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EUROPEAN ADVISORY GROUP ON THE EXPANDED PROGRAMME ON IMMUNIZATION

Report on the 12th Meeting

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1997

EUR/HFA target 5

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

At its twelfth meeting, the European Advisory Group (EAG) confirmed that the first priority for measles control was the achievement of high coverage with a single dose of vaccine, though this would not serve to eliminate the disease. The interruption of transmission needed to be maintained, and this could be achieved with supplementary vaccination, either through repeated campaigns or by the administration of second doses. Whichever approach was used, it was essential that the reaccumulation of susceptibles was prevented.

The EAG endorsed the importance of achieving very high coverage of primary immunization with DTP vaccine. This should be completed before six months of age. The first booster could be given at 16–36 months of age, with another (DT) before school entry and a third (Td) on leaving school. This recommendation applied to all European countries. In a number of countries, especially those presently experiencing or having recently experienced epidemic diphtheria, a further booster should be given during the school years. Where the risk of diphtheria was considered high, periodic booster doses for adults would be necessary to prevent resurgence of the disease as immunity waned.

On poliomyelitis, the EAG noted the significant impact of Operation MECACAR and the increasing awareness that remaining outbreaks of poliomyelitis in the Region had often followed importation of the disease. The EAG endorsed the plan of action for 1997 proposed by the Regional Office. In countries where poliomyelitis was still endemic or had become nonendemic within the past three years, the surveillance of acute flaccid paralysis (AFP) remained the recommended form of surveillance, especially for certification purposes. However, in countries where polioviruses had not been detected for many years, and AFP surveillance was not appropriate, other means of surveillance would need to be used. The EAG recommended that the Regional Office commission a position paper to review the options for laboratory-based or other surveillance techniques, so that appropriate guidelines could be issued.

Keywords

IMMUNIZATION PROGRAMS – organization and administration
PROGRAM EVALUATION
POLIOMYELITIS – prevention and control
MEASLES – prevention and control
DIPHTHERIA – prevention and control
ALBANIA
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FRANCE
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NIS
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INTRODUCTION

The twelfth meeting of the European Advisory Group (EAG) on the Expanded Programme on Immunization was held at the WHO Regional Office for Europe, Copenhagen, on 21 November 1996. The meeting was chaired by Dr Norman Begg and Dr Tove Rønne, the rapporteur was Dr David M. Salisbury, and the secretary was Dr Colette Roure, who also welcomed the participants to the Regional Office.

SCOPE AND PURPOSE

The scope and purpose of the Meeting were to:

- endorse the conclusions and recommendations of the First Technical Consultation on Measles, Copenhagen, 19–20 November 1996, in order to establish a strategic plan for measles elimination in the European Region;
- endorse the strategies for booster doses for diphtheria control;
- discuss acute flaccid paralysis (AFP) surveillance and other surveillance systems for certification of polio eradication.

MEASLES

The EAG considered the conclusions and recommendations of the expert group on measles that had met in Copenhagen on 19 and 20 November 1996. The Group endorsed the following principles for measles elimination:

- the first priority is the achievement of high coverage with a single dose of measles vaccine;
- the elimination of measles cannot be achieved with a single-dose strategy alone; the most rapid means of achieving interruption of transmission of measles virus is through the implementation of mass immunization campaigns across the whole of the age group among whom transmission is occurring; two-dose programmes at high coverage may achieve the same outcome over a longer period of time;
- the interruption of transmission needs to be maintained: this can be done through the provision of supplemental doses, either through repeated campaigns or through the administration of second doses; whichever approach is used, it is essential that the re-accumulation of susceptible individuals is prevented;
- strengthening of surveillance to include case detection, laboratory case confirmation, susceptibility and adverse events after immunization are of utmost importance.

The conclusions and recommendations of the expert group on measles are attached as Annex 1.

