EXPANDED PROGRAMME ON IMMUNIZATION

Report on the seventh WHO Meeting of National Programme Managers

Berlin
10–12 November 1997
TARGET 5

REDUCING COMMUNICABLE DISEASE

By the year 2000, there should be no indigenous cases of poliomyelitis, diphtheria, neonatal tetanus, measles, mumps and congenital rubella in the Region and there should be a sustained and continuing reduction in the incidence and adverse consequences of other communicable diseases, notably HIV infection.

ABSTRACT

The purposes of the Meeting were to introduce the European health for all policy for the twenty-first century, to discuss measles elimination, to advocate the strengthening of disease surveillance and development of laboratory networks, to present cost–benefit analysis models as tools for decision-makers, to discuss the systems of reporting on diseases covered by the WHO Expanded Programme on Immunization (EPI) and to present progress on poliomyelitis eradication/certification and diphtheria control. Essential components of a measles elimination plan for the WHO European Region were presented and the national programme managers endorsed the previous recommendation of the EPI European Advisory Group, that the elimination strategy, based on identification of susceptibility, was the most appropriate approach for the Region. Countries would need to categorize the control achieved through their current measles strategies, make appropriate analyses to estimate susceptibility and identify the appropriate way forward. The national programme managers agreed that continued efforts were needed to improve surveillance, especially for poliomyelitis, measles, hepatitis B and diphtheria. They acknowledged the progress towards poliomyelitis elimination, recognized the obstacles and reviewed the certification process.

Keywords

EMERGING DISEASES – prevention and control
IMMUNIZATION PROGRAMS
PROGRAM EVALUATION
EPIDEMIOLOGIC METHODS
MEASLES – prevention and control
POLIOMYELITIS – prevention and control
DIPHTHERIA – prevention and control
HEPATITIS B – prevention and control
HEALTH FOR ALL
EUROPE
EUROPE, EASTERN
ASIA, CENTRAL
COMMONWEALTH OF INDEPENDENT STATES
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Introduction

The seventh meeting of national immunization programme managers was held from 10 to 12 November 1997 in Berlin, Germany. The meeting was chaired by Dr Norman Begg, the Vice-Chairperson was Professor M. Koch, the Rapporteur was Dr David Salisbury and the Secretary was Dr Colette Roure. Mr Franz Bindert welcomed participants on behalf of the German Government, and drew attention to the needs and challenges of the wider Europe between countries of the north and south and countries of the east and west.

Dr Björn Melgaard welcomed participants on behalf of WHO, noting that this meeting was an opportunity to look ahead to the future. Although global coverage meant that more than 80% of the world’s children had access to at least one immunization and all countries have immunization programmes, there was still much to achieve. As regards progress towards polio eradication, the western Pacific was now virtually free of polio with notable impact being reported in Cambodia and Vietnam. India had managed to achieve more than 126 million polio immunizations in a day in early 1997 with cases dropping dramatically to below 1000 and no nationwide epidemics. This year, there have only been three cases of wild virus polio reported in the European Region, thanks in no small part to the success of Operation MECACAR. Although success in measles control/elimination was being reported in PAHO, the southern cone of Africa, the Gulf states and parts of the western Pacific, in Europe coverage was at a plateau. There remained many gaps and opportunities and new potential from a range of new vaccines already available and others soon to be available. However, there were systematic and technological challenges, particularly in immunization service delivery, including safe injection, syringe disposal and cold chain management. Health care provision was changing rapidly as health service reforms were introduced, and the EPI would need to be maintained and promoted in this changing environment.

Scope and purpose

The scope and purpose of the meeting were to:

- introduce the health for all (HFA) policy for the twenty-first century for Europe;
- keep the EPI programme managers informed about the latest developments on measles control/elimination;
- elaborate policies/strategies for the development of national plans for measles elimination;
- advocate the strengthening of disease surveillance and development of laboratory network (polio, measles, diphtheria, hepatitis);
- present cost–benefit analysis models as tools for decision-makers;
- discuss the reporting system for EPI diseases and appropriate feedback;
- present progress reports on polio eradication/certification and diphtheria control in Europe.

