use of the WHO/UNICEF Joint Reporting Form on immunization) and facilitated (in terms of both collection and feedback) through greater use of Internet-based reporting systems. The VHPB meeting underlined the importance of the quality control and representativeness of data, better analysis and interpretation of the data, and the application of the results in policy-making. Furthermore, occupational health and safety with special emphasis on vaccination coverage of health-care workers deserves more attention in many health-care facilities.

Repeat seroprevalence surveys are proposed in Bulgaria, and it is to be hoped that consideration will be given to issues such as the format and methodology for data collection and better analysis and communication of the results.

Two opportunities present themselves shortly for raising awareness about viral hepatitis and immunization: European Immunization Week (23-30 April 2011) and World Hepatitis Day (28 July). Both will enable the dissemination of information on the benefits and safety of vaccines, increasing the demand for vaccines and advocating political support and financial commitment.

Reaching vulnerable groups and under-vaccinated populations often depends on the context, meaning that tools have to be tailored or specifically designed and created, responses need to be shaped for local levels, demand has to be stimulated and access to health-care services provided. One best practice that has been identified at the European level is Bulgaria's use of the health mediator concept to reach Roma populations. This work has been a model of preparation and delivery, involving not just the health sector but several other areas as well, including the Church, municipal authorities and volunteers.

The health mediator concept needs to be expanded. At present more than 100 people have been trained and certified as mediators in Bulgaria, but it is estimated that at least 4000 are needed to reach all vulnerable and hard-to-reach groups and successfully deliver vaccination. Bulgaria has also facilitated the approach by enacting a large raft of legislative public health measures, ranging from surveillance of communicable diseases to protection of health-care workers. There are lessons to be learnt by other countries in the Union facing similar problems.

Mira Kojouharova and Johannes Hallauer
on behalf of the Viral Hepatitis Prevention Board

Burden and Prevention of Viral Hepatitis in Bulgaria, Sofia, Bulgaria, 24-25 March 2011

Background statistics and legislation: Bulgaria

Population: 7,504,868 as of 31 December 2010*
(Bulgarians 83%, Turks 9%, Roma 3%, others 5%)
Area: 111,000 km^2 (between Iceland and Greece in size)
GDP per capita: €4787 (2010)
Health expenditure per capita: US$269 (equivalent) (2009)
Birth rate: 10.0/1000 population (2010)*
Death rate: 14.6/1000 (infant mortality rate: 9.4/1000) (2010)*
Life expectancy: 73.58 years (male 70.00 yr, female 77.24 yr - both for 2008-2010)*
Hospitals: 306 (2009), including sole joint ventures 100% owned by the Ministry of Health, regional hospitals (joint ventures between regional authorities and municipal authorities) and municipal hospitals (100% owned by the municipalities)
Hospital beds: 48,000 (6.35/1000 population); 78% occupancy rate; 6.2 day length of stay (2009)
Health-care personnel: physicians, 27,998 (2009, 37/10,000); GPs, 5210, 6.5/10,000; nurses and others, 48,099, 63.6/10,000

(All data based on presentations given at the meeting or
** National Statistical Institute, http://www.nsi.bg/)*

Some recent legislation and regulations

Year	Action
1988	Selective hepatitis B immunization of newborns from HBsAg-positive mothers
1991	Universal vaccination of all newborns against hepatitis B (introduced in August)
1992	Start of routine, universal hepatitis B vaccination of newborns
1999	Framework Programme for the Equal Integration of the Roma in Bulgarian Society
2002	Establishment of the Expert Committee on Epidemiological Surveillance, Immunizations and Communicable Disease Control
	Regulation No 4 of 14 October 2002 for protection of workers from risks, related to occupational exposure to biological agents; issued by the Ministry of Labour and Social Policy and the Ministry of Health, promulgated in *State Gazette* No 105 of 8 November 2002, entry into force 9 February 2003
2003	Law on waste management, promulgated in *State Gazette*, No 86 of 30.09.2003, last amendment State Gazette, No 33, 26 April 2011
2004	Ministry of Health Order No RD 09-693 of 25 August 2004 for approval of the Guideline for protection of the medical staff from infection with the human immunodeficiency virus, hepatitis B and hepatitis C virus in medical and health institutions. *Ministry of Health Official Bulletin*, No 9, May 2005
	Ministry of Health Order No RD 09-694 of 25 August 2004 for approval of the Guideline for post-exposure prophylaxis of the medical staff for hepatitis B, hepatitis C and infection with human immunodeficiency virus. *Ministry of Health Official Bulletin*, No 9, May 2005
2005	Law on health, promulgated in *State Gazette*, No 70 of 10 August 2004, in force from 1 January 2005: • Chapter II – Health Protection Activities, section 5, Communicable disease control, Articles 57-63 • Chapter III – Medical Services, section 1, Accessibility and quality of health care, Article 82
	Regulation No 2 of 10 January 2005 on the organization of prevention and control of hospital acquired infections, issued by the Ministry of Health, promulgated in *State Gazette* No 8 of 21 January 2005
	Regulation No 15 of 12 May 2005 on the immunisations in the Republic of Bulgaria, promulgated in *State Gazette* No 45 of 31 May 2005
	Regulation No 21 of 18 July 2005 on the procedure for registration, notification and reporting of communicable diseases, promulgated in *State Gazette* No 62 of 29 July 2005
	Health Strategy concerning People in Disadvantaged Position belonging to Ethnic Minorities
2007	Medical Devices Law, promulgated in *State Gazette* No 46 of 12 June 2007, amended in *State Gazette* No 110 of 30 December 2008 and *State Gazette* No 82 of 16 October 2009
2010	Law for healthy and safe labour conditions, promulgated in *State Gazette* No 124 of 23 December 1997, last amendment in *State Gazette* No 12 of 12 February 2010
	Regulation No 39 of 26 August 2010 for approval of medical standard on prevention and control of health-care-associated infections; issued by the Ministry of Health, promulgated in *State Gazette* No 69 of 3 September 2010

Heath-care system

Organization and funding of the health system

Reforms in the 1990s led to wide-ranging changes in health-care organization, financing and delivery, with the reorganization and decentralization of the main functions of the health system, so that the Ministry of Health and its 28 decentralized regional Health-care centres develop and implement comprehensive national health programmes. Funding switched to a system based on payroll contributions [1]. The National Health Insurance Fund administers the compulsory health insurance system, raising revenue (through contributions from employers and employees), allocating resources and governing health-care providers through a national framework contract. The Ministry defines the country's health policy. Besides the 28 regional health inspectorates there are four National Centres including those on Infectious and Parasitic Diseases, Health Informatics, and Public Health. A separate department and directorate supervise surveillance of communicable diseases.

Overall, financing of public health services remains centralized, through taxes and compulsory health insurance contributions (amounting to 8% of an individual's income) into the National Health Insurance Fund (with operational activities decentralized), and formal and informal cost-sharing. Less than 2% of the population has opted for private health insurance. Individuals also make direct out-of-pocket payments for health care. As nearly 13% of the population have not paid insurance contributions, financing of health service coverage of the unemployed and the poor also comes from both central and local budgets; funding for the coverage of pensioners, students, civil servants and military personnel similarly comes from those sources.

General practitioners control access to specialist outpatient and hospital care. Outpatient care is provided by single and group practices, medical centres and independent diagnostic centres, and is financed on a per capita and fee-for-service basis by the National Health Insurance Fund. For most treatments and procedures co-payments are made, with patients being charged a flat rate for services. User charges are paid for each visit to a general practitioner, a specialist, a health diagnostic laboratory or a hospital for the use of services covered by the Insurance Fund. They amount to 1% of the minimum monthly salary per outpatient visit and 2% of the minimum monthly salary per day of stay in hospital, up to 10 bed-days per year. Moreover, cost-sharing applies to outpatient medicines, except for those for treatment of chronic diseases, and concerns all patients, except for some defined vulnerable social groups (including children, unemployed, people with salary below a given threshold, and the chronically ill). Many patients (up to 50% according to some surveys) report making informal payments in order to decrease the waiting time for services, to access a specialist without waiting for referral by a general practitioner, or to secure better conditions or better service quality in hospitals.

Inpatient care is provided by general and specialized hospitals, dispensaries, nursing homes and hospices, and hospitals providing acute, chronic, long-term care and rehabilitation. Access to such care is easy, and the waiting list is practically non-existent. The average length of stay in hospitals (6.2 days) is shorter than in most countries in the WHO European Region. Hospitals fall into the categories of sole joint ventures when they are 100% owned by the health ministry, joint ventures when ownership was shared between regional and municipal authorities, and sole legal entities when 100% owned by municipal authorities. Private hospitals exist but provide only a small number of the total of hospital beds. All public hospitals have signed contracts with the Fund. Some hospitals have signed contracts with the Fund for highly specialized activities that are paid on fee-for-service basis. The Ministry of Health covers the costs of haemodialysis centres, psychiatric hospitals, transplantation units, emergency care, expensive drugs, and similar expenditures.

Private hospitals also have signed contracts with the National Health Insurance Fund for clinical services or highly-specialized activities.Whereas physicians and centres contract with the Fund to provide statutory services, other providers can charge fees for private services.

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[1] Georgieva L, Salchev P, et al. Bulgaria: Health system REVIEW, 2007. Health System review;9(1):156.

Based on a presentation by
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Communicable disease surveillance

Several regulations from 2005-2006, including a new State law on health, have created a solid legal framework for surveillance, prevention and control of communicable diseases in Bulgaria. The list of notifiable diseases was expanded to 60. Although the list includes both acute and chronic viral hepatitis, reporting of the latter has not been a success and only acute disease will be covered in the future. The case definitions to be applied for reporting are those laid down by the European Commission in 2002. The procedures for notification and reporting of communicable diseases and outbreaks have been defined in the State's Regulation № 21 of 18 July 2005 on the procedure for registration, notification and reporting of communicable diseases and the Law on health, which came into force from 1 January 2005. (Since the meeting, Regulation No 21 has been revised and amended (8 July 2011) and the European Union case definitions of 2008 are to be applied). The list of notifiable diseases has been expanded to 62. Guidelines for investigation and management of cases and contacts were issued and different reporting forms have been designed.