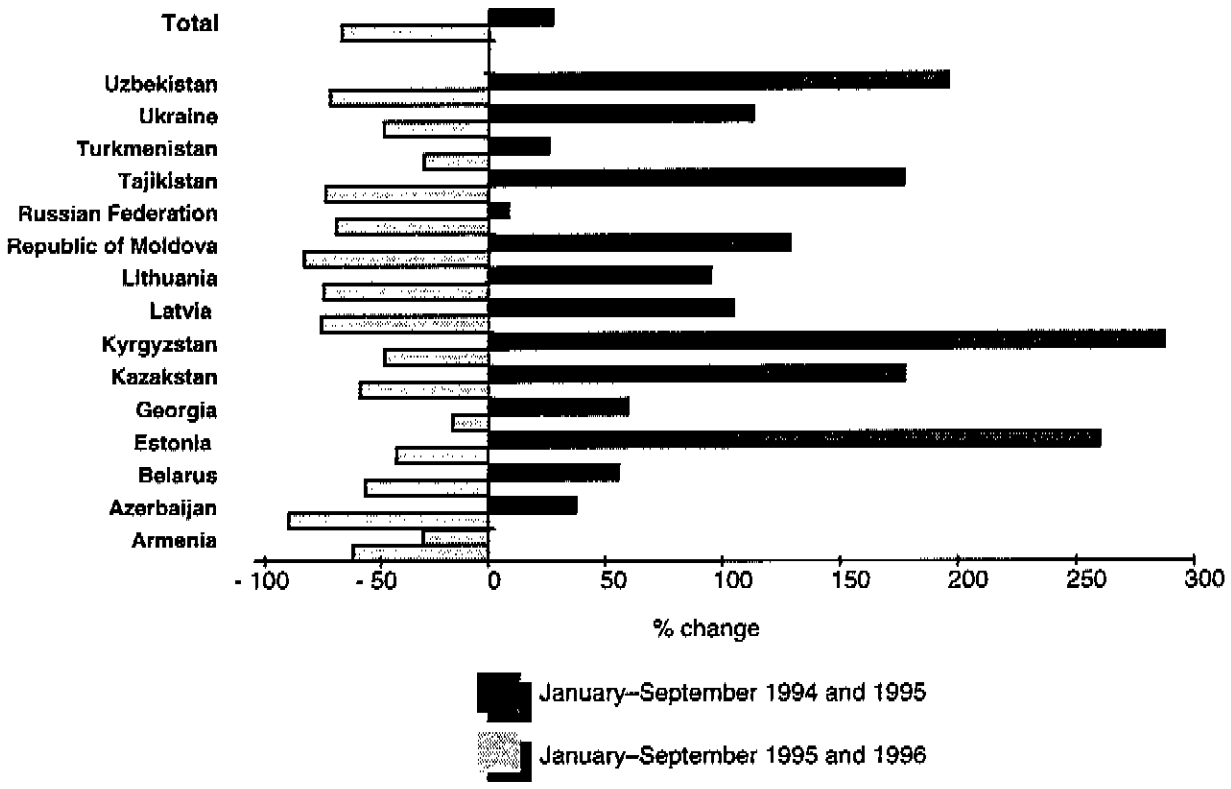
DIPHTHERIA

Overview of diphtheria in the Russian Federation and in the newly independent states (NIS)

The epidemic of diphtheria in the Russian Federation, NIS and Baltic countries appeared to have reached its main peak in 1994/1995. Some 35 000 cases were reported in the Russian Federation in 1995, whereas just 10 000 were reported by September 1996. There was also a decrease in

diphtheria incidence in all other countries over the period January–September 1995–1996 compared to the same period in 1994–1995 (Fig. 1). The decrease was particularly impressive in Azerbaijan, Lithuania, the Republic of Moldova and Tajikistan. However, a larger seasonal increase of diphtheria incidence could be expected to occur in some central Asian republics.

Fig. 1. Percentage change in diphtheria incidence in the NIS



Although considerable successes were now being observed in many of the NIS, there were still problems in implementation, notably in Georgia, Kazakstan, Kyrgyzstan and Ukraine. Particular problems came from implementation of the second dose where coverage was considerably lower at present than had been achieved at the first dose. Among the Baltic countries, Latvia was having the most difficulty in implementing the programme, but there were now signs of improvement. A meeting to evaluate serological studies on diphtheria immunity and response to diphtheria immunization undertaken in the three Baltic countries, Georgia and Ukraine had been held at the State Serum Institute, Copenhagen (conclusions in Annex 2).

Booster doses of diphtheria vaccine

Booster dose policies for children are not homogenous throughout the Region. Three doses are given before the second birthday in some countries and four in others. Some countries use preschool boosting and there is variation in the number of booster doses given throughout the school years. Full-strength diphtheria vaccine is given combined as either DTP or DT in children under five years, while older children are given Td. In individuals who have been primed, a good boosting response is obtained from a single dose of diphtheria vaccine and good responses have been observed at all Lf doses investigated. In individuals who have not been primed, two doses may not be sufficient to give adequate immunity and the Lf dose is much more important.

