



Prevention and control of viral hepatitis
in Greece: Lessons learnt and the way
forward

Athens, November 15-16, 2007

meeting conclusions

Objectives

- Overview of surveillance systems for infectious diseases in Greece;
- Update of the epidemiological situation on viral hepatitis in Greece;
- Evaluation of current prevention and control measures on viral hepatitis in Greece;
- Successes, problems and barriers to overcome, and the way forward

Sequence of conclusions presentation

- Organization of health care system in Greece
- Surveillance systems in Greece
- Diagnostic tools and epidemiology of viral hepatitis
- Vaccination policies for hepatitis A&B
- Lessons learnt and challenges

Organization of health care system in Greece

- Complex organization
- Mixed type of health care system with 3 sectors:
 - National Health Services (ESY)
 - Social Insurance Services (mainly IKA foundation)
 - Private Sector
- Primary HC centres developed mostly in rural areas, as part of NHS
- In urban areas:
 - IKA funded services
 - Large private sector – large number of private doctors and diagnostic centres

Organization of health care system in Greece

- Hospitals: 44% public (larger), 54% private (smaller);
but beds: 69% public, 28% private; meeting the WHO requirement for beds/population
- Ratio public/private expenditure has evolved to approx. 50/50, but public expenditure is mainly for hospitals, while private expenditure is mainly for primary HC

Organization of health care system in Greece

- Greece has the lowest level of public health expenditure in Europe, leading to:
 - Social/health inequalities in the access to health services (unorganized primary HC)
 - fragmented responsibilities between ministries, eg prevention; poorly regulated private sector (no evaluation and no control)
 - inadequate management of health care resources (eg nurse shortage, political management of hospital)

National Program for Viral Hepatitis prevention and control (HCDCP/KEELpno)

- HCDCP independent centre (established in 1992) responsible for :
 - surveillance and control of infectious diseases in Greece, with focus on viral hepatitis, eg HEPNET cohort study for HBV and HCV
 - implementation of immunization recommendations, eg HAV and HBV
 - education and training
 - guidelines for medical management, eg treatment and improvement of HBV and HCV patient healthcare

National Board of Immunization (NBI)

- NBI:
 - Advisory Committee to Greek MOH
 - Members mainly paediatricians (but also responsible for adult recommendations)
 - Reviews Immunization program (new vaccines) and recommendations for targeted patient groups
 - Ensures availability and distribution of vaccines
 - Responsible for report of vaccine related safety issues

Overview of HBV Immunization program in Greece

- 1982: risk group vaccination
- 1993: start campaign for UMV
- 1998: hepatitis B vaccine in national programme
 - 2,4,6-18 Mo
 - birth dose + 1-2,6-18 Mo for infants of HBsAg+ mothers

Overview of HAV Immunization program in Greece

- 1995: HAV vaccine available
- Recommended for risk groups
- Recommended but not included in NIP
- Havrix, Vaqta, Epaxal
- 1/3 of children vaccinated
 - Most private pediatricians vaccinate at entrance in DCC
- targeted versus UVM

HAV vaccination policy

- Difficult to estimate the disease burden
 - Asymptomatic
 - Underreported in surveillance system
- Natural immunity higher in the North, vaccination coverage higher in central and South
- HAV vaccine widely used, but not necessarily for those that need it most

HAV vaccination policy

- What is the way forward?
 - New cost-effectiveness studies to assist decision making process (incl. indirect costs, herd immunity effect, ...)
 - Introduction in the NIP?
 - Competition with introduction of other vaccines:
 - HPV, varicella, pneumo, rota, ...
 - Extend targeted policy to other risk groups: immigrant children, ...

Viral Hepatitis Surveillance in Greece (HCDCP)

- Objective: Disease identification, monitoring and prevention
- Mandatory notification system for selected diseases (based on case definition and standardized notification form on a weekly basis)
- Notification mainly from hospitals, but considerable non-compliance from physicians leads to major under reporting
- Future possibility: introduction of a separate laboratory notification system for viral hepatitis infections (asymptomatic versus symptomatic)

Experience from Surveillance of infectious diseases during the Olympics

- enhanced surveillance systems (daily reporting) and new syndromic surveillance system implemented
- SOPs for data interpretation
- significant expertise built among the staff of the HCDCP

HAV and HBV vaccination uptake in child population of Greece – National survey 2006