The most important part of the surveillance system is the first, or peripheral, level (see Figure next page). Notification is done by general practitioners, private physicians, laboratories, outpatient and health centres, specialized health-care facilities, and hospitals; all these parties are responsible for identifying cases

and completing and sending forms within 24 hours to one of the 28 regional health inspectorates. Reporting is done by mail, telephone, e-mail or fax.

These regional health inspectorates (RHI) undertake epidemiological investigations of outbreaks and contact tracing, collect reports and send aggregated data to the central level: the National Centre for Health Informatics (NCHI), the National Centre of Infectious and Parasitic Diseases (NCIPD) and the Ministry of Health (for outbreak information). Reports are submitted on a daily, monthly and annual basis. In addition, they provide feedback to the peripheral level. Besides mail, e-mail and fax, they use web portals, the internet-based technology being introduced a few years ago for influenza surveillance. They also are responsible for liaising with local media. Computerized data processing, analysis and interpretation are done at the central level, and data are fed into international data systems such as the European and WHO surveillance systems. Outbreaks and other events of public health importance are clearly defined at the upper levels of the information process. Results are issued weekly and annually through a variety of outputs, including the media.

Increasing use is being made of the Internet as a vehicle for information exchange. The National Centre of Infectious and Parasitic Diseases publishes on its website (http://www.ncipd.org/?news=disease) its weekly epidemiological bulletin and surveillance data on influenza and acute respiratory infections [1]. Greater use of such applications is planned for the future.

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[1] *Bulgarian weekly epidemiological bulletin and surveillance data on influenza and acute respiratory infections. Available at: http://grippe.gateway.bg/lab.php (Accessed 7 September 2011).*

Based on a presentation by
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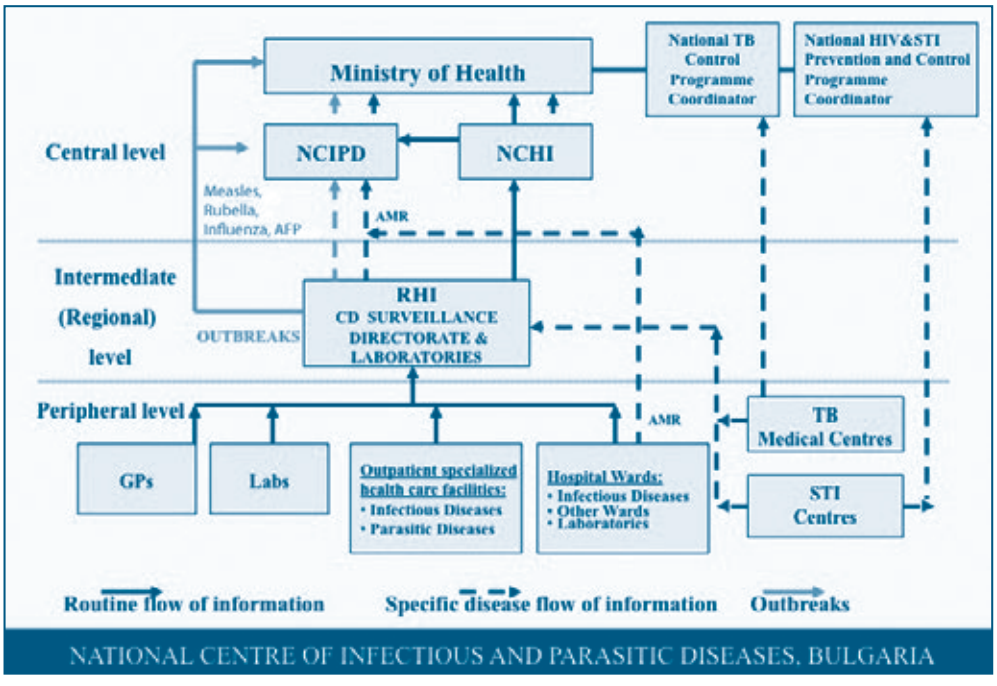
National immunization programme

The legal framework for the prevention and control of communicable diseases dates back to the introduction of compulsory immunization against smallpox in 1897 and a law on protection of public health enacted in 1903, when notification of tuberculosis, diphtheria, pertussis, measles and mumps became mandatory. Subsequent legislation regulated the introduction of compulsory immunization programmes, although no formal written national immunization programme existed.

The registration of acute viral hepatitis (all types together) in Bulgaria was introduced in 1952 and complete information is available since 1955. In 1983 the separate registration of acute cases of hepatitis A, hepatitis B and (as it was then called) non-A, non-B hepatitis was begun. Hepatitis B vaccination was introduced in 1991.

In 2005 the Health Law was completely revised, but it retained the specification of prevention and control of communicable diseases through immunization, including the definition of schedules, target groups, vaccine characteristics, and establishment of an expert committee to provide advice to the health minister about national immunization policy. In cases of outbreaks, the Minister of Health is empowered to introduce additional vaccination programmes, including vaccines not in the immunization calendar and other extraordinary measures. Regulation 15/2005 specifies compulsory immunization against 11 communicable diseases, and also authorizes targeted vaccination programmes for those professionally at risk against rabies, typhoid and Crimean-Congo haemorrhagic fever.

Flow of information for communicable disease surveillance in Bulgaria. Based on a presentation by Professor Mira Kojouharova



The overall immunization schedule and specific type of vaccine to be used have been changed many times, and the example of mumps illustrated the complexity of the situation. Routine immunization was stopped for four years before being restarted in 1986. In 2001 the dose schedule was increased to two doses at 13 months and 12 years in order to ensure coverage of all the population, including those at risk because of earlier practices and schedules, and in 2004 the more immunogenic Jeryl Lynn virus strain was used in MMR vaccines. Vaccines without mercury-containing preservatives for use in children up to the age of 6 months were introduced in 2005. Other recent developments include the replacement of oral poliovirus vaccine with inactivated vaccine and reduction of doses from six to five in 2007 and change to acellular DTP vaccine in 2009.

A special provision of the Regulation 15/2005 allows recommended vaccination of people in other age groups than those covered by the immunization calendar, and vaccines against: yellow fever, meningococcal infections, influenza and human papillomavirus infection. These vaccinations are, however, voluntary, and the vaccines and their administration have to be paid for by the individual.

Compulsory health insurance was introduced in 2000 but recognition that some marginalized groups were not reached led to revised legislation in 2002 in order to ensure access of all children up to the age of 16 years to medical care, including immunization, irrespective of whether the families had paid health insurance contributions. Vaccinations under the Expanded Programme on Immunization are mandatory and free of charge for the parents. Successful coverage depends, however, on parents being aware and supportive of the goals of vaccination programmes.

Except for vaccinations given at birth such as administration of hepatitis B vaccine, general practitioners are the main providers of immunization services. They have annual contracts with the National Health Insurance Fund and are responsible for the planning and performance of vaccine administration and the registration and reporting of data thereon. The regional health inspectorates also provide immunization services. The Ministry of Health plans and procures vaccines and syringes for use at national and regional levels, and monitors performance. Funding comes from the global State budget as well as from the health ministry and regional authorities.

The development and introduction of multivalent vaccines put new pressures on the immunization calendar. New means need to be found to extend coverage to underserved groups and to deal with outbreaks such as the recent measles epidemic. Further, different mechanisms have to be found for reimbursing the costs of vaccines against diseases of high public health importance (besides influenza, others are also under consideration) that are currently only recommended.

Based on a presentation by
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Health-care policy for vulnerable groups, especially Roma

In 2004, the National Council for Cooperation on Ethnic and Demographic Issues was established, under the chairmanship of the Deputy Prime Minister, as the governmental body in charge of coordination and consultation of minority issues and of the general regular monitoring of the implementation of the integration policies. Its membership includes representatives of the Government and civil society, particularly organizations of ethnic minorities. Its purpose is to influence governmental decision-making. The Council gained considerable experience in formulating, implementing and coordinating various international projects and programmes financed by the European Union.

The health-care reforms in Bulgaria brought to light some alarming features of the health status of the Roma population: high morbidity, high mortality and low life expectancy. Infectious diseases, with high prevalence rates in particular of tuber-

Bulgarian immunization calendar

Age	At birth	1 mo	2 mo	3 mo	4 mo	6 mo	7 mo	12 mo	13 mo	16 mo	6 yr	7 yr	11 yr	12 yr	17 yr	>25 yr (every 10 yr)
BCG	●						(●)[2]					(●)[2]	(●)[2]		(●)[2]	
Hep B	●	●				●										
DTPa, IPV, HIB			●	●	●					●						
Pneumo			●	●	●			●								
MMR									●					●		
DTPa, IPV											●					
Td														●	●	●

()[2] indicates absence of tuberculin sensitivity.
(BCG: Bacillus Calmette-Guérin; Hep B: hepatitis B; DTaP: Diphtheria, Tetanus, acellular Pertussis; IPV: inactivated polio vaccine; Hib: Haemophilus influenzae *type b; Pneumo: Pneumococcal conjugate; MMR: Measles, Mumps, Rubella; Td: Tetanus, Diphtheria low dose.)*

culosis and viral hepatitis (A and B), exact a heavy toll on the Roma. According to data from one pulmonary hospital in 2009, 30% of the patients were of Roma origin and in another hospital 60% of the tuberculosis patients were Roma. In one study in three towns one quarter of the large number of cases of tuberculosis were in children. In addition, the number of physically and mentally disabled Roma is six times higher than the rest of the Bulgarian population.

The main causes of ill-health lie in massive unemployment (with the consequence that only a small part of the adult Roma population has paid health insurance contributions) and consequent poverty, poor nutrition, bad living conditions and lack of proper sanitation. Moreover, there are few or no prevention activities or health promotion, educational levels are low with poor knowledge about health, and the medical system is often very bureaucratic. Relations between the medical staff and the Roma communities are hampered by the fact that many general practitioners who work in Roma neighborhoods are not familiar with the cultural differences and traditions of their patients. Poor Bulgarian language skills of many Roma people only aggravate the problem.