In some countries, tetanus toxoid is no longer provided as a single antigen but is always combined with low dose diphtheria (Td). This preparation can be used for combined tetanus diphtheria boosting as routine or for tetanus prevention in wound management. Routine boosting with Td is recommended at 26 and 46 years in some countries and at 10-year intervals through adult life in others.

Conclusions

The EAG endorsed the importance of achieving very high coverage of primary immunization with DTP vaccine. This should be completed before six months of age. The first booster may be given at 16–36 months of age, and boosters given before school entry (DT) and on leaving school (Td). This recommendation applies to all European countries. In a number of countries, especially those experiencing or having recently experienced epidemic diphtheria, a further booster is given in the middle period of school years. Adult diphtheria booster strategies need to be considered in the light of the perceived risk of diphtheria, the opportunities that exist for provision of boosters, and the sensitivity of surveillance so that rapid responses could be implemented should diphtheria be introduced. Where the risk of diphtheria is considered high, periodic booster doses for adults will be necessary to prevent its resurgence in adults as immunity wanes.

POLIOMYELITIS

Global overview

The recommended WHO strategies for achieving high coverage through routine immunization, supplemental immunization through national immunization days, and surveillance to identify the final change of transmission are now being increasingly applied with corresponding successes. Global coverage has now reached 83%, with coverage in Africa the lowest, and there has been an explosion of interest with countries now undertaking or committing themselves to national immunization days. It was estimated that 100 countries would have held NIDs by the end of 1996. AFP surveillance is increasingly being implemented and the global laboratory network is progressively extending. Surveillance indicators are showing signs of improvement but there is still some considerable way to go. The decline in paralytic polio cases over the last eight years is estimated to have been 80%. The major reservoirs are Bangladesh, India and Pakistan. India, however, held two NIDs in 1995 when more than 90 million children were immunized in a single day. Further NIDs are planned in India in 1996/1997, with a target population of 125 million children.

European Region overview

In 1995, 210 cases of paralytic poliomyelitis were reported from the European Region, whereas in 1996 there had been 159 to date. At first impression, it appears that there has been little overall improvement within Europe but some striking successes have been achieved, overshadowed by a number of outbreaks. Operation MECACAR achieved 95% coverage with 58 million children immunized (17 million in the European Region and 41 million in the Eastern Mediterranean Region). Operation MECACAR had had a dramatic impact in the affected countries; thus far there had been very little evidence of the usual seasonal increase as had occurred in previous years. Detailed analysis, including genotypic differentiation, suggests that there is little endemic poliomyelitis in the Region and that most cases result from importations from outside the Region, especially from south-east Asia.

Surveillance of AFP is progressively improving but is not yet up to satisfactory levels. The overall rate for AFP, in those countries where this is now carried out, was 0.65 per 100 000 in 1996, but analysis of other surveillance indicators suggest that detection of cases is better than investigation. Reporting is still not done on time and the use of surveillance indicators is poor. Although there have been improvements in the laboratory network, it is not yet adequate.

Regional plan of action – proposals

Three main areas of activity are planned for 1997. In the **political** area, the support of the Regional Committee will be sought for special action in poliomyelitis, an article on certification will be submitted for publication in the Lancet, and efforts will continue to mobilize mass media interest in polio eradication and to develop certification documentation. In the **technical** area, there will be further emphasis on surveillance activities at coordination meetings, national workshops, workshops for the national chairmen of certification committees and AFP workshops, and guidance developed on alternative methods for polio surveillance for certification. **Managerial** activities will include implementation of case definitions that include virologically based definitions, further improvement and maintenance of AFP indicators, improved performance of the laboratory network, preparation of certification activities and improved communication to local levels.

Laboratory-based surveillance

Global polio laboratory network

The purpose of the polio laboratory network is to detect and identify wild poliovirus and to transmit information rapidly to those responsible for implementing polio eradication strategies. The basic structure of the network is in place with the establishment of 6 specialized, 16 regional reference and over 60 national laboratories. Specimen referral exists and appropriate technical expertise is available at each level. However, there is wide variation between regions and countries in laboratory competence, and constant monitoring of performance indicators is needed. Although 85% of the laboratories performed well on proficiency testing in the African, Eastern Mediterranean and Western Pacific regions, the percentage of laboratories reporting within the stipulated 28 days was 30%, 46% and 75%, respectively. Certification of polio eradication will require laboratories of proven competence, and a system of accreditation of WHO network laboratories will be put into place in 1997. This will be based on six criteria, recently approved by a meeting of the global network: performance and proficiency tests, ability to isolate enteroviruses other than polio, confirmation of virus typing by a reference laboratory, testing an adequate number of specimens, rapid reporting of results and the use of good laboratory practices and procedures.

