Objectives

- Review surveillance systems for infectious diseases
- Update the epidemiological situation on viral hepatitis
- Evaluate current prevention and control measures for viral hepatitis
- Discuss possible implementation of new prevention strategies, control measures and monitoring systems
- Identify successes, problems and obstacles, and the way forward
General observations

- The more we know the more we don't know
- Changing epidemiological patterns and behaviours (for hepatitis A, B, C and E)
- Seemingly contradictory views
  - E.g. rising global HB immunization coverage will affect epidemiology (implied reduce need for immunization) vs global pressure for universal immunization
  - advocating wider screening to prevent later mortality but not advocating universal vaccination
- Transformation of hepatitis B and C: from non-preventable and non-treatable to preventable (hepatitis B) and treatable (hepatitis B and C)
- Very high standard of measurement and documentation in the Netherlands, with response to problems identified (committees formed, guidelines produced)
- The Netherlands shows high competence in programmatic issues
- In the Netherlands, clinicians and epidemiologists/public health specialists hold different perspectives; debate is vigorous and open
- Lack of knowledge about viral hepatitis persists nationally, among public and professionals (GPs)
Dutch health-care system

- Ministry of Health
  - National Institute of Public Health and Environment (RIVM) (NIP)
  - Netherlands Vaccine Institute
  - Health Council
  - Sets research direction
- Municipal health authorities (GGD)
- National Hepatitis Centre
- Other stakeholders (NGOs, civil society…)
- 1 December 2008: new Public Health Law
Programme and its future being reviewed
Assessment framework created for informed decision-making
Criteria (7) defined for provision of vaccine to given groups
All 15 vaccines in the National Immunization Programme meet these criteria
Criteria applied to 23 candidate vaccines: no unqualified recommendation, but 4 require additional analysis (including universal vaccination against hepatitis B)
Scientific advisory report on universal hepatitis B vaccination due to be submitted to the Ministry of Health end-December 2008
Hepatitis B vaccination in the Netherlands

Introduction of vaccination:
- 1989: vaccine given to children born to carrier mothers
- 2001: health-care workers vaccinated (intensified programme)
- 2002: policy of targeted programmes (intensified activities)
- 2003: children with at least one parent from country with high or intermediate endemicity vaccinated

National findings:
- Vaccination coverage of children born to infected mothers reported to be very good
- Assessment: universal vaccination would be more effective and feasible than targeted approach but questions about priorities
Surveillance and systems

- Surveillance of infectious diseases is the task of the RIVM Centre for Infectious Disease Control
- Web-based notification system exists
- New Public Health Law (December 2008) will replace three existing laws
- 42 diseases are now notifiable, including hepatitis A, B and C (the latter only if acquired less than one year before)
- Clinicians, laboratories and heads of institutions must report
Surveillance and systems

- Numerous databases and documentation systems
  - National: Population register, Osiris (infectious diseases), Praeventis (all infant vaccines); occupational health databases, data from cohort studies, others; seroepidemiological studies – national samples (B and C); no national register of people with high-risk behaviours

- Current system performs powerfully

- National Hepatitis Centre
  - Knowledge clearinghouse; web site, printed publications, information resource
  - Prevention and health promotion
  - Coordination and promotion of studies

- Several pilot projects on surveillance of hepatitis C infection (including specific groups, such as pregnant women and STI clinics), but no routine active surveillance

- Passive reporting system for adverse events
Surveillance and systems: limitations

- **Hepatitis A:**
  - seroprevalence (Pienter) study
  - significant under-reporting (~50%)
  - vaccination not recorded

- **Hepatitis B**
  - seroprevalence (Pienter) study
  - asymptomatic infections not registered in reporting system
  - occupational vaccine coverage not aggregated
  - few seroprevalence data for high risk groups
  - mortality difficult to assess

- **Hepatitis C:** asymptomatic infections not detected
- **Problem of lack of knowledge about denominators**
Epidemiology – hepatitis A