Given the deterioration of health indicators in the Roma population, in 2003 a project [1] under the pre-accession Phare Programme was undertaken to improve access to good-quality education and health care for vulnerable minority groups. A special focus was placed on Roma, in the context of the Framework Programme for the Equal Integration of the Roma in Bulgarian Society and the Bulgarian National Health Strategy and Action Plan for the period 2001-2006. The project focused on improving access to health-care services and strengthening medical staff, preventive services and health promotion. Training on working with the Roma community was instituted in selected universities and nursing colleges and some 50 "health mediators" were educated in order to link the Roma with the health-care system. Five mobile units providing prophylactic care were brought into the communities.

In 2004 a further three-year project [2] was launched in order to systematically improve the situation. The first phase focused on the improvement of maternal and child health through implementation of health-care educational programmes for disadvantaged ethnic minority women and children, implementation of an outreach examination pilot programme for preventive maternal and child health care, and further training of physicians, family practitioners and nurses. Emphasis was placed on preventive family health care, and, in the pilot phase, physicians, family practitioners, nurses and radiology technicians were trained in primary health care aimed at 12,000 disadvantaged ethnic minorities women and children. Ten mobile units, providing gynaecological, paediatric and mammographic services, were delivered.

Another Phare project, in 2005, introduced an outreach programme for screening and early diagnostics of tuberculosis, cancer, heart and congenital diseases, with a comprehensive programme and action plan. It also featured a health promotion campaign with local and regional stakeholders for reaching the disadvantaged ethnic minorities, with a special focus on Roma, and provided additional training to health professional, social workers and nongovernmental organization staff for work with Roma communities. Finally, it assessed the needs and studied the possibilities for upgrading the existing health information and monitoring system.

During 2010 a series of meetings were held in nine cities throughout the country under the aegis of the "Initiative of health and vaccination". The main themes were the importance of timely vaccination and extending the coverage of immunization in vulnerable groups, as well as the introduction of new multivalent vaccines and a new vaccination calendar. The role and value of health mediators was also covered (see later). Further work planned for 2011 includes implementation of preventive programmes, creation of appropriate health-education materials, and health awareness activities in schools and child-care centres in Roma communities.

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[1] PHARE Contract BG2003/004-937.01.03: Educational and medical integration of vulnerable minority groups with the special focus on Roma. 2003 Available at: http://ec.europa.eu/enlargement/fiche_projet/index.cfm?page=410708&c=BULGARIA. (Accessed June 2011).

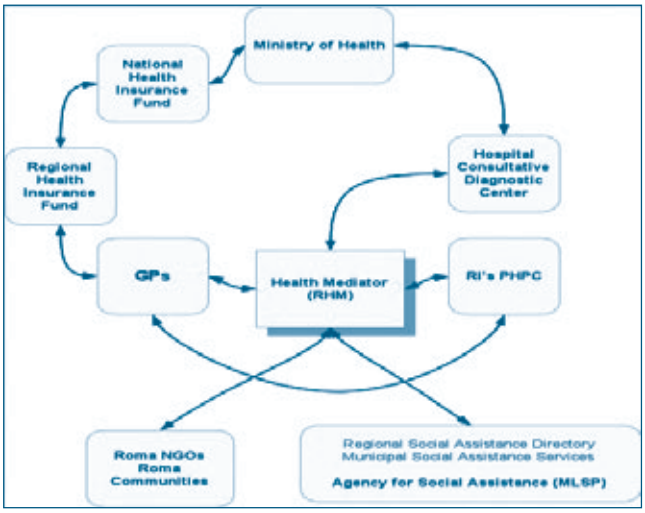
[2] PHARE BG2004/016-711.01.03: Improvement of the situation and inclusion of the disadvantaged ethnic minorities with a special focus on Roma. 2004 Available at: http://ec.europa.eu/enlargement/fiche_projet/index.cfm?page=410708&c=BULGARIA. (Accessed June 2011).

Based on a presentation by
Rositsa Ivanova, National council for cooperation for ethnic and demographic issues at Council of Ministers, Sofia, Bulgaria

Ensuring access of minorities to health care in Bulgaria: concept of health mediators – history, job description and mediator's activities

Although according to official statistics native Bulgarians make up 83% of the population, other estimates identify different ethnic groups as comprising between 10% and 30% of the population. Some of these ethnic communities were said to be "virtually deprived of health care", with the Roma (themselves a diverse community with groups and subgroups based on characteristics such as occupation, religion, and language) experiencing social and economic isolation and associated health problems despite socio-economic progress in the rest of the country. The Health Strategy concerning People in Disadvantaged Position belonging to Ethnic Minorities, adopted in 2005, aims to rectify that situation by institutionalizing the role of health mediators as coordinating figures between health institutions and members of minority groups and communities (see Figure for scheme of their role). It also stresses the need to improve constantly the skills of health-care providers for working in a multiethnic environment and with disadvantaged groups.

The role of health mediators as coordinator between health institutions and minority groups



RI: Regional Inspectors PHPC: Protection and control of public health

Indicators of the disadvantages facing ethnic Roma in Bulgaria include the following: a poverty rate of 84%, unemployment at 50% to 80% (depending on the definition of unemployment), more than 40% have not attended school or completed primary school and 40% have only primary school education. Poor living conditions render Roma communities susceptible to tuberculosis and viral hepatitis. Almost half the people with Roma background and two thirds of ethnic Turks live in underdeveloped rural regions with inadequate infrastructure, lack of water and electricity supply, in small settlements and overcrowded housing. Chronic disease is rampant, and the frequency of disability (often due to accidents) is up to six times the national rate. Life expectancy for Roma is about 10 years shorter than the national average, with the highest mortality rates in the 40-49 year age group, mainly due to heart disease. According to 2003 data, the child mortality rate, at 28/1000 is nearly three times the figure for ethnic Bulgarians, and 20% of Roma children have not been immunized or only partially. For most (55%) access to health care is difficult, a fact compounded by the high mobility of some groups, and less than half have health insurance.

The Government's health programme has set a series of strategic objectives [references 1-3]:

1. To overcome and discontinue the negative tendencies for the health of people in a disadvantaged position, belonging to ethnic minorities, and create conditions for improving their health
2. To secure equality of access to health services for people in a disadvantaged position, belonging to ethnic minorities
3. To raise the health knowledge and secure access to health information
4. To overcome the cultural barriers in communication and any forms of discrimination
5. To expand the coverage of health-insured people in a disadvantaged position, belonging to ethnic minorities.

Corresponding actions have been defined, and include: improving sexual and reproductive health, preventing violence against women, developing a network of health mediators [4] (http://www.zdravenmediator.net/), improving both the training and the status of doctors and nurses working with ethnic minorities, improving access to and quality of primary outpatient care (including emergency care) and bringing services closer to populations, raising the knowledge of disadvantaged populations about prevention, services available and the rights and duties of patients, innovative means of health education together with improving communication skills, action by health professional organizations to counter discrimination, and new legislation to extend health insurance to disadvantaged people.

Specific indicators to be measured include: child mortality rate (with pre- and peri-natal services, births in hospital, and timely immunization), maternal mortality ratio, number of teenage pregnancies and consanguineous marriages, and infectious disease morbidity rates.

The concept of health mediators is relatively new in Bulgaria, with the health mediation programme being launched in 2001, compared with, for example, France and Spain which have 20 years or more experience. These health workers have appeared under different guises in different countries: intercultural mediators in Finland, ethnic health educators in The Netherlands, sanitary mediators in Romania and Republic of Moldova, and field health workers in Serbia. The concept has proven its efficiency in many European countries for improving access of Roma to health and social services and for overcoming discrimination, and its introduction in Bulgaria successfully built on the experience of Romania and the Netherlands. In 2003 a Phare programme supported the training of 51 health mediators, 30 general practitioners, and 30 nurses from 15 towns in Bulgaria with concentrations of Roma populations. Unfortunately, following the completion of their training in 2004, most of these graduates were not appointed at their institutions and those who practiced were able to do so through projects financed by international donors. The national Health Strategy for Disadvantaged Persons Belonging to Ethnic Minorities adopted in 2005 gave health mediators a significant place and an indicator of the Strategy's successful implementation is the number of health mediators employed by the Government. Training continued, with 45 more health mediators in 2006-2007 and 19 in 2008 in one centre from municipalities where thus far there have not been any trained health mediators. A new training programme with a curriculum of 150 academic hours has been developed, and two medical colleges for training of health mediators had been licensed. In 2008-2011 105 health mediators were appointed in 57 municipalities through earmarked budgets to the municipalities.

Health mediators are selected first through selection committees in cooperation with the local authorities and health institutions in each town and by interview. Candidates are

expected to have completed secondary school education and health ministry-approved specialized training; knowledge of Romany or Turkish language as well as familiarity with health and social legislation are advantages. Their work covers work with the patient and the health service provider, assistance with communication with the National Health Insurance Fund and other State agencies, health education and promotion, as well as reporting with recommendations to appropriate bodies (see Figure). Recently health mediators have been active in programmes on tuberculosis control, prevention and control of AIDS and sexually transmitted infections, control of a large outbreak of hepatitis A, measles prevention and genetic screening. They have also been active in encouraging disadvantaged populations to use mobile clinics for clinical examinations such as cervical screening. In more than 10,000 subsequent obstetric and gynaecological examinations, the first such examination for most of the women, about half were found to have pathological signs. More than 10,000 children have been also examined in mobile clinics. Health mediators have promoted good nutrition, breast-feeding, immunization and prevention of drug and substance abuse.

Although the approach was acknowledged as a successful first step, it was observed that altogether 4000-5000 such staff would be needed to meet the objectives in a sustained way. The cost of outbreak containment, however, might be a useful argument in gaining funding, especially in resource-constrained times.

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[2] Health Strategy for Disadvantaged Persons Belonging to Ethnic Minorities, adopted by the Council of Ministers of the Republic of Bulgaria in September 2005; Action plan for Strategy implementation, 2005-2007, adopted by the Council of Ministers on 8 September, 2005 (Decision No 36.1), Action plan for implementation, 2011-2015, adopted by the Council of Ministers on 27 July, 2011. Available at: http://www.strategy.bg/StrategicDocuments/View.aspx?lang=bg-BG&Id=658 http://www.government.bg/cgi-bin/e-cms/vis/vispl?s=001&p=0228&n=2632&g (Accessed on 7 September 2011).