Laboratory network in the European Region

In the European Region there are now more than 40 countries which have at least one laboratory taking part in activities supporting polio eradication. Additionally, there are four specialized reference laboratories, four regional reference laboratories and two subregional laboratories. Action taken in 1996 to strengthen the laboratory network comprised evaluation by questionnaire of the potential and needs of all participating laboratories, distribution of a proficiency panel of unknown strains to all laboratories, and field visits by experts to selected laboratories of strategic importance. Rapid appointment of a laboratory coordinator for the European Region will be needed to optimize further programmatic action, such as the integration of the laboratories with the surveillance systems for poliomyelitis and for wild poliovirus circulation, for cooperation between network laboratories and development of referral channels from countries without a

qualified laboratory. Results from the 1996 proficiency test for isolation and typing are very promising: 20 out of 30 laboratories that have reported results have passed the test with a score of 80% or more – 5 laboratories had an optimal score of 100%. Five laboratories just missed the passing score, but little corrective action will be needed to improve their proficiency. In the case of another five laboratories, the proficiency test revealed severe lacks in competence to function as WHO network laboratories. Comparison with results from the previous year's test showed that important progress in the build-up of the EURO laboratory network had been made. Continued efforts are needed to complete the network, as only a Region-wide laboratory network fulfilling all required proficiency indicators will be able to document the absence of poliovirus circulation, as needed for the certification of a polio-free European Region.

Genetic analysis of polioviruses

In most western and mid-European countries, there is no longer evidence of endemic circulation of wild polioviruses. Few wild poliovirus strains have been isolated in these countries in recent years. A number of outbreaks have occurred in the 1990s, particularly in Albania, Bulgaria, the Netherlands and Romania. Cases have been more frequent in some NIS and Turkey. Genetic analysis of the wild type 1 strains reveal that they belonged to four different genotypes, two of which circulate predominantly in the Caucasian, central Asian and middle eastern countries. The epidemic viruses from Bulgaria and Romania belong to these genotypes. The third genotype consists of mainly Egyptian strains (so far), and the fourth genotype contains many wild type 1 viruses, probably originating in the Indian subcontinent. The Albanian epidemic virus belongs to this genotype. There is virtually no information on recently circulating wild poliovirus type 2 strains in the Region but several type 3 strains were obtained from the NIS. Three genotypes were detected. The first is represented by strains that were isolated in central Asian republics, the second is from the Mediterranean region, and the third appears to have its origins in the Indian subcontinent but has a very widespread distribution. The Netherlands epidemic virus belongs to this genotype.

Alternative surveillance approaches

Enterovirus surveillance

Polioviruses belong to the genus of enteroviruses and share many characteristics of these viruses, such as their site of replication, clinical course of the infection, mode of transmission, general epidemiological pattern, and the approach needed to diagnose them,. Thus, in principle, one may expect to find polioviruses in the same materials and at the same sites as the other enteroviruses. In a programme dedicated to poliovirus surveillance, it is appropriate to examine patients and materials from which enteroviruses were isolated. For diagnostic purposes, laboratory examination by virus culture is carried out in large numbers of patients with various clinical symptoms suggestive of a possible enterovirus infection of, for example, the central nervous system or the respiratory or gastrointestinal tracts. Enteroviruses are frequently isolated from these patients, mostly from stool specimens. Between 1981–1992 the Dutch virus diagnostic laboratories reported between 652 and 1332 patients with enterovirus infection each year (average 910). The mean annual number of enterovirus isolates from patients with neurological symptoms was 215 (range 115 to 512). Approximately 80% of the isolates were recovered from faeces. The mean number of faecal specimens examined by virus culture in Dutch virus diagnostic laboratories is estimated to be between 9000 and 10 000 per year. Polioviruses are sporadically isolated but these are mostly vaccine-derived viruses. Although the larger proportion of enteroviruses are typed, those that are not typed or remain untypeable are important as they may contain unrecognized polioviruses. This is borne out by quality assessment of laboratories undertaking isolation of enteroviruses, which is done relatively well, although the correct

identification of enterovirus serotypes, especially in mixtures with polioviruses, is not being so well done.