- Vaccination largely carried out in private sector (67% hepB – 88% hepA)
- Results valid for responders
- HepB
 - High vaccination coverage in young school-children (95%) but less in adolescents (85%)
 - Evenly distributed coverage among regions
 - Good coverage of immigrants (except Greek Roma children)
 - Delay in starting vaccination / completing primary course
- HepA
 - not included in NIP
 - vaccination coverage in young school-children 37% and adolescents 22%, with large differences in coverage between regions and social groups; high risk groups (minorities) vaccinated less

Migration and viral hepatitis

- Immigrants account for 7-10% of Greek population, mainly from Albania, other Balkan countries and former USSR countries, leading to a change in HBV and HAV epidemiology in Greece
- No routine serological testing performed
- Higher prevalence levels: eg up to 22% HBsAg+ in Albanian immigrants, 96% HAV+ among Albanian pregnant women, up to 2.3% HCV+ in immigrants living in Athens
- Implications for immunization policies
 - Need to reinforce HAV vaccination in susceptible children of immigrant families travelling back to home country for vacation
 - Need to implement early HBV vaccination of infants and catch up of children and adolescents of immigrants with chronic HBV infection
- Prevalence data among immigrants is underreported because only available for legal individuals – and in a fragmented way

Surveillance in Blood Bank

- implementation of ID-NAT technology, in addition to serology, reinforces the safety of blood supply, supporting the value of establishing NAT as a routine screening test
- implementation of NAT technology is particularly relevant for occult blood infection (OBI) cases, missed by HBsAg screening
- the clinical significance of OBI and the impact on donor management should be further studied in order to fully assess the benefit of NAT testing in terms of reduced morbidity and mortality

Epidemiology of HAV in Greece

- No reliable national data on disease burden (high variability of results from small studies) and significant underreporting
- Overall HAV incidence is decreasing over time.
- Greece is a country of intermediate HAV endemicity, with higher incidence in the Northern part, rural versus urban and minorities
- Surveillance data showed age shift
- Up to 17.9% of unvaccinated children 1-14 yrs (2007) with past natural infection warrants the implementation of UMV against HAV

Epidemiology of HBV in Greece

- Greece is a country of intermediate HBV endemicity (>2%) with higher incidence in the Northern part, minorities and high risk groups
- HBV incidence is decreasing over time
 - Impact of immunization
 - Socio-economic improvements
 - Health care system improvement
- Intra-familial spread of HBV still documented
HBV incidence is highest among 15-24 yrs old
- Factors influencing the current epidemiology include modes of transmission, travelling, immigrants (high HBsAg rate, high eAg+)

HCV epidemiology in Greece

- Greece is a country of low HCV endemicity (<2%) with highest incidence in Athens region (IDU)
- A higher incidence is also observed in minorities and high risk groups (blood transfusion, IDU etc)
- Surveillance data indicate that HCV incidence is decreasing over time

HDV epidemiology in Greece

- No HDV data representative of general population in Greece
- Mainly in IDU or specific areas, higher rates in immigrants (study in Albanians: 12,7%)
- High risk groups include IDU, prisoners, HIV+, prostitutes, minorities

Epidemiology HEV

- Little data available
 - Healthy blood donors: 0.23%
 - Healthy workers: 2.2%
 - Higher prevalence in hemodialysis patients
- No evidence of endemicity from few existing data
- Further research could be considered on environmental link and animal reservoir

Molecular epidemiology of HBV and HCV

- HBV genotype D most frequent in Greece, followed by A and G
- Several HCV genotypes detected, predominance of genotype 1 (particularly in older ones), with fast increase in prevalence of genotype 3 since 70's (esp. in younger ones)
- Distribution of HCV genotypes in Greece is different from other Mediterranean countries.

HBV, HCV patients and HIV co-infection

- Hepnet = uniquely large cohort of chronic HBV and HCV patients followed up since 2003 in a retrospective-prospective study
- Early diagnosis of infection – data may be used to improve prevention and control
- Prevalence of HCV co-infection in Greece is relatively low among HIV patients
- HBeAg+ incidence is high in co-infected HIV patients unlike HIV neg patients in Greece

Overall: lessons learnt/ challenges/ the way forward

- High involvement of private sector in HC services leads to social inequalities
- High involvement of private sector in immunization practices (>60%) may leave unvaccinated population unprotected and contribute to shifting epidemiology to older age groups
- Delay of first HBV dose increases risk for chronic carriage
- Absence of national hepatitis seroprevalence data
- Absence of reliable surveillance systems
- Lab notification of hepatitis cases would help reducing underreporting by private physicians
- Development of several approaches to obtain national seroprevalence data, eg use of residual serum from routine testing
- Shortage of data of immunization status of HCW
- Higher HAV, HBV and HCV incidence in immigrants deserves special attention in terms of immunization policy