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Based on a presentation by
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Epidemiology

Viral hepatitis in Bulgaria

Since 2005 surveillance of viral hepatitis (A, B, C, D and unspecified) has been brought into line with the requirements of the European Union, with adoption of the latter's case definitions of 2002. In addition, data are broken down by age, sex and category. At present the list includes only acute viral hepatitis and not chronic viral hepatitis see previous section on communicable disease surveillance (page 3).

Data from surveillance reflect recent exposures, contacts and acute cases, while seroprevalence data reveal exposure at young ages, the lifetime serological heritage and the level of immunity in a population. For HAV infection almost no national seroprevalence data have been collected for the past 20 years, whereas data for HBV infection come also from studies in the pre-vaccination era and investigations of specific groups and nosocomial outbreaks - data on HCV infection is also provided by the latter type of investigation.

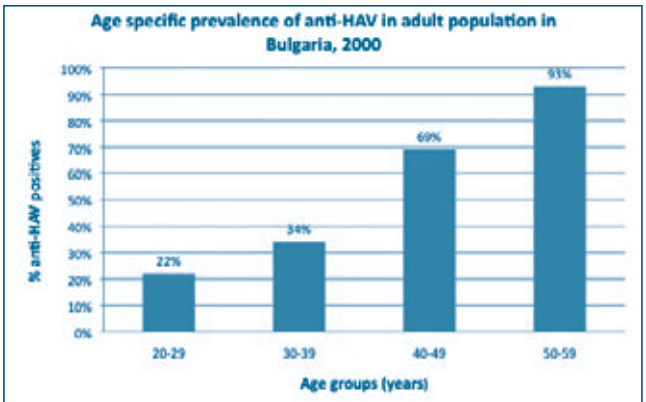
HAV and HBV are present with intermediate endemicity. A small study in 2000 demonstrated that, out of a total of 781 tested persons aged 1 to 59 years, 293 (37.5%) were positive for anti-HAV antibodies. The age-specific prevalence of anti-HAV in the adult population in Bulgaria in 2000 is shown on next page (Table and Figure).

Nationally, the carriage rate of HBsAg in the population is in the intermediate range (2-7% of the population) but the annual incidence of cases of acute hepatitis B reported has fallen from 35/100,000 in 1984 to 5/100,000 in 2010. The endemicity of HCV is low, anti-HCV prevalence being about 1.3%. Figures for the period 1998-2010 show that most cases of acute viral hepatitis are due to HAV (average 77%), followed by HBV (17%), HCV (2%) and HDV (0.1%). Deaths are mainly due to hepatitis B.

Hepatitis A

Over the past 25 years the annual incidence rate has been falling steadily, apart from the country's largest outbreak in 1990-1991 (41,060 registered cases, see Figure below). Most cases are in children aged 1-14 years, particularly in schools, orphanages and centres for special care, but there are also large cohorts of susceptible adolescents and adults. As mentioned above, no

Age specific prevalence of anti-HAV in adult population in Bulgaria, 2000

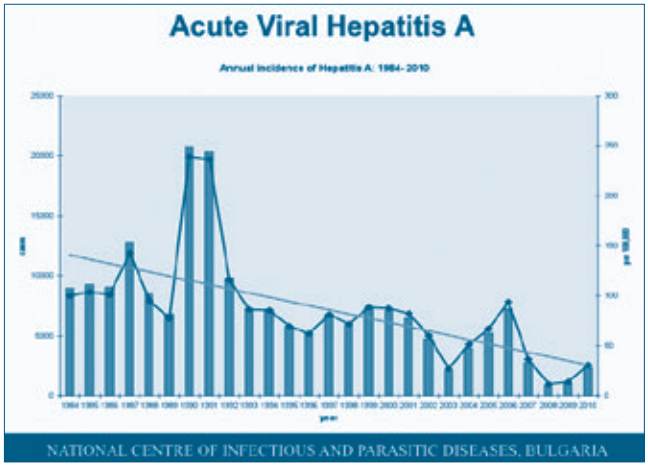


Age group (years)	20-29	30-39	40-49	50-49
Proportion anti-HAV positive	22%	34%	69%	93%

Source: Mira Kojouharova, Hepatitis A Advisory Panel (Eastern Europe - Middle East - North Africa). 18-19 December, 2006, Istanbul, Turkey

national data for HAV seroprevalence exist but for the region of Plovdiv a few studies on the seroprevalence of different types of viral hepatitis have been performed and the results published. One study found an average seroprevalence rate of 68% for HAV in the region of Plovdiv [1]. The most significant cluster of outbreaks in recent years is attributable to the floods in the summer of 2005 and to the large outbreak of hepatitis A in Plovdiv with person-to-person transmission in 2006, particularly affecting Roma communities.

Annual incidence of acute viral hepatitis A in Bulgaria, (1984-2010)



In 2006, two simultaneous outbreaks of hepatitis A occurred in communities about 200 km apart. There was no evidence of any links between these two centres. Inconsistencies in the results of testing for anti-HAV antibodies prompted the sharing of samples with colleagues in the Public Health Agency of Canada. A subsequent meticulous phylogenetic analysis, using the VP1/2A junction region of the genome (most commonly used in the genetic analysis of mutants of HAV), revealed that at least two genetically related but distinct strains of HAV had been transmitted in parallel in both outbreaks. In the course of the prolonged outbreaks, the viruses rapidly evolved into a quasispecies of viral sublineages in individual hosts. The data did not support the idea of immune-escape variants of HAV.

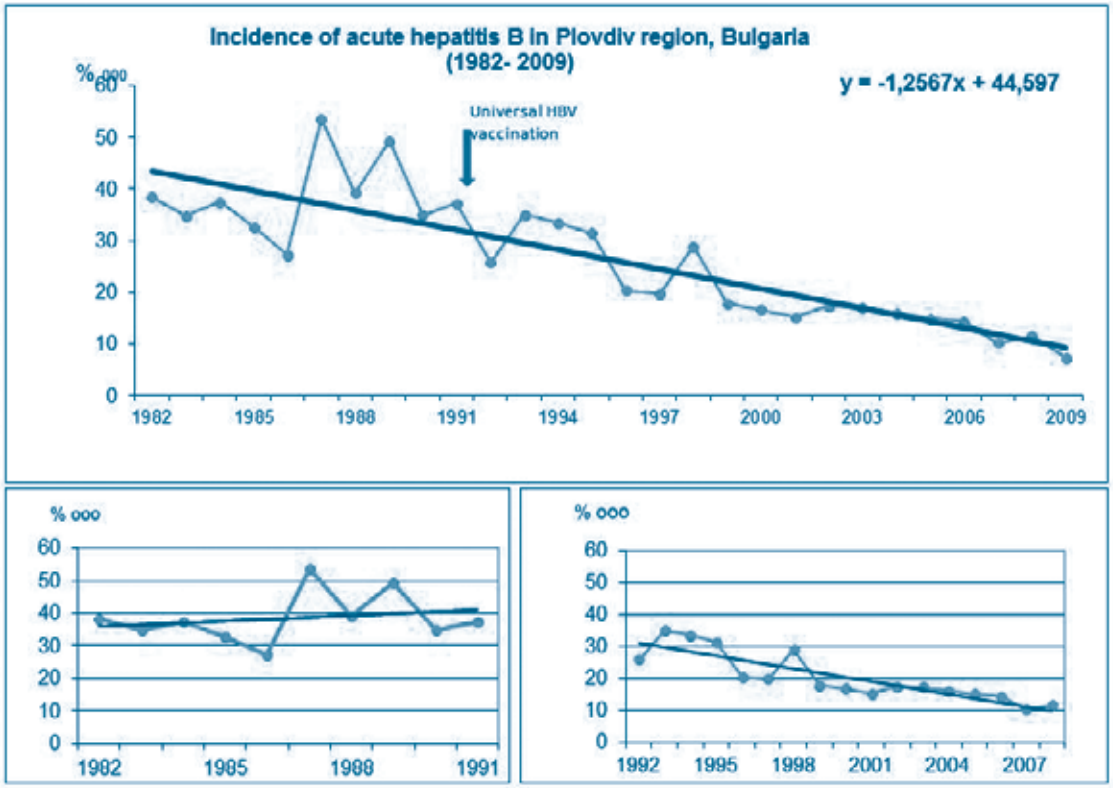
One outbreak occurred in Plovdiv in a Roma community of about 45,000 people that had seen no investment in infrastructure for more than 20 years and where a boom in illegal housing had led to severe problems with regard to electricity and water supply, sewerage and waste disposal. After controlling the epidemic, the local authorities spent the equivalent of US$ 650,000 in clearing up and improving sanitation. Soap and washing powder were distributed, refuse (including human excreta) was removed, areas between housing blocks were drained and asphalted, and all children were immunized. Concern was expressed, however, that soon afterwards the living conditions had not improved and the danger existed that the epidemic would repeat itself in five years' time.

In 2010, a slight cyclic increase in HAV incidence was registered in the country (2350 acute cases were reported). Cases were reported mainly in three regions of the country and the Roma minority again was the most affected population in two of these regions. Although the socio-economic circumstances in which many minorities live make it likely that many children develop immunity to hepatitis A, the economic transition in the country raised pressing questions about the need to immunize at-risk populations with hepatitis A vaccine.

Hepatitis B and D

The quantitative changes in the incidence of acute hepatitis B over the past decades are most clearly demonstrated by the incidence trends. Between 1982, when separate registration of viral hepatitides was established, and 2009 the incidence of hepatitis B decreased more than five-fold, from $38.41/10^5$ in 1982 to $7.39/10^5$ in 2009 (see figure next page). The changes correlate with the introduction of the universal vaccination programme. Particularly noteworthy are the rising trend of the incidence of acute hepatitis before the introduction of vaccination (1982–1991) and the subsequent decline in incidence after its introduction (1992–2008). The policy of universal immunization of newborns was introduced in August 1991 (with full routine vaccination from 1992 onwards). The impact has been dramatic: between 1992 and 2010, incidence rates per 100,000 population fell from 8.0 to zero for the 0-1 year age group, from 23.8 to 1.4 for the 1-3 year age group and from 58.7 to 8.4 for those aged 15-19. Most acute cases in Bulgaria in 2010 were in the 20-24 year age group followed by the 25-35 year group. All acute cases of hepatitis B are investigated, including their history of vaccination against hepatitis B; within the three years 2008-2010, a total of 272 cases in children and young people aged 0-19 years were registered and investigated. About 60% were either born before universal immunization was introduced or not vaccinated. However, 24% (38 cases) of those for whom immunization status was known had received three doses of vaccine.