Summary of recent EAG activities

The EAG activities since the last meeting of national programme managers were summarized. A measles elimination target by 2007 had now been recommended for countries of the WHO European Region and a strategy is being developed. This will be based on identification of susceptibility with countries categorized according to their measles control
activities and outcomes. The WHO Regional Director for Europe has proposed to bring the measles elimination strategy to the Regional Committee in 1998.

For polio eradication, it has been recommended by EAG that there should be a minimum of three annual national immunization days (NIDs) where there is evidence of recent polio virus circulation. NIDs may need to continue to be held until sensitive surveillance shows that they are no longer necessary. Since a number of recent polio outbreaks have been linked to gypsy populations, it is recommended that there should be a regionwide initiative to work with gypsy communities to ensure polio immunization. EAG reaffirmed that OPV was the vaccine of choice for polio eradication purposes.

Whilst the diphtheria epidemic in the newly independent states (NIS) seemed to be waning, it remained essential that high coverage be achieved with three doses of diphtheria-containing vaccine by six months of age and three further doses be given before adulthood (16–36 months, school entry and school leaving). Adult booster doses were not recommended as routine unless there was a perceived risk of diphtheria, with opportunities for immunization where appropriate.

The EAG confirmed that where there was evidence that high quality whole cell pertussis vaccine was in use, then this should be the mainstay for routine immunization and that acellular vaccines were most suitable as booster vaccines since they are costly and may not offer any advantage in terms of efficacy. Where perceived reactogenicity to whole cell vaccine has been a problem, acellular vaccines may be better accepted. The reported interference between acellular vaccines and Hib vaccine requires further elucidation. In the case of Hib vaccine, it was considered essential that the burden of disease should be assessed so that the cost of introducing Hib vaccine could be justified. There was a need for specialized laboratory support, and this may require collaboration and cooperation between countries where such facilities may not already be present.

**Measles**

**Global measles overview**

Measles coverage at global level appeared now to be static at around 80% and is of concern. The proportion of countries with more than 80% coverage is declining and the number of notified cases has increased in 1996 compared with 1995. There were still an estimated one million measles deaths globally, half of them in Africa. Major issues that were holding back measles immunization in industrialized countries were misconceptions about disease severity, although studies in a number of those countries revealed 10–20% of cases to be associated with complications and 2% were hospitalized. As large parts of the world are achieving measles control or elimination, the role of international seeding of measles becomes increasingly important.

**European Region**

An analysis was presented of the 1996 regionwide survey of measles. Ninety per cent of countries, representing 98% of the population of the Region, had returned the questionnaires. These dealt with the national history of measles immunization, service provision, coverage, epidemiology, surveillance and elimination goals. This survey will be published in the very near future. However, poor surveillance was noted including lack of statutory notification, particularly in three European countries. The lack of specificity of clinical diagnosis requires laboratory services to be employed for case confirmation. In some countries, measles control was hampered by low coverage, whilst even in high coverage countries, outbreaks continue to occur because of gradual accumulation of susceptibles. The strategic plan for the WHO European
Region, designed to further reduce the morbidity and mortality for measles in the Region and eventually to eliminate indigenous measles from Europe by the year 2007, was described. The objectives of the strategy were to reduce the estimated proportion of measles susceptibles in the population to low levels by the year 2005, and to maintain these low levels of susceptibility until 2007, by when elimination was estimated to be attained. The proportion of susceptibles in each age group must not exceed 15% in children aged 1–4 years, 10% in 5–9-year-olds, 5% in 10–14-year-olds and 5% in each cohort of adults above this age. These levels of susceptibility are those felt to be sufficient to lead to interruption of measles transmission. Key steps in the achievement of the objectives are:

1. establishment of political commitment to measles elimination;
2. developing a measles elimination plan based upon assessment of local epidemiology;
3. achieving and maintaining high routine immunization coverage for the first dose of measles vaccine, and ensuring high coverage in all geopolitical units;
4. strengthening the surveillance of measles by:
   • monitoring measles vaccination coverage;
   • instituting or continuing the national statutory reporting of suspected measles;
   • use of a standard case definition;
   • establishing the laboratory resources to assist measles surveillance tasks;
   • laboratory support to perform confirmation of diagnosis, to attempt virus isolation and to assist with serological surveillance;
   • providing regular analysis and feedback of surveillance and coverage data;
5. estimating the age specific proportion of the population who are susceptible to measles;
6. choosing an appropriate strategy to accelerate measles control;
7. choosing an appropriate strategy to maintain measles elimination.