- Hepatitis A – "not a serious public health problem but a problem for public health"
- Seasonal epidemics in Turkish and Moroccan communities after travel to home countries; subsequent outbreaks in communities
  - Decreasing; limited transmission chains; effective contact tracing; decreasing endemicity in source countries; possibility of use of combined hepatitis A+B vaccine (although difficult logistically)
  - Proposal to vaccinate (or fund vaccination of) children in source countries
- Continuing transmission in men who have sex with men
  - Contact tracing not possible because of anonymous sex
  - Possibility of use of combined hepatitis A+B vaccine (although difficult logistically) through hepatitis B vaccine programme
- Food-borne transmission
  - Enhanced surveillance
  - European collaboration
Epidemiology – hepatitis B

European Union: ECDC year report referred to 7500 new cases/year; male/female ratio ~2; clustered in risk groups; prevalence varies widely

Netherlands:
- Seroprevalence (1995; Pienter study): 2.1% anti-HBc, but results of 2007 study due soon; >1400 new chronic cases notified per year; 700 pregnant women (mostly immigrants) found HBsAg+ each year. Despite the different database systems there is still a lot of variation in the reported cases.
- In 2006: 240 acute cases were reported, 1.5 per 100,000 inhabitants. (RIVM)
- Chronic infections of hepatitis B increasing in men but overall stable for 5 years, with major contribution from perinatal transmission
- Acute infections in MSM with circulation of virus in that population
- HIV deleteriously effects hepatitis B (including faster progression to cirrhosis)
- Migrants contribute strongly to chronic infections burden
- Mortality statistics for hepatitis B ignore mortality due to cirrhosis and hepatocellular carcinoma: their inclusion puts mortality at several times higher than HIV, and rising, despite introduction of antiviral therapy; confirmed by modelling
- Low national prevalence rate can hide areas of higher endemicity in the country
- Targeted screening will increase access to treatment
Epidemiology – Hepatitis C

European Union: 27,000-29,000 new cases of hepatitis C diagnosed each year; male/female ratio ~2; clustered in risk groups including migrants from endemic countries (but no sexual transmission); prevalence varies widely

Netherlands:
- Low prevalence (lower end of WHO European Region range, i.e. 0.1 – 4.5%)
- Little known about general population – general population surveys (0.08-0.6%) and Health Council estimate (11,000-46,000 people) are both underestimates; possibly 12,600 cases in immigrants (from prevalence of source countries)
- Main risks: injecting drug use (ever), recipient of blood before 1987, haemophilia and haemodialysis, men having sex with men (notable epidemic in HIV-positive men), first generation immigrants
- No heterosexual transmission
- Unexpected and rapid spread of HCV in HIV-positive men who have sex with men
Epidemiology – Hepatitis C

- Blood donors: a few cases are detected each year
- The predominantly asymptomatic course of infection means that 75-80% of infections are not yet diagnosed
- Incidence is falling in injecting drug users
- Improved treatment regimens led the Health Council in 2004 to urge information for those at risk and further epidemiological studies
- Coinfection with HIV: HIV increases cirrhosis and rate of progression in HCV-infected subjects; treatment is less successful
Epidemiology – hepatitis E

- Hepatitis E is not notifiable
- Seroprevalence is about 2-3% and about 6% in acute hepatitis patients
- Until recently, hepatitis E was related to travel; non-travel risks include older age, underlying disease, consumption of raw pig meat (anecdotal, but no proof) or pig meat more than once a week, and receipt of a blood transfusion in the incubation period
- Currently, endemic infections are due to genotype 3 of the virus (US/swine)
- The virus is found in surface waters and in pigs (which form the reservoir, with a 50% seroprevalence)
Epidemiology – new tools

- Molecular typing of genotypes of hepatitis A, B, C and E viruses
- May be powerful tools for:
  - Identifying sources of food-borne HAV infections (national study)
  - Evaluating effectiveness of targeted vaccination programmes
  - Identifying new sources of infection and population dynamics
  - Detecting spread of antigenic variants, resistance and immune escape mutants
  - Predicting route of infection in general population (e.g. HCV)
Of the Netherlands' 16 million population 10% are first generation migrants and 10% second generation migrants.