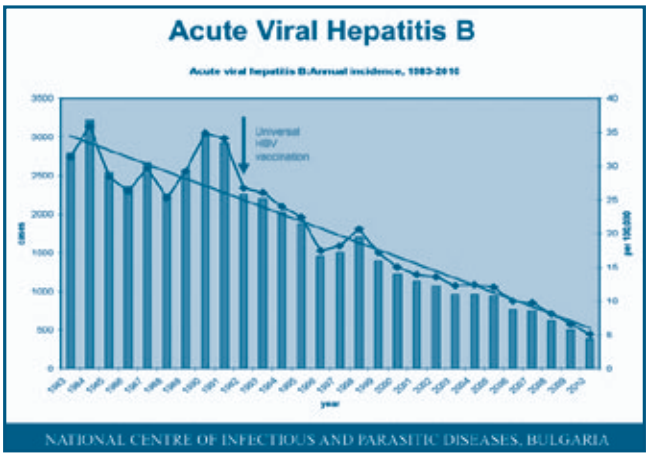
Annual incidence of acute viral hepatitis B in Plovdiv region in Bulgaria, (1982-2009)



Two serological studies of seroprevalence in the general population were conducted 10 years apart. Data from the European Union's Interreg II multicentre project, a seroepidemiological study in 1999-2000 of 11,597 unvaccinated people, showed a carriage rate of HBsAg of on average 3.87% (ranging from 1.96% to 5.26% in five cities) and immunity to HBV in 23.6% (varying from 16% to 34% by city) [2]. A study in 2010 in the Plovdiv region demonstrated an HBsAg prevalence rate of 4.8% (similar to the data from the first study in 2000, when the prevalence rate in Plovdiv was 4.19%) and a significantly higher rate (7.4%) in minority groups (mainly Roma). Family contact was a significant risk factor for HBsAg positivity.

The steady rate of chronic carriage of HBsAg remains a continuing problem in the country. The lack of change in the proportion of chronic carriers over time is due to the extremely low rate of vaccination with recombinant hepatitis B vaccine of people older than 20 years (in a study of 667 people over 20 years of age, only two were vaccinated, i.e. <1%). Nevertheless, there is a steady reduction in the incidence of acute hepatitis B (see figure left below).

Annual incidence of acute viral hepatitis B in Bulgaria, (1984-2010)



At the same time as the vaccination programme was introduced, immunization of health-care workers and medical students was recommended. Pregnant women are not screened for HBsAg as all children are now vaccinated (nearly all births take place in hospitals) and HBIG is not available - there is no local production. It was observed that screening pregnant women in those circumstances would not be a good use of resources. Besides the very important contribution of vaccination, other factors that have contributed to the striking decrease in incidence of acute hepatitis B include improved laboratory diagnosis, screening of blood, blood products, donated tissues and organs, application of standard precautions in health-care and laboratory settings, use of disposable syringes, and training of medical personnel. At the same time, patients' associations and the pharmaceutical industry have been active in providing information and health education. It was further pointed out in discussion that behavioural changes resulting from the prevention and control campaigns relating to AIDS will also have had an effect.

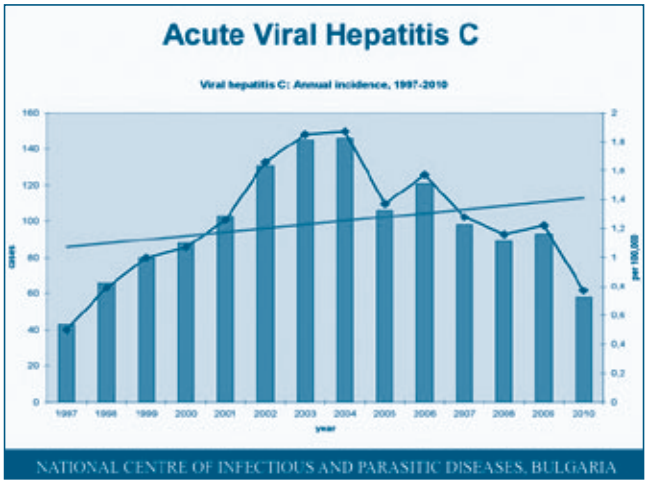
Genotyping of isolates from patients with either acute or chronic hepatitis B showed that genotype D predominated, alone or, to a lesser extent, in combination [3].

Between 1997 and 2010, on average, about six acute cases of hepatitis D have been detected each year, with a slightly rising incidence trend.

Hepatitis C

A very low incidence of hepatitis C is reported (less than 2 cases/100,000 population, see Figure below), with only 58 acute cases being notified in 2010. Cases were identified in most regions of the country and, although in most cases the source or route of transmission was unknown, 29% were in people at-risk for blood-borne diseases, mainly injecting drug users. Haemodialysis and multiple medical interventions, or dentistry were also risk factors. Nosocomial outbreaks were seen in hospitals and haemodialysis units and were mainly attributable to failures in infection-control procedures, including unsafe injections [4-6].

Annual incidence of acute viral hepatitis B in Bulgaria, (1984-2010)



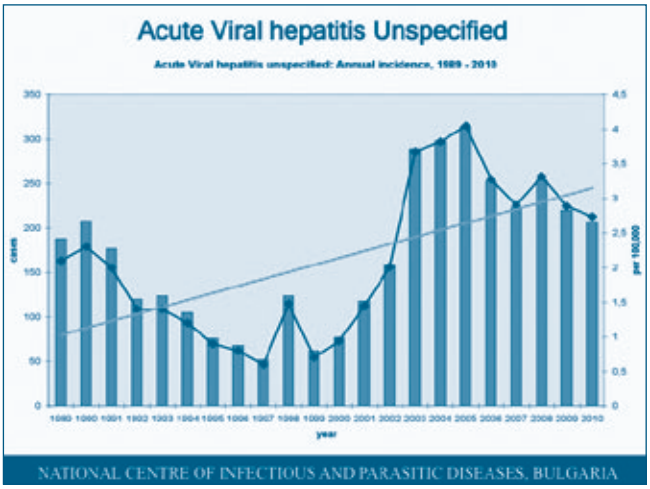
Genotype 1b predominated in patients infected with HCV in Bulgaria, although considerable genotypic diversity was seen in isolates from injecting drug users, with genotype 3a being often found as well as, less frequently, other subtypes [7, 8]. Such molecular epidemiological techniques proved valuable in identifying a nosocomial outbreak in patients on a urology ward. Genotypes 4 and 6 (usually seen in Africa and the Russian Federation, respectively) have been recently detected in Bulgarian patients.

Data on HCV infection from the two serological studies mentioned above for hepatitis B indicated a seroprevalence rate of 1.28% for anti-HCV in the five major cities (range 1.1-1.6%) in 1999-2000 [2]. In the Plovdiv region in 2010, the prevalence had fallen significantly from 1.13% in 2000 to 0.9%. In one study in Plovdiv which covered a period of 15 years (between 1993 and 2006), high seroprevalence rates of anti-HCV were found in haemophiliacs (116 out of a total of 120 cases, 97%), haemodialysis patients (45%), and injecting drug users (161 out of a total of 230, 70%) [9]. Studies for HCV prevalence among medical staff are still insufficient. One study conducted among 31 health-care workers working in haemodialysis unit, found four persons positive for HCV (12,9%) [10]. In 2007-2008, another study of 324 health-care workers in acute care hospitals in four regions found none to have anti-HCV antibodies [11].

Unspecified viral hepatitis

In the past decade the annual incidence of acute cases of unspecified viral hepatitis has risen, with 207 cases (three deaths) having been reported in 2010. Cases have been found in all age groups and tested negative for anti-HAV, HBsAg and anti-HCV.

Annual incidence of acute viral hepatitis unspecified (negative for anti-HAV, HBsAg, Anti-HCV), (1984-2010)



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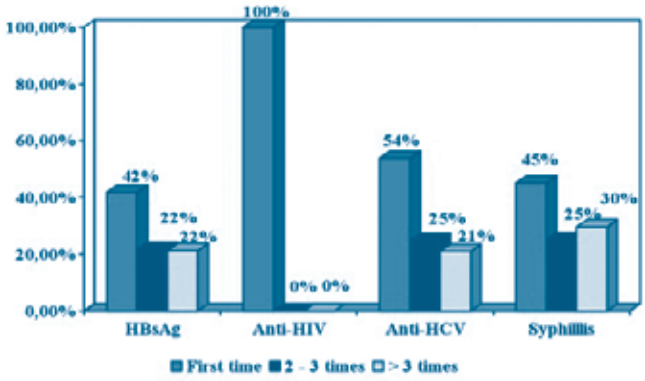
Blood donors

The blood transfusion system is based on a national centre, four regional blood establishments and 23 hospital-based centres. Donation is voluntary and non-remunerated (except for a small group of donors with rare blood groups), with established criteria for selection of donors. Some 90% of donors are repeat donors. Donations are screened for markers of HBV, HCV, HIV infection and syphilis. Algorithms are in place for confirmatory testing and false-positive or indeterminate results, and data are collated nationally. A steady supply with a policy of rational use of blood and blood components renders the country self-sufficient.

Data from screening of some 60,000 donations show 1.62% of male donors (range 1.04% to 3.30% between the regions) and 1.41% (0.85-3.50%) female donors to be positive for HBsAg, a rate that is comparably high to that in neighbouring South-Eastern European countries. The percentages for HCV-positive donors are: males 0.26% and females 0.15%. Positive results are likely to be found in first-time donors, but, despite a policy of deferral of positive donors, more than 20% of seropositive donors were found to be donating for the second time (see Figure). The problem was identified as one of communication, indicating a need to improve information and to define who provides counselling. Other problems identified were the need for new legislation on the prevention of viral hepatitis and the misuse of plasma, and it was argued that the rational use of blood and plasma for direct clinical purposes needs to be improved. A national programme for safe blood was instituted in 2005, and every year energetic drives are held to encourage and recruit young donors, with considerable success.