Based on the national epidemiological data and coverage data, countries will be classified into three groups, namely those countries close to elimination, those with good control but with potential for future outbreaks and those with poor control. In the case of each category, there are specific tasks necessary either to remain in Group 1, or to move progressively from lower groups to higher groups.

Mathematical modelling of data available in France demonstrated that the present strategy, involving the two dose programme administered after the first birthday and at age 11–13 years, with a catch-up programme available at 6 years, would not suffice at present levels of coverage to prevent regular measles epidemics. With reduced but not interrupted transmission, there would be a progressive shift of measles towards cases in older ages, with consequent higher morbidity and mortality. Operational difficulties meant that a nationwide campaign to reduce the pools of susceptibles and interrupt transmission would be extremely difficult. It had therefore been recommended that the second dose of MMR vaccine should be given routinely at age 6 years along with efforts continuing to be made to raise routine coverage.

The economics of different measles interventions were presented, using economic analysis to provide a basis for priority setting in relation to measles vaccination. The model was based on an economic evaluation of different strategies in a hypothetical western European country examining two different scenarios, namely a past history of routine single-dose vaccination with 70%
coverage and also with 90% coverage. Policy options examined were: no change in policy; addition of a second dose at either 70% or 90% coverage; increase in coverage of the first dose to 95%; a two-dose policy with higher coverage for both doses; a two-dose policy with higher coverage for both doses with the implementation of one-time mass vaccination campaign aimed at older age groups with susceptibility levels higher than 5%. It was found that any of the options were better than that of maintaining pre-existing coverage at either 70 or 90%. With either starting coverage, it is better to increase coverage of single dose vaccination to 95% than to introduce a two-dose strategy, particularly with poor coverage of both doses of a two-dose programme. With a history of low coverage (i.e. 70% or less) and once coverage of 95% is established for the first dose, it is preferable to move on to a strategy with both a routine second dose and a mass campaign to reduce susceptibles, than a strategy employing two doses without a campaign to eliminate susceptibility in older age groups. With a history of high coverage (i.e. 90% or more), sustained for a long period, it seems more cost effective to attain a 95% two-dose vaccination strategy without an additional mass campaign, than with an additional campaign.

**Outcome of measles workgroups**

**Group A (mostly EU and northern European countries)**

Problems identified, that were inhibiting measles elimination, included the application of false contraindications, difficulty in access for immigrant populations, refusals from “informed” parents, paucity of data from private sector providers and lack of appreciated severity of measles. Specific actions needed included working with “hard to reach” groups, maintaining coverage when perceived risk of diseases is low, providing practitioner or nurse training on counselling for parents, working with media and marketing experts, and providing updated information for parents, particularly on adverse events. Efforts to improve surveillance would include heightened primary care reporting, the use of salivary diagnosis for confirming measles infection rather than blood samples, increasing laboratory testing, and ensuring consistency in diagnostic methods used in laboratories.

**Group B countries (mostly central or south European countries)**

Countries in this grouping were categorized as either III or II status and all except five representatives disagreed with these classifications. Causes for disagreement were relatively minor, usually centred on the interval between epidemics, or length of time that high coverage had been attained. Although laboratory testing was available in all countries, the rate was usually unknown. Frequency and quality of coverage measurement needed improvement. There was general agreement that the main priorities were to achieve high coverage and political commitment. Perceived obstacles to measles elimination were professional and public perceptions over measles severity, divided responsibilities between different government departments with responsibility for immunization or resource provision, vaccine safety concerns, infrastructure weaknesses in immunization service provision, especially where there was a significant contribution from the private sector, competing resource needs and scepticism over the feasibility of measles elimination. Greater publicity should be given to international importations of measles.