The surveillance of enteroviruses from clinical specimens, especially those in patients with neurological disease, may well provide an acceptable alternative to AFP surveillance in those countries where virological examination is well established and AFP surveillance will be impracticable.

Surveillance of aseptic meningitis

There are a number of options for surveillance of poliomyelitis in addition to the WHO recommended AFP surveillance, including the rate of vaccine-associated poliomyelitis and the surveillance of the rate of aseptic meningitis (AM). AM surveillance may be particularly appropriate for polio-free industrialized countries to detect any wild virus circulation or to contribute to information for certification and might also be appropriate for application in small countries. When comparing the AFP rates with aseptic meningitis rates in countries with a population of 2 million, 5 AFP cases could be expected in children under 15 years per annum compared with 41 cases of AM in children under 5 years old, assuming a rate of AM of 27 cases per 100 000 persons under 5 years of age. The increased sensitivity of AM surveillance comes about because the risk of AM is of the order of 10 times higher than that of paralytic illness following wild polio virus infection, and AM surveillance can potentially be built on established enterovirus reporting systems. Provided that validation can establish the true rates of AM and the indications for investigations, it might be possible to establish performance indicators based on AM. Given that 11 European countries are routinely monitoring AM through laboratory surveillance, this offers distinct possibilities.

COUNTRY REPORTS

Albania

Between 1960 and 1978, poliomyelitis was endemic and epidemic in Albania with an outbreak of polio virus type I involving 71 cases in 1978. OPV was introduced on a routine basis in 1980 since when the number of cases has significantly declined. Between 1980 and 1995, there was AFP surveillance with mandatory notification of clinically suspected cases of polio. During this period, 93 AFP cases were reported and the incidence of AFP per year was 0.6 per 100 000 inhabitants. Eleven cases were considered to be poliomyelitis with polio virus isolated from 6 of them. In 4, polio virus type 2 was isolated, and in 2 polio virus type 3. These were all characterized as sabin-like strains. In the remaining 5 cases, isolation in sub-culture was negative and diagnosis was based on clinical symptoms, residual paralysis or serological data. Between 1991 and 1995, AFP cases and their contacts were studied and although polio viruses were isolated, they were always sabin-like strains; other viruses were also identified. These data suggested that there was a lack of circulation of wild polio virus in Albania in that period. However, in 1996 there was a polio outbreak between April and November, involving 140 cases. To date, isolation had been successful for samples from 63 out of 93 cases with type 1 wild polio viruses in 55, negative samples in 9, and investigations in progress in 19. Following this outbreak, national immunization days had been held, with the first round on 7–14 October. The total estimated population in the age group 0–50 years was 3 million inhabitants, of whom 2.5 million were immunized, an estimated coverage of this group of 81%. The corrected vaccination coverage of the population aged 0–50 years, after allowance had been made for inhabitants who had immigrated, was 90–97%.

Denmark

Data being prepared for submission for certification of polio elimination in Denmark would take account of the long stability of the immunization programme with high coverage of polio immunization since its introduction in 1955. Coverage rates for the previous decade had been in excess of 95%, and coverage had been validated. The last indigenous case of type 1 polio was in 1976 and the last imported case in 1983. There had been no recent cases of vaccine-associated polio. Serological surveillance had demonstrated high sero-immunity levels against all three polio virus types in all age groups, on a number of occasions. A further sero-survey would be undertaken in the near future. The Central Enterovirus Laboratory at the State Serum Institute tests around 1200 specimens per year and identifies OPV and other enteroviruses. In order to improve enterovirus surveillance, it was planned to remind clinicians actively of appropriate samples and relevant patients, but this was becoming increasingly difficult as virological investigations were increasingly carried out with PCR rather than viral culture. An informal technical group had been established at the State Serum Institute and the National Board of Health had been asked to establish the formal National Certification Committee.