Frequency of donation of seropositive donors



Based on a presentation by
Svetla Bakalova, National Center of Transfusion Hematology, Sofia, Bulgaria.

Injecting drug users

In 2008, a national representative study in the general population in Bulgaria on the use of, and attitudes towards, different psychoactive substances indicated that 5.2% of the adult population had a lifetime experience of drug use. Heroin has been the illicit drug associated with the highest level of drug-related problems, and the number of heroin users is estimated, on the basis of those seeking treatment, to lie between 20,000 and 30,000. That figure has remained steady, or even declined a little, in recent years. On the other hand, more young people are injecting amphetamines. There is even a large black market for methadone to use including for injection. Sharing injection equipment, although declining over the past decade, is still common (44% of users report sharing).

Testing of injecting drug users in Sofia between 2000 and 2010 showed figures of 50-60% positive for anti-HCV antibodies and data from 2004 to 2008 for 10 cities gave a corresponding figure of 64% - the rates are generally comparable with those in other countries in Central and Eastern Europe. Some 9% of injecting drug users became positive within the first two years after beginning injection and the same proportion in the next two years. Views diverged as to whether this (relatively low) rate represented an opportunity for prevention. The prevalence of HBV infection is steady at around 6% although a fall has been seen in the rate in people younger than 25 years. A worrying trend is the sharp rise in HIV infections - eight-fold over four years, albeit still at low levels (to 2.7% in 2009). The treatment of addiction and harm-reduction activities are successful types for prevention of drug-related infectious diseases.

Based on a presentation by
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Haemodialysis patients

Patients in dialysis units and the medical personnel who work in those units are at raised risk of infection with HBV and HCV. A multicentre observational study in 2004 looked at seroprevalence rates in a large cohort of nearly 2300 patients. The proportions infected with HBV (9.1%) and especially HCV (25.2%) were higher than the rates in the general population (respectively 8.0% and 1.5%). These data are comparable with those in other southern European countries.

Very few (1.4%) of the patients had been vaccinated before starting haemodialysis (and only 26% during treatment), even if vaccination and revaccination were recommended. The

serological status of such subjects was not checked systemically (indeed, seldom before starting treatment); it is recommended that patients be tested for HBV and HCV infection markers every six months. The implication is that communication between general practitioners and nephrologists needs to improve.

Significant rates of positivity for markers of HBV and HCV infection were found in dialysis unit personnel; 13% (4/31) (in particular nurses) were positive for anti-HCV. Standard precautions and other preventive measures need to be more strictly imposed and practised (see section on health-care workers).

False serological results mean that all haemodialysis patients and patients with disturbed immune response should have at least one polymerase chain reaction test for HCV RNA, irrespective of serological status. Approaches to reducing infection also include the wider use of erythropoiesis-stimulating agents in order to diminish the amount of risk full blood transfusions and peritoneal dialysis.

Based on a presentation by
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Health care

The impact of patients' associations

Hepasist - the National Association for Fighting Hepatitis - was founded in 2005 with the aims of informing the general population about hepatitis, including testing and prevention, and militating for patients' rights [1]. It runs a website (http://hepasist.org), provides free medical consultations, holds awareness-raising events and undertakes campaigns to promote screening for HBV and HCV infection and hepatitis B vaccination. In 2006 it organized protests against the limits being placed on a hepatitis C treatment programme, which resulted in a change in policy, and since 2009 treatment for hepatitis is reimbursed in the same way as treatment for other diseases. In 2007 the association continued its activities with a European campaign for Bulgarian patients with hepatitis C. It has successfully negotiated with the National Health Insurance Fund for a chronic viral hepatitis treatment programme with separate funding, organized expert meetings, raised viral hepatitis issues in the National Assembly, organized prominent actions around World Hepatitis Day, and vigorously campaigned for hepatitis A and B vaccination with many media interventions and a toll-free telephone service. Its media campaigns have been internationally acknowledged, and its activities have resulted in high levels of public awareness and the Government giving viral hepatitis a high priority and ensuring that treatment is reimbursed and access to treatment and therapy meet the highest international standard.

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Based on a presentation by
Stanimir Hasurdjiev, Hepasist, Sofia, Bulgaria

Health-care workers

Although no comprehensive nation-wide data exist for infection of health-care workers with viral hepatitis, several investigations provide indicative findings, even if the results are not always consistent. A multicentre study in 2007-2008 showed no HCV infection in health-care workers, although another smaller study showed a high rate: 13% of health staff in a haemodialysis unit had been infected with HCV [1]. An outbreak due to HCV genotype 1b in six patients on a urology ward resulted in one death, one case of chronic HCV infection and complete recovery in four cases; transmission was attributed to use of a common syringe to administer intravenous heparin flushes.

Prevention of exposure should be the primary strategy to eliminate or reduce the risk of occupational blood-borne pathogens. The importance of adhering to standard precautions including the prevention of sharps injuries (the subject of a recent European Council Directive) was emphasized, together with practice of internationally agreed management of occupationally exposed health-care workers and the need for awareness raising, information and training. Under specific legislation (Regulation 4/2002) people at risk of occupational infection are entitled to vaccination, at the expense of the employer, and senior managers in medical institutions are responsible for evaluating the risks of infection of health-care personnel and ensuring their protection. In discussion it was mentioned that a new document on protection of health-care workers is being prepared for the health ministry with a view to strengthening the legislation.

Participants also underlined the need to issue guidance or legislation on restricting the work practices of health-care personnel infected with hepatitis viruses. Also, although one medical school was said to have had a programme of immunizing all students before entry, there was no general condition for medical and nursing students to be vaccinated before starting their studies as exists in some other countries and to keep registers of the immune status of health-care workers. Such a policy should be considered, it was argued, especially as both low pay and a risk of infection would be likely to further encourage health-care workers to emigrate, and to take steps to improve legis-lation.

In a multicentre survey of more than 1400 health-care workers from 29 hospitals (doctors, nurses and laboratory technicians) in 2008, 76% reported in response to a questionnaire that they were fully vaccinated against hepatitis B; 0.4% had markers of HCV infection [2]. Barely half fully appreciated the value of vaccination or post-exposure prophylaxis, and continuing training in infection prevention and control was reported by only 21%. Serological results showed that 5% carried HBsAg (a similar rate to that in the general population) and 36% were not immune to HBV infection. A subsequent study conducted in three regional hospitals (227 doctors, 666 nurses) in 2010 revealed wide differences in the proportions of doctors (0-67%) and nurses (10-76%) vaccinated against hepatitis B. The worrying conclusion was that an estimated 36,500 health-care personnel were unvaccinated with 30,000 susceptible non-immune personnel working in the health system in the country. Both vaccination coverage and protection were significantly higher in staff who worked in hospitals with an established infection control team and strong and visible support from higher management. Strategies to improve the situation are being developed and implemented, including strengthening hospital infection control programmes, developing a national protocol for post-vaccination screening and vaccination of non-responders [3], and building on the successes of "champions" of infection control.

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Based on presentations by
Rossitza Vatcheva-Dobrevska, Head of National reference centre for health-care associated infections, National Centre of Infectious and Parasitic Diseases, Sofia, Bulgaria;
Nina Gatcheva, President of the Board of Bulgarian association for prevention and infection control, Sofia, Bulgaria.

Clinical aspects and treatment

A group of 135 patients (56% male) with acute hepatitis B (average age 35 years) were followed between 2006 and 2008. Overall, infection was acquired sexually in 44% of patients but through gynaecological, dental or other medical interventions in 17% and blood transfusions in another 7%. The high figures for gynaecological and other medical interventions as a possible route of transmission of virus were noted with concern and underlined the need for better enforcement of standard pre-cautions.

Genotypes of hepatitis B virus and their influence on severity and outcome of acute disease were studied in 23 patients in the group. Genotype D predominated, mostly alone but also in combination with types A, E and F, and in most cases was associated with moderate or severe illness; in 81% of cases the patients recovered whereas 19% developed chronic infection. Among the smaller number of patients with multiple genotypes, outcome tended to be worse with more chronic infections and even one case of fulminant disease. Real-time PCR analysis of 45 patients showed that concentrations of HBV DNA did not correlate with genotype.

Another study looked at 238 patients (78% male) with acute hepatitis C. Most had probably acquired infection through injecting drug use (59%) but 14% through surgical interventions, piercing or tattooing and 8% through blood transfusions. The clinical course was mostly mild or moderate, but more severe in patients with co-infection with HBV (usually injecting drug users). Young HBsAg-positive injecting drug users tended to be superinfected with HCV, experience more severe illness and often developed chronic infection. Spontaneous recovery was more frequently seen in younger patients with lower bilirubin concentrations.

Early start of treatment of patients with acute hepatitis C with interferon led to biochemical and virological response in 62%. The likelihood of recovery was higher when treatment was started in the third to sixth month rather than after one year. After 8-10 years of follow-up spontaneous viral clearance was seen in 58% of patients with acute hepatitis C. Recovery was more likely in patients under 30 years of age and those with bilirubin concentrations of less than 100 µmol/l.

Treatment of HCV infection has evolved from alpha interferon alone to repeat therapy with pegylated alpha interferon and ribavirin. The latter combination gave sustained virological responses in 80% of cases, including all patients infected with genotype 3 and 79% of those infected with genotype 1; patients infected with genotype 3 were significantly younger than those infected with genotype 1 and had much lower concentrations of HCV RNA. In chronic genotype 1 infection, better sustained virological responses were associated with the presence of the CC subtype of IL28B polymorphism than with CT or TT subtypes. Careful selection of patients improves the outcome; the presence of steatosis reduced the effectiveness of the pegylated interferon/ribavirin combination. Clinical trials are in process of new interferons (locteron and multiferon), a ribavirin analogue (viramidine) and immunomodulators.

Whereas the goal of treatment of hepatitis C is cure, that of hepatitis B is different: suppression of viral replication leading to prevention of disease transmission, disease progression and improved quality of life (for which an assessment tool has been developed). Lamivudine was introduced in 2000 and other

nucleoside analogues in 2009. Clinical trials are investigating cyclic treatment with interferons, new compounds and even with a therapeutic vaccine. HBeAg-negative chronic hepatitis B patients are being seen more frequently, especially older subjects; treatment of these patients with interferon rarely resulted in sustained virological response, irrespective of dose. In HBsAg-positive patients treated with nucleotide analogues, loss of HBsAg and anti-HBs conversion were observed. Trials with tenefovir (alone or with adefovir) in more than 500 subjects are showing extremely good and sustained responses over four years in both HBeAg-positive and HBeAg-negative patients.