**Group C (central European and Baltic countries)**

These countries were all in categories II and III. The first priority was to improve coverage for the first dose and it was appreciated that two countries (Albania and the Republic of Moldova) would need to introduce a routine second dose. Five countries identified a need for measles immunization campaigns to interrupt transmission. Although there was political commitment, it was appreciated that there was often tension between competing programmes for
resources. Seven out of nine countries would need further laboratory support to improve measles surveillance and seven out of nine would require external support. The importance of achieving high coverage in all geopolitical units, rather than national averages, was stressed.

**Group D (eastern European and central Asian countries)**

These countries were all classified as group III countries although one was approaching group II. There was no disagreement with the categorization. Priorities were the achievement of high coverage, achievement of the implementation of appropriate strategies, improving surveillance including laboratory services and the requirement for external resources. Coverage would need to be increased along with public awareness and social mobilization, particularly to deny false rumours over vaccine safety. National immunization days (NIDs) may be needed along with catch up initiatives in high-risk groups, and polio NIDs could be used for some catch up work but not for joint measles and polio NIDs. Surveillance and coverage monitoring required improvement and laboratory services would need to be upgraded along with efforts to improve human resources. External support would be particularly needed for cold chain equipment.

**Recommendations**

At the 1997 meeting of EURO national programme managers, the March 1997 recommendations of the EAG were endorsed.

The EAG was convinced that the elimination strategy, based on identification of susceptibility, was the most appropriate approach for the European Region. Countries will need to categorize their present measles strategies and make appropriate analyses to estimate susceptibility and identify the appropriate way forward. In some countries this will be done using serological surveillance, while in others it will be done on the basis of estimates using immunization coverage data and disease-reporting data. Countries that do not have such historic data could proceed rapidly to identification of susceptibility through the use of sero-sampling. The elimination of measles will require the maintenance of high coverage and the absence of disease in some countries for a significantly long period of time. Under such circumstances, the potential seriousness of the disease is no longer apparent and parental and professional concerns of adverse events appear more significant. The global eradication of measles would then allow the stopping of measles immunization and such concerns would no longer be relevant. The EAG agreed that the target date for elimination should be set at 2007 but this could be accelerated especially if some western European countries, where measles control is presently of low political priority, were to make a full commitment to elimination.

A number of actions will be necessary for implementation of the measles elimination objective. A plan of action will be necessary for regional activities, including operational milestones and cost estimates. This will require endorsement by the Regional Committee and referral to national governments for action. Each country will have to interpret the regional plan of action in the light of its own circumstances and develop its national plan of action. All opportunities should be sought to recruit support of national and international agencies as soon as possible.

Starting from the existing scheme of country categorization, national programme managers will need to identify the steps needed to achieve country Group 1 status. By autumn 1998, countries should have developed operational plans for measles elimination activities, ready for submission to WHO/EURO. By this time, WHO/EURO will have completed a regional plan of action for measles elimination with key milestones identified and resource requirements detailed.
**Strengthening surveillance – laboratory support**

**Poliomyelitis**

The Global Commission for the Certification of Eradication of Poliomyelitis has identified the critical importance of laboratory surveillance in the process of eradication of wild polio virus. All laboratories in the European Region will require WHO accreditation and the process starts this year. Transportation of specimens will need to be monitored with appropriate performance indicators, particularly in countries where AFP surveillance will be the mainstay. The laboratory network in the European Region will have four specialized reference laboratories (Bilthoven, Helsinki, London, Paris) and these laboratories and one in Moscow will act as regional reference laboratories. Sub-regional laboratories will be in Rome and Sofia and possibly Almaty and Tashkent. At the beginning of the laboratory network development in 1993 proficiency testing scores were around 65%; in 1997 these had risen to 91%.

**Measles**

Many rash and fever illnesses have similar clinical presentations as measles and as the disease incidence declines, so does diagnostic specificity; at younger ages, specificity of diagnosis is also low. The role of measles laboratories will include monitoring and verifying transmission through confirmation of outbreaks, confirmation of cases, and sequencing and mapping of isolates. Laboratories will also contribute to the monitoring of susceptibility profiles through identification of age distribution of susceptibles, ideally through opportunistic serosampling rather than dedicated studies, measuring the impact of campaigns and providing validation of model predictions. As with polio, there will be national laboratories that can confirm diagnoses, undertake quality assurance and epidemiological surveys; regional laboratories will have training responsibilities, do further quality assurance work, and undertake virus detection and research. Global laboratories will undertake quality control, set up strain banks, undertake proficiency testing and provide technical advice and research.