Finland

High coverage with IPV had been achieved since this vaccine was introduced in 1957, and IPV campaigns covering the entire Finnish population in 1960/1961 had resulted in the disappearance of poliomyelitis and polio viruses in 1964. No cases were reported until there was an outbreak in 1984, when 9 paralytic cases of poliomyelitis and widespread circulation of the causative wild type 3 polio virus had been seen. The most likely reason for the outbreak was a combination of the relatively weak immunogenicity of the IPV preparation used and an antigenically aberrant virus strain. The virus was later shown to belong to the Mediterranean genotype. The outbreak had been contained by an intensive vaccination campaign consisting of an extra dose of IVP to children aged 18 years or less, and a dose of trivalent OPV to the entire population with coverage of 94%. No cases of wild poliomyelitis had been reported in Finland since January 1985 and no wild type polio viruses had been isolated from patients or the environment during the previous 11 years. Immunization coverage had been shown to exceed 98% for the first three doses of IPV. Sero-surveys assessing the prevalence of neutralizing antibodies are carried out at 5–7 year intervals; the last one in 1994 had revealed a prevalence of 98% or more to all three sero-types in all adult age groups. Although no active AFP surveillance is carried out, all physicians are obliged to report any documented or seriously suspected cases of poliomyelitis. Approximately 20 AFP cases are evaluated each year, and in addition to attempted virus isolation from faecal specimens, serum and CSF specimens are examined for polio virus specific IgM. Faecal specimens are frequently, but not regularly, collected from patients with suspected CNS infections and examined by virus isolation. Some 500–600 specimens are tested annually in the five virus laboratories, outside KTL. Any polio viruses isolated are immediately sent to KTL for confirmation of identity and further characterization. All laboratories involved in the primary examination of the samples participate in the UK PHLS Quality Assessment Programme.

Sewage specimens collected twice a week from two separate locations in Helsinki are screened for polio virus. In addition, from July to December monthly specimens from four other towns are similarly tested. The method used is able to detect polio virus circulation if 1 out of 1000–2000 individuals is infected with polio virus. Children adopted from countries with endemic polio virus infection are medically examined at arrival and are also screened for polio virus excretion. One to three children annually present with excretion of polio virus, usually one of the OPV-derived strains. Isolation of a wild strain is a rare occurrence; in such cases, contacts and local sewage are

examined to discover potential spreading of the virus. A special plan for outbreak containment had been revised in 1994 and approved by the National Council for Communicable Diseases. The plan had been tested in winter 1995 when the IgM test used had suggested a polio virus infection in a patient with GBS-like disease. All designated steps in the containment plan had been initiated but were withdrawn when it turned out that the IgM had given a false-positive result.

The National Committee for Poliomyelitis Certification has been established.

France

In France, poliomyelitis had been a statutorily notifiable disease since 1936. The surveillance of poliomyelitis depended on compulsory notification of cases and deaths, epidemiological investigation of cases and contacts, virological or serological investigation of suspected cases through the national network of laboratories, measurement of immunization coverage, and surveillance or screening for circulation of wild polio virus in the population and in the environment. Immunization coverage for the first three doses was over 95% and coverage up to the age of 40 years was over 80%. Serological data in 1991 showed high levels of protection of the younger half of the population. The last wild virus case of poliomyelitis had occurred in 1989, although there was one imported case in 1995. There had been no vaccine-associated cases for many years as IPV was used almost exclusively. The National Centre of Public Health coordinated a network of about 25 virological laboratories; during the period 1990–1993, 28 678 samples had been investigated for enterovirus identification, of which 1002 were from patients with viral meningitis. Enteroviruses were isolated in 675 of these (67%). None were polio virus. Some cases of acute paralysis, including GBS, had been investigated. From 1991 to 1996, 45 GBS cases had undergone virological examination, and no polio viruses had been found, although four enteroviruses were isolated. Between 1993 and 1996, 136 CSF samples had been examined from cases of aseptic meningitis and 112 enterovirus strains had been isolated (82%). In Paris and its suburbs, the surveillance of polio virus circulation had been carried out since 1973, and strain differentiation performed by the National Reference Centre for Enteroviruses. Samples were collected from sewage which reflected a population of 79 million inhabitants. The last wild polio virus had been found in 1988, one undifferentiated polio virus type 1 and 1 sabin-like type 2 had been found in 1993, and one sabin-like type 3 was found in 1995. A Certification Committee was being appointed.