An innovative approach with intermittent or cyclical treatment with 1.5 MIU of pegylated interferon α2a showed a markedly lower relapse rate (38% compared with 63% in the control group at 24 months), which sustained up to 48 months. The regimen consisted of an initial 12-month course followed by a rest period of 3 months and then four cycles each of interferon (135 µg/wk) for 3 months and a rest period of 3 months. Better approaches are needed, especially given the presence of HDV infections (even though interferon suppressed HDV replication), and the duration of nucleoside analogue treatment remains undefined.

Access to treatment is free and good, with an elapse of only several weeks between diagnosis and start of treatment, although patients in underserved populations may not have good access. The strict application of patient selection criteria has contributed significantly to the extremely good success rates. The criteria include consideration of age, general clinical state (e.g. absence of steatosis), virus genotype, and favour a good outcome. With limited resources, cost is a major factor: about 300 patients are being treated each year at a total cost of about €6 million. For that reason, patients older than 60 years and those with other conditions, patients on methadone treatment, and those with alcohol-related liver problems are not selected. In addition it is recognized that interferon produces many side effects, and alternative therapies should be used when they become available.

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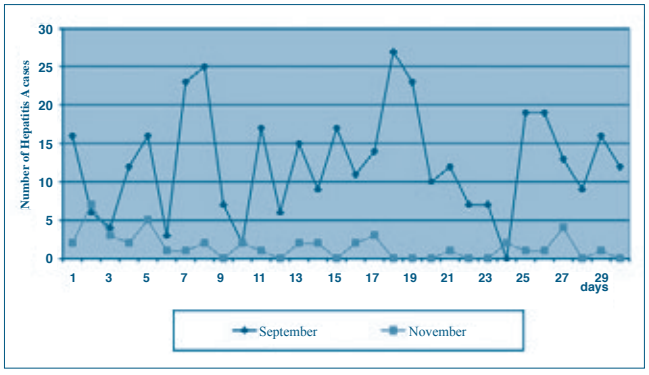
Prevention and control

Control of hepatitis A

The major outbreak of hepatitis A in the Roma community in the Stolipinovo suburb of Plovdiv in 2006 was the biggest in Europe in the past 10 years, and the effect of post-exposure vaccination of contacts with inactivated hepatitis A vaccine was studied. More than 1000 patients (mostly aged 1-9 years) were admitted to hospital and 5500 contacts were followed up. A total of 8835 children were considered eligible for immunization but 1244 (14%) were not vaccinated for a variety of reasons. The morbidity dropped markedly in the month after vaccine was administered. It appeared that postexposure vaccination of contact persons played a fundamental role in limiting the spread of the infection; as the Figure shows, the daily number of cases dropped dramatically in November after vaccination was introduced in October. It was evident, however, that without substantial changes in the living conditions and the behaviour of the population, better public health cannot be provided. The health of the Roma population is not so much a public health issue as social, economic and political matters whose solution needs the involvement of society as a whole.

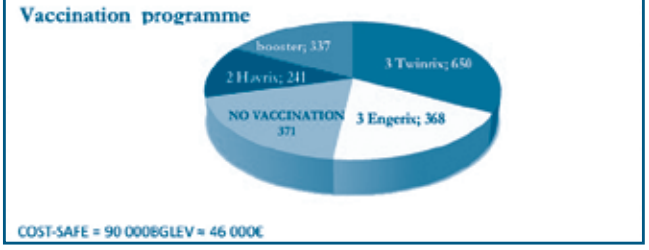
Number of cases of hepatitis A during outbreak 2006 in Stolipinovo, Plovdiv, before and after vaccination (October)



Based on a presentation by
Angel Kunchev, Communicable Disease Surveillance Department, Ministry of Health, Sofia, Bulgaria;
Monika Troyancheva, Regional health inspector, Directorate communicable disease, Plovdiv, Bulgaria.

Screening and vaccination programme in military personnel (2005-2010)

Result screening programme	Persons	Percentage
Non Immune against HAV & HBV	650	33,05%
Immune against HAV & HBV	371	18,86%
Non-immune against HAV	241	12,25%
Non-immune against HBV	368	18,71%
Partial immunity (A or B)	337	17,13%



Military personnel

Military personnel are recognized as a group of high risk for contracting both HAV and HBV infections. Vaccination is obligatory against hepatitis B but recommended against hepatitis A. After consultations, a policy of selective immunization of military medical personnel against hepatitis A and B following screening for markers of immunity was proposed. A five-year investigation in 2005-2010 of nearly 2000 military personnel showed that 19% were immune to infections by both viruses and 17% had partial immunity; the rest were then appropriately vaccinated. The screening programme resulted in considerable savings (the equivalent of €46,000).

The policy was thus shown to be ethically and economically justified. It also ensured that personnel were informed about their immune status and were appropriately protected. Moreover, non-responders were enabled to take appropriate steps for protection.

Based on a presentation
Colonel Andrey Galev, Center of Military Epidemiology and Hygiene, Military Medical Academy, Sofia, Bulgaria

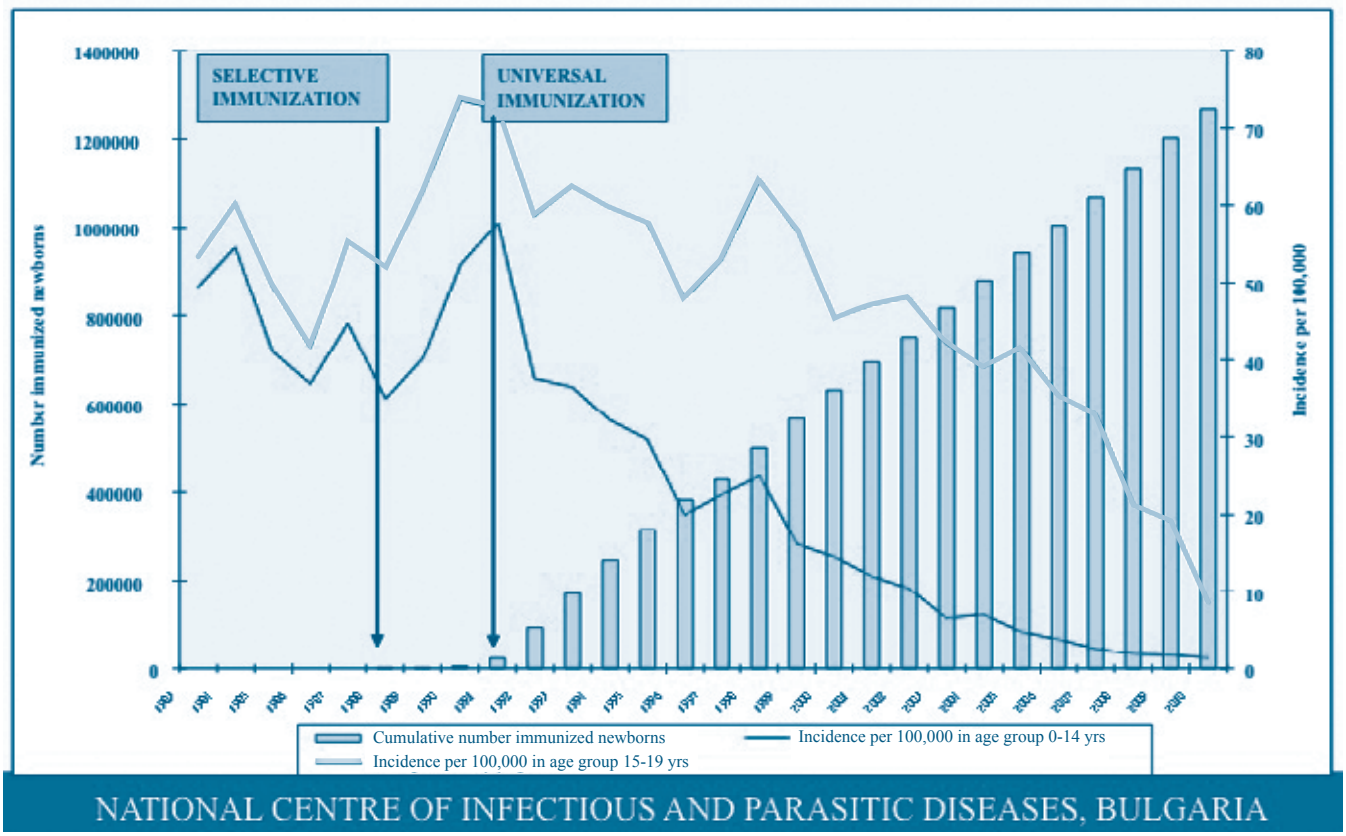
Cost-benefit analyses

Cost-benefit assessment of introduction of universal hepatitis B vaccination programme of newborns

After the introduction of hepatitis B vaccination in 1988 in Bulgaria, a total of 1,270,618 children had been fully vaccinated by the end of 2010. When the policy of universal vaccination was fully implemented in 1992, the annual coverage with three doses rapidly increased and has remained at high levels since 1993. As a result it is estimated that for the period of the universal hepatitis B vaccination (1992-2010) 1,246,018 of all 1,356,290 newborn children had been fully vaccinated (an average vaccine coverage rate of 91.87% for the whole period). The incidence of acute hepatitis B steadily fell to 1.4/10^5 in children aged 0-14 years and 8.4/10^5 in the 15-19 year age group (see Figure). The target of immunizing all adolescents is expected to be reached in 2011. Currently, the highest annual incidence of reported cases of acute hepatitis B is among young adults aged 20-24 years old (17.6/10^5).

