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Report on the

Intercountry meeting on measles and rubella control and elimination

Sharm El Sheikh, Egypt
27 September–1 October 2009

World Health Organization
Regional Office for the Eastern Mediterranean

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Annexes

1. INTRODUCTION

An intercountry meeting on measles and rulbella control and elimination was held in Sharm El Sheikh, Egypt on 27–30 September. Participants included national managers of the Expanded Programme on Immunization (EPI) and laboratory staff, members of the Regional Technical Advisory Group (RTAG), experts from the Centers for Disease Control and Prevention (CDC), a Gates Foundation representative and staff of the WHO Regional Office for the Eastern Mediterranean (EMRO) and headquarters. The objectives of the meeting were to:

- Review the progress toward and discuss barriers to measles elimination in the WHO Eastern Mediterranean Region
- Discuss the feasibility of measles eradication in the Region
- Review the criteria, parameters, and process for documenting and confirming measles, elimination in the Region.

The meeting was opened by Dr Nadia Teleb, Medical Officer, WHO EMRO, who delivered a message from Dr Hussein A. Gezairy, WHO Regional Director for the Eastern Mediterranean. In his message, Dr Gezairy welcomed the participants and noted the impressive progress towards achieving the goal of measles elimination by 2010. It was now time to build on this success and consolidate the gains. Routine immunization still needed strengthening, as did measles and rubella surveillance. Improvements in these areas would continue to be at the forefront of the regional agenda.

He emphasized the importance of utilizing the experience and capacity of polio eradication initiative staff to support measles surveillance. He closed by urging participants to sustain the success, strengthen national plans for measles elimination as part of the national comprehensive multi-year plans for immunization and regularly monitor the implementation of the measles elimination activities. He also urged partners to continue providing the support needed in order to sustain the gains.

The meeting was chaired by Dr Ibrahim Mousa. The programme and list of participants are attached as Annexes 1 and 2, respectively.

2. GLOBAL AND REGIONAL UPDATES ON MEASLES AND RUBELLA CONTROL AND ELIMINATION

2.1 Measles elimination: global overview

Dr E. Hoekstra, UNICEF/HQ

Each WHO region has a measles elimination, pre-elimination, or mortality reduction goal. The Eastern Mediterranean and Europe both have elimination goals for the year 2010 whereas the Americas goal was the year 2000. Additionally, Africa has a pre-elimination goal by the end of 2012 and set the goal of measles elimination by 2020. The Western Pacific set their elimination goal by 2012. Only the South-East Asia Region remains without a goal. Currently they have a mortality reduction goal.

Over the past 3 years, the Strategic Advisory Group of Experts (SAGE) has provided some more guidance on measles immunization policy to accomplish these goals. This guidance includes recommending:

- that two doses of measles vaccine should be standard;
- that the optimal age for MCV1 and MCV2 in a country with high transmission is 9m and 15-18m respectively;
- that the optimal age for MCV1 and MCV2 in a country with low transmission should be 12m (MCV1) and either 15-18m or school entry (MCV2);
- that a follow-up supplementary immunization activity needs to be conducted when the number of susceptible preschool-age children approaches the size of a birth cohort;
- that MCV2 should be routine when MCV1 > 80% for 3 consecutive years (WHO/UNICEF estimates); and
- that supplementary immunization activities can be stopped once MCV1 and routine MCV2 reach ≥ 90%–95% nationally.

WHO/UNICEF MCV1 coverage estimates show that global coverage has increased to over 80% as of 2008 compared to approximately 15% in 1980. All countries have a two-dose MCV strategy (MCV1 routine and MCV2 either in supplementary immunization or routine) except India where only 1 MCV dose is offered. Only one region (the Americas) has achieved <1 case per million population. During 2008, the rate per million per year in the Eastern Mediterranean was between 1 and 10 cases.

Measles supplementary immunization activities provide an effective delivery platform for other child survival interventions. The integration of multiple interventions with measles campaigns is now common practice in Africa. Vitamin A supplementation is the most frequently added intervention. In 2008, 14 of 15 campaigns in Africa were integrated with at least one other intervention and about 57 million doses of vitamin A, 49 million doses of polio, 24 million de-worming tablets, and 5 million ITNs were distributed during measles campaigns in the course of the year.

The impact of these accelerated activities is seen in the reduction of global measles mortality which decreased 74% from an estimated 750 000 deaths in 2000 to 197 000 deaths in 2007. The reduction in measles deaths among the 47 priority countries accounted for 96% of the global reduction in measles deaths during this time period. In the Eastern Mediterranean, there has been a 90% reduction in total and under five measles deaths from 2000 to 2007.

Routine MCV1 coverage is a critical component of the measles elimination strategy. While all countries have implemented a first dose of MCV, coverage in many countries remains well below the 90% target. Countries with less than 50% MCV1 coverage include Chad, Somalia and Laos. Additionally, of 21 million infants in 2008 who missed receiving their first dose of measles vaccine through routine immunization services by the age of 12 months, 60% reside in 6 large countries (India, Nigeria, China, Democratic Republic of Congo, Pakistan and Ethiopia).

The burden of measles disease has shifted from Africa to India. India now accounts for an estimated 67% of global measles mortality. Ten states in India account for over 95% of the estimated measles deaths in India. To reach the 2010 goal, an estimated 204 million children between nine months and 10 years of age in these states need to receive measles immunization by 2010.

Some progress has been made in India however. The Indian National Technical Advisory Group on Immunization met in June 2008 and recommended that a second opportunity for measles immunization be introduced either through routine services (in states with routine coverage >80%) or through supplementary immunization. In 2009, the government met with 4 high priority states (Uttar Pradesh, Bihar, Rajasthan and Madya Pradesh) and agreed to set up measles surveillance and begin to formulate plans of action for mass campaigns.