United Kingdom

IPV was introduced in England in the late 1950s and OPV in the early 1960s. Thereafter poliomyelitis in the United Kingdom had remained under excellent control. The last confirmed case of wild virus poliomyelitis had occurred in England in 1983. Poliomyelitis is a compulsorily notifiable disease and doctors are obliged to report suspected cases. There is weekly reporting including zero reporting from all health districts (approximately 150). All cases of suspected poliomyelitis are classified as wild virus (indigenous), wild virus (imported), vaccine-associated/recipient (VAR), vaccine-associated/contact (VAC), or unknown. Since 1987, there had only been one case of unknown aetiology and that was likely to have been caused by Coxsackie infection. The most recent imported case, two years earlier, had been in a child returning from India with an established diagnosis of acute poliomyelitis. The child was no longer excreting wild virus and was admitted to hospital simply for confirmation of the diagnosis. Cases are sought from routine identification sources, laboratory reporting, death certificates that identify polio as contributing to the cause of death, adverse event reporting of vaccine-associated poliomyelitis from the Medicines Control Agency, and applications for vaccine-damage payment following vaccine-associated poliomyelitis. Rates of detection of

vaccine-associated poliomyelitis are equal to or higher than those reported by other authorities. AFP surveillance had been implemented between 1991–1994 with an overall reporting rate of 0.35 cases per 100 000 population under 16 years of age. GBS cases accounted for approximately 60%. During 1994, 200 polio virus strains had been received by the PHLS Enteric and Respiratory Virus Laboratory for characterization; 183 isolates so far characterized had proved to be sabin-like strains, almost equally distributed between the three polio virus types. This surveillance was being widened to include all public health laboratories. Enterovirus identification had been undertaken with centralization of results from this testing. In the previous three years 1200 enteroviruses had been identified, none of them polio viruses. Aseptic meningitis samples are also available through the PHLS. A Certification Committee is being set up.

CONCLUSIONS

The EAG noted the significant impact of Operation MECACAR and the increasing awareness that remaining outbreaks of poliomyelitis in the Region have often followed importations.

The EAG endorsed the Plan of Action for 1997 proposed by the Regional Office.

In countries where polio is still endemic or has recently become non-endemic (i.e. within the previous three years), surveillance of AFP remains the recommended form of surveillance, especially for certification purposes. However, in countries where polio viruses have not been detected for many years and AFP surveillance would not be appropriate, other means of surveillance would need to be used. These surveillance techniques may include laboratory-based surveillance for enteroviruses, aseptic meningitis surveillance and surveillance of paralytic poliomyelitis through vaccine-associated cases where OPV is used.

The EAG recommended that the WHO Regional Office commission a position paper to review the options for laboratory-based or other surveillance techniques so that appropriate guidelines can be issued.

The EAG endorsed the application to IICC regarding funds for heightened surveillance activities in the European Region.

Annex 1

CONCLUSIONS AND RECOMMENDATIONS FROM THE FIRST TECHNICAL CONSULTATION ON STRATEGY FOR CONTROL/ELIMINATION OF MEASLES IN THE WHO EUROPEAN REGION COPENHAGEN, 19–20 NOVEMBER 1996

Current state of measles eradication in Europe

Conclusions

1. The elimination of measles in the European Region is feasible within the next 10–15 years, and sooner in a number of countries.
2. Many countries are, however, still not meeting the EPI operational targets.
3. Failure to control measles in some countries is mainly due to a lack of political will and a belief among health professionals and parents that measles is not a severe disease, but also due to incomplete implementation of strategies.

Recommendations

1. The goal of measles elimination in Europe should be promoted widely by all Member States and by the WHO Regional Office.
2. The WHO Regional Office should help secure political commitment to measles elimination through the Regional Committee and other relevant professional groups.
3. An executive summary of the technical consultation on measles should be prepared by the Regional Office, which can be used by countries when seeking support for elimination strategies. The Regional Office should also prepare a measles elimination strategic plan which will provide detailed operational guidance, definitions and specifications for surveillance activities.
4. The survey on measles epidemiology and control strategies carried out by the Regional Office should be completed by encouraging non-responding countries to reply. The results should be presented at the next meeting of EPI managers in the Region.
5. The current EPI operational targets for measles elimination remain appropriate and should be regularly followed up by the Regional Office in monitoring progress towards elimination.

Strategies for measles eradication

Conclusions

1. Elimination of measles cannot be achieved with a single dose strategy alone. A second dose should be delivered either through mass campaigns or routine immunization services. In some situations, more than two doses may be required.
2. The key to measles elimination is ensuring that the number of susceptible individuals in the population is kept below the level required to sustain transmission.
3. Outbreak investigation is helpful in identifying unvaccinated populations and can provide useful data on vaccine efficacy. Outbreak immunization is however very labour-intensive and has only a limited contribution to elimination.