**Hepatitis B**

Hepatitis A, B, C, D, E and G cannot be differentiated on clinical grounds and laboratory services are essential. Although services are available to identify HbsAg to separate B and non-B cases, diagnostic facilities for other types are not available in much of the Region. Nevertheless, special studies can be implemented to define the relative contribution of the different types. Since acute disease surveillance considerably underestimates the disease burden, and there is an inverse relationship between the likelihood of chronic infection and symptomatic presentations, laboratory facilities are of utmost importance. Except for Hepatitis B vaccine coverage, routine surveillance is not a major factor in hepatitis B control. Hepatitis B screening and Hepatitis C screening of blood products is however essential. Routine surveillance does play a part in identification of outbreaks of hepatitis A and E.

**Diphtheria**

The European Laboratory Working Group on Diphtheria (ELWGD), initially developed to contribute to laboratory diagnostic services in response to the NIS diphtheria epidemic, now involves 18 countries of west and east Europe, USA, Australia and south-east Asia. The objectives of the working group are: to define a network of laboratories that collaborate in diphtheria surveillance, to improve information exchange and laboratory surveillance, to standardize methodologies, to develop novel or new techniques for diagnosis (including rapid
tests), train personnel, undertake quality assurance for diagnosis and typing methods, and to establish international databases of strains classified by molecular methods. As part of its work in contributing to services in response to the NIS diphtheria epidemic, the working group, in collaboration with the WHO Regional Office for Europe, has coordinated the provision of more than 60 laboratory kits to NIS countries, each sufficient for the microbiological investigation of 100 index cases investigations and 1000 contacts or secondary cases. The working group has been involved in workshops in all NIS countries. Due to the collaboration between the group members, a new *Corynebacterium* species was identified, and has been named *Corynebacterium imitans*.

**EPI reporting and feedback**

The objectives of the surveillance system include:

- determining the effectiveness of disease control strategies;
- identifying problems in immunization delivery;
- identifying high risk areas in population groups;
- demonstrating the impact of immunization services at district and country level;
- increasing motivation of reporting facilities by giving feedback; and
- helping sustain or increase financial support by showing effectiveness of immunization in reducing morbidity and mortality.

Effective use of surveillance data includes input into the allocation of cost-effective resources; determining priorities for vaccines; supporting vaccine research and development; monitoring of immunization safety; and assessment of disease reduction targets.

The present information system comprises a cycle for provision of annual data on diseases, coverage and performance indicators with data collected in February, analysed and processed and made available in May of each year. For diphtheria, measles, polio and acute flaccid paralysis surveillance data is collected on a monthly basis. Performance indicators include completeness of annual or monthly reporting and timeliness of annual or monthly reporting. Targets are 90%. There is high compliance for reporting of diphtheria and polio with over 95% performance indicators attained. Reporting compliance for measles is lower at 70–80% and for hepatitis B reports are considerably in arrears. Approximately 20% of Hib reports are achieved in a timely fashion. Goals therefore are for more efficient reporting and management of data with improved quality and relevance of data. At present, much information is provided in paper form and this needs to be exchanged for an electronic information system.

**Poliomyelitis**

In 1997, there have been only three confirmed isolations to date of wild polio virus with the last occurring in Turkey on 5 September. Provided that there are no more confirmed wild virus cases, the Region could be certified by September 2000. It is therefore appropriate that efforts are now accelerated to prepare documentation for polio certification in EURO countries. Critical steps in the regional polio elimination process have included attainment of high coverage, national immunization days, AFP surveillance (in 31 countries), mopping up and supplemental activities (done in all MECACAR countries). Operation MECACAR has had a dramatic impact brought about through political commitment, public health initiatives, and epidemiologically appropriate strategies.
With the apparent decline in polio in the Region, increasing emphasis will now need to be put on the quality of surveillance indicators and the preparation of certification data. The process will start in 1998, beginning with Denmark, Poland, Sweden and the United Kingdom with western European countries in the first main tranche and culminating in 2000 with the Russian Federation and recently endemic countries.