Most migrants come from countries with historically intermediate prevalence rates of hepatitis B and C (Turkey, Suriname, Morocco, Indonesia).

Migrants were under-represented in the previous (Pienter) seroprevalence study, but that factor has been corrected in the recent study.

About 60-70% of all chronic hepatitis B patients were born abroad in high-endemic countries.

In 60% of heterosexual cases, source was a partner from a region endemic for hepatitis B.
HCV prevalence rates range between 1% and 5% in the main source countries (Turkey, Indonesia, Morocco and Egypt).
The prevalence of HCV in first generation migrants is estimated to be 2.2%.
First generation migrants are responsible for 56% of HCV infections (besides injecting drug users and transfusion recipients).
Residence >5 years abroad may be a risk factor.
Prevention and control

- Treatment of chronic hepatitis B is a successful public health measure, but a study predicts halving of clinical benefits if resistance not addressed.
- Guidelines for prevention of occupational HBV infections exist – with a higher threshold for exclusion of infected health-care workers than in EU policy; no guidelines for HCV-infected health-care workers, but they will now be prepared.
- Guidelines on screening of newborns for HBV have been updated to include guidance on management of HBsAg+ mothers (including monitoring and treatment with lamivudine).
- Migrants and close contacts are a major target for screening and treatment for hepatitis B and C.
- Universal screening and/or vaccination of all new migrants against hepatitis B would be good prevention, but feasibility is an issue.
- Culturally sensitive information on all aspects of viral hepatitis needs to be provided in appropriate languages in order to support care.
- Two tailored pilot screening programmes for migrants are being designed for Turkish and Chinese migrants.
  - Intention to be screened found to be strongest in people firmly rooted in their ethnic group, who have high regard for Dutch health services and who are self-confident, but negatively linked with associations of hepatitis B with sexuality and sexual behaviour.
Vaccination programmes

- New vaccines being introduced in many European countries; introduction of HB vaccine was model for that of other, new vaccines
- WHO, European Parliament and British Medical Association call for universal immunization of infants against hepatitis B; targeted programmes are "supplementary"
- WHO in disagreement with Dutch policy
- Universal immunization showing good results in implementing countries (e.g. Italy)
- In the Netherlands:
  - high rates of coverage of HBsAg-positive mothers
  - effective perinatal transmission prevention programme
  - good coverage of infants of immigrants (leading to the conclusion that it is "not difficult to reach target groups"); impact difficult to assess
  - transmission stopped in injecting drug users, but not due to HB vaccine programme
  - 7% of MSM vaccinated (but could be much higher in subgroups); those with risk behaviours more vaccinated? Impact difficult to assess, but number of hepatitis B virus infections decreasing; focus on MSM "not very effective"
  - risk-group programmes said to be cost-effective (but subject of debate), stigmatizing?
  - effect of financial crisis, given commitment to human papillomavirus vaccine?
  - vaccine free for MSM not heterosexuals (despite proportion of transmission by "heterosexual" and "unknown" being >50%)
  - strong arguments marshalled for universal vaccination programme, vigorous defence of exclusive vaccination of risk groups
Future – needs/developments

- Need for integrated approach
- Need to monitor programmes and spread of antiviral resistance
- Molecular typing, including surveillance of antiviral resistance, access to treatment and behaviour, new phylogenetic methods
- Consider incentives for reporting data
- Need to detect and monitor chronic hepatitis B and C patients
- Full economic burden of hepatitis B (including treatment and management of chronic liver disease and cirrhosis) needs to be established
- Annual screening for HCV of health-care workers performing exposure-prone procedures
- Economic, up-to-date analysis for different vaccination approaches
Lessons learnt