Recommendations

1. The Regional Office should prepare a strategic framework for the elimination of measles in Europe, based on the four categories of countries.
2. All countries that have not already done so should develop a national plan of action to achieve elimination of measles. This plan should be based on minimizing the number of susceptible individuals through an initial mass campaign and delivery of a second dose, either through routine services or follow up immunization. Extra efforts to reach groups with socioeconomic problems should be made, and clear information to avoid simple misunderstandings should be given to health professionals and parents.

Surveillance

Conclusions

1. Surveillance is critical to measles elimination. It is still inadequate in some countries and must be strengthened.
2. Adequate laboratory support for measles elimination is essential, to confirm or discard suspected cases, to undertake serological surveillance, and to monitor circulation of virus strains.
3. Information about disease burden and costs and benefits of measles elimination is limited in most countries.

Recommendations

1. Measles should be made notifiable in all countries of the Region as soon as possible, with minimum data including age and vaccination status.
2. Countries should develop surveillance strategies to achieve and confirm measles elimination. These strategies should include serological surveillance and monitoring of adverse events following vaccination, and – where the incidence is below 1/100 000 – the laboratory investigation of all suspected cases.
3. When campaigns and second doses are implemented, countries should ensure that high coverage is achieved, monitored and maintained.
4. The Regional Office should establish a laboratory network to support measles elimination. This network should establish a bank of genetic sequencing data on circulating measles viruses.
5. Studies should be carried out at country level to provide economic evaluation and mathematical modelling of the impact of elimination strategies.

Annex 2

CONCLUSIONS FROM THE MEETING ON DIPHTHERIA AND VACCINATION ORGANIZED BY THE STATE SERUM INSTITUTE COPENHAGEN, 18 NOVEMBER, 1996

1. After reviewing the available knowledge on the effects of pre-existing antibody level, preparation and potency of toxoid, and adjuvants, results of serologic studies conducted in Ukraine (Kiev and Odessa), Georgia, Estonia, Latvia and Lithuania were presented and discussed. These studies support that a single dose of diphtheria toxoid is effective in boosting antibody levels in persons with prior primary vaccination. This effect is independent of gender, military status, or Lf content of the preparation (studying 2, 3, 5, or 6Lf; a study of 12Lf is pending).

2. This booster effect supports the WHO/UNICEF strategy of supplying a single dose of diphtheria toxoid to as many persons in the population as possible under 60 years of age as quickly as possible ($\geq$95% coverage in children, $\geq$90% coverage in adults). All NIS countries and Baltic states have initiated mass vaccination, with some reaching over 90% coverage. The effects of high coverage have been observed in these countries.

3. Some countries continue to have substantial reported disease in children under age 15, indicating the need for completing booster vaccination in that age group. Children who have received adult type tetanus and diphtheria toxoids (Td) as primary vaccine cannot be considered to be protected against diphtheria.

4. As already recommended, routine fourth doses of toxoid as DTP are recommended in NIS countries as well as booster doses (with DTP or Td as appropriate) at school entry and leaving. Boosters of Td are recommended every ten years thereafter.

5. Distinct age groups have been shown in these serologic studies to have a lower response to a single dose of vaccine and respond in a manner indicating a lack of primary immunization in a substantial subgroup. The specific age groups varied based on the study, such as 30–50 years of age in the studies in the Ukraine, 30–59 in the Georgia study (especially those 40–49), and different age groups in the Baltic country studies within the 40–55 year age group. Overall, about 20–40% of persons in the study age groups at risk fail to respond with a titre considered to be protective at 0.1IU/ml level to a single dose of toxoid.

6. This is consistent with the WHO/UNICEF strategy of providing a primary series of three doses for a distinct age group, in most countries being 30–50 years of age. Immunizing this age group can be guided by these serologic studies for these countries, and the current epidemiology of reported cases. The screening of immunization history in this age group is not practical in public health practice.

7. The issue of which Lf content of toxoid is best to use for primary immunization in adults is not answered; there is some suggestion that 2Lf vaccine may not be optimal. However, it is not possible to identify who such persons are within the higher risk age group, and use of 2Lf toxoid for the entire age group can be continued.

8. Further follow-up at five years in some of the serologic studies may be helpful in addressing the persistence of antibody. No additional serologic studies similar to these presented appear necessary. Additional research on adjuvants would be interesting for addressing routine primary vaccination in the future.

Annex 3

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