Participants in the meeting commended the achievement of such high coverage but asked about the representativeness

Cumulative number of immunized newborns with with HBV vaccine and hepatitis B incidence (per 100,000) in children 0-14 and 15-19 years of age in Bulgaria, 1983-2010

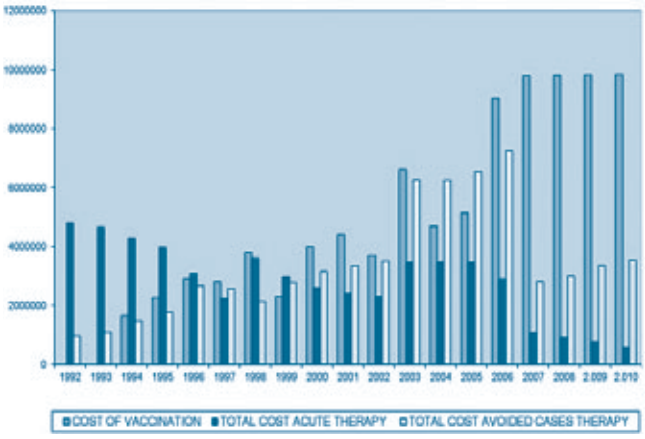


of the data. The figure of 95% annual coverage since 2003 is indeed an average, which means that there may be gaps in immunization coverage generally, as the recent measles epidemic indicated. With regard to the Roma communities, it appeared that the coverage was reasonable, although the rate for the third dose at 6 months could be improved. The fact that measles vaccine is given only at 13 months of age, when it was more difficult to bring children to the medical services, might explain why hepatitis B vaccine coverage was good and yet there had been a measles outbreak. The use of seroprevalence surveys of the whole population with standardized methodology and reaching every district (including Roma communities), which had been discussed at an ECDC conference on childhood immunization held only two weeks before the present meeting [1], would help to provide timely and more complete data.

A model-based economic assessment, based on a static model of the evolution of acute and chronic HBV infection, was made when universal infant HBV vaccination was introduced in Bulgaria. Several input settings were used in this model: the 1992 birth cohort (88,000), official and published data and estimates for age-specific mortality rates and HBV prevalence, vaccine efficacy and coverage, and duration of immunity. The direct medical costs of treating HBV infection and official data from public tenders for hepatitis B vaccine purchase were used for analysis. The assessment covered a period of 100 years. The analysis showed that universal vaccination of all newborns would significantly reduce the expected number of HBV cases and deaths and total medical costs related to infection. Vaccination would be both medically and economically beneficial (with benefit-to-cost ratio of 1.21). The economic effect of the vaccination would be realized 19 years after introduction of the programme when the benefits should exceed its costs. The benefit-to-cost ratio was sensitive to the discount rate on vaccine cost and treatment cost. The higher vaccine cost and lower treatment costs influence negatively on benefit-to-cost ratio [2].

Another study examined economic, social and medical costs and savings of the vaccination programme, using actual epidemiological data and retrospective costs for the period 1992-2010. The number of reported cases of acute hepatitis B fell from 2268 in 1992 to 387 in 2010 and conversely avoided cases and infections rose to 2330 in 2010. Costs due to complications and admissions to hospital fell proportionately, but the costs for cases avoided rose because of the cost of treatment (see Figure). The cost of vaccination has plateaued since 2007. In this analysis the cost of immunization and therapy of acute cases decreased but was still higher than the benefits in terms of avoided cases and their therapy. The determining variables were the cost of immunization (including the cost of vaccine) and treating chronic cases.

Cost of vaccination, cost of infected and avoided cases per year in Bulgarian Lev (BGN)



It was pointed out that use of direct medical costs rendered models very conservative and that inclusion of real costs and allowing for benefits from relief from suffering and illness would increase the cost-effectiveness. Also, use of a static model rather than a dynamic one will also underestimate cost-effectiveness.

In a discussion about transparency in view of the European Commission's current consultations of updating the Pharmaceutical Transparency Directive, it emerged that information about prices and tenders are published on the websites of the Ministry of Health and the Bulgarian Public Procurement Agency (http://www.aop.bg/index.php?ln=1) and in official publications. The Ministry has a pricing committee and a mechanism for pricing all medicinal products that uses data from seven reference countries. Actual prices of vaccines are needed for good cost-benefit analyses, but many countries keep the price paid confidential.

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Based on presentations by
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Conclusions

Needs, issues and observations

It almost went without saying that resources remained a major preoccupation, but in the current financial crisis funding was even more problematic. Discussions are focusing on potential mechanisms to reimburse some recommended vaccines of high public health importance (such as those against influenza). Another pressing consideration is how to insert new and combined vaccines (including hepatitis B antigen) into the already crowded immunization calendar as they become available. Innovative ways need to be found to extend the coverage of routine immunization programmes in order to reach vulnerable and underserved populations (e.g. Roma children, among whom tuberculosis is common, and in response to the recent measles outbreak).

Despite the good overall vaccination coverage rates, the questions raised about the documentation and validation of those data needed answers in order to provide a sounder base for setting priorities, guiding policy and ensuring more transparency about the epidemiological situation. Similarly, it was recognized that the seroprevalence data for blood donors were not necessarily representative of the general population, and care is needed in determining the nationwide epidemiological situation based on those data. Bulgaria was to be congratulated on the wealth of data that exists.

The vulnerability to infection of numerous health-care staff, as well as the lack of protection of many medical and nursing students, underlines the need for full implementation of national legislation on protection of the work force. Necessary measures include leadership in medical institutions to educate about infection control, immunization of future health-care workers, strengthening the infection-control teams, and capitalizing on the role and experience of "champions".

Comments in discussion highlighted the potential value of European-wide dialogue between the governmental health sector and industry and the benefits from transparency about prices and policies. This approach was relevant globally, and national experiences range from complete openness to confidentiality. The Viral Hepatitis Prevention Board has experience of eliciting information about costs paid for vaccines and published such information in the report of a meeting in 2001 on introducing hepatitis B vaccine in Central and Eastern Europe (St Petersburg, Russian Federation, 24-27 June 2001)[1]. There were calls for all vaccine-related contracts that were paid for with State funding to be published on the government's website, although in response the Government indicated that the information was available. There would seem to be a need for better communication of that information, which is also valid for other countries in the Region. Better data on the costs of treatment as well as socioeconomic costs of viral hepatitis are needed.

Finally it was observed that together the presentations and the data therein made a compelling story of remarkable progress, which reflected the considerable efforts of health workers, politicians and civil society in Bulgaria.

In terms of the global context, in May 2010, the World Health Assembly adopted resolution WHA63.18 which requests WHO to draft a comprehensive strategy and endorses World Hepatitis Day, one of only six official WHO "health days". The resolution legitimates governments to act. Work is well under way for producing materials to support Member States marking the Day on July 28, and steps are being taken at WHO headquarters and the Regional Office for Europe to develop global and regional strategies on viral hepatitis.

Possible future steps and recommendations

At the central level, it was recommended that public health tasks should be better prioritized and that the extensive reforms over the past few years should be evaluated.

Clear guidance should be issued for health education and medical institutions regarding vaccination of medical and nursing students and health-care workers in general. Further guidance was needed on possible restrictions on work practices for infected health-care workers (exposure-prone procedures) [2], and on implementing existing legislation. In addition, it was recommended that a special legal framework or regulation be created for establishing registers of the immune status of health-care personnel and students. A mandate should be given to infection-control teams for leadership in training, and educational institutions should be fostered. Education about standard precautions should start during training at medical and nursing schools, and the strict applica-

tion of standard precautions should be subject to continuous monitoring.

A recommendation was made that the legislation on blood safety control needed to be revised for viral hepatitis, in particular with regard to responsibilities for counselling infected blood donors.

Another area needing attention was prevention for, and treatment of, viral hepatitis in injecting drug users and ethnic minorities. Opportunities for prevention of hepatitis A, B and C need to be identified. Work should focus on innovative approaches for bringing routine immunization programmes closer to vulnerable populations, building on successful models such as the health mediator concept. Consideration should be given to use of hepatitis A vaccine as epidemiological pattern changes. The low rate of infection of injecting drug users with hepatitis C virus during first two years after starting drug use represented an opportunity for prevention.

Existing systems of reporting from the peripheral level are based on paper or e-mail, and consideration should be given to introducing or extending the use of web-based reporting systems, although that would need investment in training staff and developing or adapting systems. Regarding the data themselves, attention should be paid to quality control in the generation of the data (including determination of the extent to which prevalence was possibly underestimated, as for instance may be the case for hepatitis D), to improving their analysis and interpretation, and to the greater application of the conclusions in policy-making. Auditing the quality of data is essential for supporting evidence-based decision-making and providing greater transparency.

Given the relatively large rural population, better breakdown of the seroepidemiological data for rural and urban populations was recommended. The age-specific seroprevalence study should be repeated but with expanded aims and should be designed so as to be representative for the whole population in Bulgaria, and to examine the impact of the hepatitis B vaccination programmes. Clear case definitions and protocols should be developed for laboratory testing in acute viral hepatitis surveillance. Surveillance of hepatitis D should be continued, and consideration should perhaps be given to surveillance of hepatitis E virus infections, which are not yet covered.

Concern was expressed about the lack of trained epidemiologists, virologists and other microbiologists in the near future, as many experienced professionals were retiring. It was recommended that the Government consider a “business continuity” plan for training more epidemiologists, virologists and other microbiologists - increasing their numbers would bring benefits not just in the field of viral hepatitis but for work in all areas of infectious diseases.

Given the variable nature of viral hepatitis, cutting across several disciplines, it was recommended that public health experts, vaccinologists, gastroenterologists, liver specialists, infectious disease specialists, internists, general practitioners, other experts and civil society should be closely involved in the decision-making process. This could be achieved through a strategic committee or national immunization technical advisory group with a focal point or other forum for discussion, with a view to provide a mechanism for ensuring that objectives were met and to coordinate policies and programmes.

The Viral Hepatitis Prevention Board offered to provide support to health authorities and other relevant bodies in formulating proposals for policies on surveillance, control and prevention of viral hepatitis.

It was concluded that Bulgaria is making significant progress in reaching underserved and vulnerable populations. The country’s application of the health mediator model provides a valuable example for accessing hard-to-reach populations. Although 105 such mediators have already been trained and qualified, it was estimated that some 4000 would be needed to reach all vulnerable groups adequately. An even greater advance would be to consolidate the supplementary immunization activities currently being undertaken in that area into more permanent routine activities. Such action would enable Bulgaria to become a role model in Europe.

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Based on a presentation by David FitzSimons

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