- Ethical issues can be resolved, e.g. issues such as:
  - "positive discrimination" in favour of migrants
  - insurance and HBsAg-positivity
  - access to treatment
- Think big – at European Union/Region level (for support and joint programmes)
  - e.g. EuroSIDA (HCV/HIV), European Study Group for Viral Hepatitis
  - Management of HCV-infected health-care personnel
  - European Immunization Week
- Current immunization programme validated by assessment criteria and retains public confidence (high coverage rates)
- Existing interventions offer opportunities for added interventions and data collection
- New public health law will strengthen data and evidence base
- Guideline on prevention of iatrogenic hepatitis B has power of law; guideline for HBsAg+ pregnant women resulted in more HBV+ women seeing a specialist
- Share methods to achieve high coverage of infants of HBsAg+ mothers and immigrants with other countries
- Dedicated person overseeing immunization of infants of HBsAg+ mothers
Lessons learnt

- Impact of prevention not easily measured in target groups
- Impressive declines reported for universal programmes, e.g. Taiwan, Italy
- Powerful new surveillance tools (e.g. molecular epidemiology and modelling), but too early to produce answers to questions about evaluating vaccine programmes
- Behaviours can change/be changed (e.g. move from injecting drugs) but not all: unsafe sex in travellers and (high (increasing) levels) in HIV-positive men who have sex with men
- Continuing need for advocacy (themes: hepatitis B and C "silent killers"; chronic diseases: interventions will need 30-50 years to prove full effects; hepatitis B vaccine is an anticancer vaccine)
- Need for better screening for, monitoring of, and treatment of chronic HBV infection
- Screening annually for acute HCV advised in some risk groups
- Good treatments available (including combination therapy in HIV/HBV patients); early treatment valuable (tertiary prevention); but liver toxicity and concerns about resistance
Lessons learnt

- Good information essential; still need to overcome barriers of ignorance (general practitioners, general population) and prejudice, but anti-vaccine messages seem to be weakening
- Needle-capping *still* a risk factor for occupational infections; inexperienced staff involved; some personnel unimmunized – programmes being introduced to raise awareness
- The alternative to increasing the number and complexity of targeted programmes is universal vaccination
- Targeted programmes do not reach all those at risk
- In low-endemic countries without universal HB vaccine programme travel and immigration increasing prevalence of chronic infections and risk of HBV infection
- Ireland introduced HB vaccine also on health economic grounds; Italian data show large savings
- "All countries can be turned into low-endemic areas"
- Netherlands has a very strong infant immunization programme and wants to protect it; evidence from other countries shows that introduction of new vaccine does not undermine, indeed can increase coverage
**Challenges**

- What is "burden" of disease? – it depends on individual, country, region...
- Discrepant data (coverage rates, national variations)
- Gaps in reporting/data on which different policy decisions about universal vaccination are made in low endemic countries
- Data on and protection of health-care workers not seen as a high priority
- Cost effectiveness vs affordability
- Outreach to groups at risk; more than 30% of people with acute hepatitis B have no identifiable risk factors and would be missed by risk-group approach
- Questions about success of prevention programmes and behavioural change; changes in practices; consequences of HIV becoming a chronic and manageable disease
Challenges

- Improvements in technology may need re-thinking guidelines (e.g. infected health-care workers)
- Screening needs more attention
- Lack of standardization of surveillance in the WHO European Region
- Surveillance focused on acute infections which are not seen
- Increasing migration and travel
- Immigrants screened for tuberculosis but not other infectious diseases
- Treatment: antiviral resistance; questions about impact on perinatal transmission; general practitioners' concerns/lack of knowledge about treatment in pregnancy
- Increasing political commitment and involvement of private sector
- Universal vaccination versus targeted approach: "simplicity" vs "public health priorities"
- Targeted approach would be continued
- Globalization and financial crisis
- Is prevention of hepatitis B a priority for the Netherlands?