Lessons learnt

- HAV:
 - Decreasing with changing epidemiology
 - Migration related; risk factors known
- HBV:
 - Need for data in the general population
 - Residual reservoirs of carriers known
 - Migration and socio-economic related
- HCV:
 - Low level
 - Genotype 3 increasing
 - Higher data in some groups need better understanding and follow-up actions
 - Risk factors remain through failure of prevention in medical practice

Research challenges

- As epidemiological data are often fragmented and not based on representative samples:
- Figures are sometimes puzzling
- Need for verification in larger representative cohorts
 - In particular for HCV prevalence data
- different approaches for a national sero-prevalence study were presented and discussed to document:
 - prevalence (age-specific)
 - Burden of diseases
 - Impact of preventative interventions

Research challenges (con't)

- 4 alternatives:
 - Based on current data, to build a prediction model through back calculation methods
 - Sero-prevalence study based on residual samples (ESEN-like)
 - Population based sero-survey
 - National health survey
- All have their pros and cons
- Funding will be a major issue
 - Linking with HIV sero-prevalence could be a possibility

Research on surveillance and vaccination uptake

- Set up campaigns to stress the importance of timely hepatitis B vaccination
- Use of combined vaccines could be promoted
 - Pay attention for the financial issue
- Vaccination coverage study to be repeated

Need for further research

- Need for further research on the potential implication of high HCV in HCW in some hospitals
 - Issue of further spread
 - Issue of exposure and universal precautions
- Planned research within the Hepnet study

strengths

- Group of remarkable scientists, doctors and public health experts
 - Tackling the well known problem of viral hepatitis
 - Large research output
- Clear early identification of viral hepatitis as a public health burden

strengths

Aware of the limitations of some data

- Willingness to design and perform additional epidemiological studies
- Issuing and updating documents and recommendations (HCDCP)
- Coordinating a large nationwide cohort study (hepnet-study)
 - Which improves collaboration (30 centres)
 - Confirms results from other smaller studies
 - Common standards of care can be introduced
 - To achieve more effective treatment need for early diagnosis of HBV and HCV (through better screening and surveillance)

strengths

- Use of EU case definition in the surveillance system of hepatitis A and B
- Enhanced surveillance system during the Olympics could be maintained for routine surveillance by HCDCP
- Child Health Booklet is a unique source of data on immunization status of children in Greece

challenges

- Private public health system
 - Rapid introduction of new vaccines
 - No immediate guarantee to cover the whole country
 - Inequalities remain
 - In particular in immigrant population (7-10%)
 - In lower socio-economic population

challenges

- Decision on UVM HAV vaccination
- Bring the Israeli experience into practice
 - Decision making process
 - pros and cons
 - Area of endemicity in transition
 - High contact rate between high and low socio-economic risk groups – number of outbreaks?
 - Fulminant hepatitis A?
 - Priority setting
 - Cost-benefit analysis
 - Long-term view!

challenges

- Many issues have been raised regarding the HBV-HIV and HCV-HIV co-infections
 - Diagnosis, influence on progression, efficacy of treatment, therapy completion, drug interactions, ...
- Increasing experience with treatment of HIV-HBV and HIV-HCV co-infected patients, but further need for LT follow-up
- Attention should be paid to strengthen primary prevention: harm reduction measures, needle exchange programmes, ...
- Enhance HBV vaccination policy
- HBV and HCV treatment in HIV+ should be enhanced
- Data relating to preventive measures taken to reduce HIV/HBV/HCV infections in IDUs should be made available

recommendations

- As higher HCV prevalence reported to be associated with some iatrogenic practices (use of glass syringes, non-disposable material, dental practices, surgery, hospitalisation, ...)
 - Attention should be paid to:
 - how to control this
 - Implement standard precaution measures
 - Emphasize importance in (para)medical education

recommendations

- Design large representative cohort studies
- Consider vaccine coverage study in younger age groups, if feasible
- Hepatitis A vaccination programme for immigrant children before visiting endemic home country
- Need to document health issues in migrant population as there are implications for immigrants as well as for the Greek population
- Clinical significance of occult HBV infection needs to be further explored