**Diphtheria**

The diphtheria epidemic in the Russian Federation and NIS is now declining, reflecting the resource mobilization and immunization activities undertaken by affected countries in collaboration with international agencies.
In 1996, 80% of the global cases of diphtheria came from the European Region; projected estimates for 1997 suggest that this will fall to 50%. Further work is still required to consolidate the successes achieved, completing mass immunization in affected countries, following the principles outlined in the WHO/UNICEF strategy, and employing the now expanded laboratory support.

**Pertussis**

Despite more than 95% coverage, there were more than 1000 cases of pertussis in the Netherlands in the first three months of 1997. There were no deaths. This epidemic is thought to be explained by genetic shift in *B. pertussis* involving a pertactin gene and less efficacious protection from the RIVM-manufactured pertussis vaccine, known to have high pertactin content but low PT content. The Dutch national authorities are presently considering an appropriate response which may include bringing forward the date of first immunization from three to two months, adding a booster dose at four years and possibly changing to an acellular rather than whole cell vaccine. This epidemic attracted considerable media interest with fears raised over Europe-wide pertussis epidemics, but there has been very little evidence to support these fears from other countries. After achieving excellent control of pertussis in Poland, there appears to have been a very small increase in the number of cases during the 1990s, particularly in younger children. This may be a result of the relatively late starting date for pertussis immunization with some failures to complete immunization. Although there had been media reporting of increased pertussis in Denmark, cases in 1997 did not appear significantly different from those reported in other years recently. The continuing cases were thought possibly to be related to a poor quality vaccine and excessive application of contra indications, with significant drop out rates due to adverse events. The Danish immunization schedule had recently been modified to provide three doses of diphtheria, tetanus, acellular pertussis vaccine and IPV, with Hib vaccine, at 3, 5 and 12 months. Consideration was now being given to introduce an acellular booster at five years.

**Hepatitis B – countries of east Europe and newly independent states (CEE and NIS)**

Although original estimates had suggested HbsAg prevalence of 2–8%, results ranged from 2% carriers in Baltic and northern countries, 2–7% in the Russian Federation, and 5–10% in Albania, Bulgaria, the Republic of Moldova, Romania and some central Asian republics. Mathematical modelling, using conservative assumptions on disease burden and costs suggested that in countries of central and eastern Europe and NIS, average costs per death averted were $543 (not discounted), and $2055 discounted, assuming 95% vaccine efficacy and hepatitis B vaccine coverage equivalent to DTP3 coverage. The cost per life year saved was on average $22 not discounted and $138 discounted. Thus, implementation of hepatitis B vaccine in these countries could be seen as highly effective use of health resources. Furthermore, a number of other factors, in addition to traditional patterns of transmission of hepatitis B, reinforced the likely benefits from routine provision of hepatitis B immunization. In a number of parts of the CEE/NIS, there are inadequate supplies of needles and syringes, injections are often given outside of health settings, there are inadequate or non-functioning sterilization facilities, and there is great popularity of injections as a routine form of therapy.

**Health for all in the 21st century**

In 1984 immunization targets for the European Region were developed at the Karlovy Vary Conference and were in turn adopted as health for all by the year 2000 targets. These were agreed by all EURO Member States but, despite the optimism when they were developed, have not yet been attained. Factors that have led to these difficulties were the political, social and
economic changes in the 1990s along with some underestimation of the difficulties of achieving the targets. As the new HFA 2020 strategy is being developed, so there will be a need to prioritize infectious disease targets so as to build on those identified as achievable from HFA 2000 along with new objectives reflecting the likely changes over the next 20 years. Early indications suggest that there will be a limited number of elimination targets, operational targets that will include the provision of immunization services and encouragement of opportunities to introduce new vaccines in the control of diseases not presently controlled through immunization. Cornerstones of the new strategy will be political will, resource allocation, strategic planning and multi-agency collaboration.
## Annex 1

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