Most of the priority countries with highest disease burden are highly dependent on donor funds for supporting supplementary immunization activities. If funding and completing campaigns were to stop, we would see a slow increase in cases/death and by 2015 we would be back to where we were in 2000. GAVI and IFFM have decided not to give funds (traditionally have been giving one fourth of funds) – now have to find new funders.

Conclusions include:

- measles strategy works for every country
- global mortality reduction goal will be achieved – realistically though it will be delayed (primarily because of India)
- achievements (3 out of 4 deaths globally are being prevented compared to 2000),
- 4 of 6 regions reached their measles mortality reduction 2010 goals
- 2 of every 3 deaths due to measles are occurring in India
- 3 out of 6 dollars needed for 2010 have been pledged.

2.2 Regional measles elimination progress

Dr B. Naouri, WHO/EMRO

The Eastern Mediterranean Region has made substantial progress toward measles elimination since 1997, when all countries of the Region resolved to eliminate measles from the Region by 2010. The regional MCV1 coverage reached 83% and the number of confirmed measles cases decreased dramatically from about 88 000 in 1998 to 11 600 in 2008. The 90% reduction in global measles mortality was reached in 2007, three years early from the year target. Eight countries are moving very rapidly towards measles elimination and WHO EMRO is in the process of developing the guidelines for the validation of measles elimination.

However, the Region is still facing many challenges and constraints toward measles elimination. Polio remains endemic in three countries; insecurity is a big barrier towards implementation of strategies for measles elimination; and funds are still needed to support supplemental immunization activities in GAVI countries. During the past two years, several

countries experienced large outbreaks resulting from low measles coverage due to failure of "keep-up" strategy, or to the immunity gap among some groups.

The Regional Office will keep moving toward measles elimination by providing financial and technical support to all countries to reach measles elimination in the short-term future.

2.3 Regional measles/rubella laboratory network progress and challenges

Dr H. Ahmed, WHO/EMRO

In support of measles and rubella surveillance, the regional laboratory network has made considerable progress in 2005 and 2006 by expanding and completing establishment of a national measles/rubella laboratory (NML) in all countries in the Region with full serology capacity. In addition 16 countries have measles virus isolation or detection capacity and 4 countries have the virus sequencing capacity two of these are the Regional Reference laboratories (RRL) in Tunisia and in Oman.

All countries have moved to measles case-base surveillance with laboratory confirmation. 19 of these countries are implementing nationwide, and three countries (Morocco, Pakistan and Somalia) in addition to south Sudan are performing in identified sentinel sites. Thus the serological testing had increased, approximately 13 630 serum samples were tested in the EMR LabNet for measles IgM in 2008 compared to 6684 samples in 2006, an increase of 49%.

Laboratories are functioning at a high level of proficiency and meet performance indicators and timeliness of reporting criteria on measles case-based surveillance with laboratory confirmation reported in the monthly measles bulletin. High quality of the testing achieving more than 90% concordance results with external quality control. Countries Initiated shipping dried serum sample on a filter paper for serum validation and concordant results were obtained by RRLs in Egypt, Islamic Republic of Iran, Morocco, Sudan and Syrian Arab Republic.

Of the 22 laboratories which received the global annual proficiency testing panel in 2007, 100% passed the measles component and 100% passed the rubella component. Annual accreditation review has been conducted between 2005 and 2008 at the national measles/rubella laboratories in the Region, 20 passed successfully and two countries remain to be reviewed in which one has achieved less than the passing score and areas of improvement were identified during the review mission.

The Region has improved its virological surveillance for measles and rubella. The Regional Office has organized two intercountry training workshops one in March 2007 at the RRL in Muscat, Oman and the other in May 2008 at the RRL Tunis, Tunisia for 16 countries that have facilities for virus isolation or molecular techniques for virus detection. In addition individual training is conducted because of staff turnover. There has been a remarkable increase in filling the measles genotype information gaps in countries of the identified measles

genotypes are: C2, B3, D4, D5, D6, D7 D8 and H1. The predominant genotype is D4, with 14 countries in the Region having detected D4.

- Progress has been made in the identification of measles /rubella genotypes circulating in the Region
- It is vital that plan of action for surveillance are coordinated between epidemiologists and laboratory personnel
- Molecular epidemiology data is useful in tracking viruses in documentation of measles elimination, collecting throat swabs specimens in a timely manner and also considering using Oracol devices for virus detection
- In an elimination setting, rapid exchange of sequence data is a critical component of laboratory surveillance.

As more countries of the region move toward the measles elimination goal by 2010, the need for enhanced surveillance, allied to rapid and accurate measles virus diagnosis is required to monitor the success of this important programme. In this regard, it is vital that plan of action for surveillance are coordinated between epidemiologists and laboratory personnel and vigilance and readiness to detect any circulating measles virus in a timely manner becomes very critical. WHO/EMRO encourages countries to scale-up virological surveillance; samples for virus isolation must be obtained from every chain of transmission and from all congenital rubella syndrome cases in the first six months of life. If genetic information regarding circulating genotypes is enhanced, molecular epidemiological data will help to document viral transmission pathway, classify cases, and confirm the elimination of endemic transmission. Finally, the genetic data for rubella virus circulation in the Region needs continued support.

Discussion

- For an elimination target, rates of cases per district should be used rather than absolute numbers (as is done in AFRO).
- SAGE recommended that countries that had a first measles dose coverage under 80% should have a campaign for their second dose. Those countries with at least 80% coverage with MCV1 for 3 years or more then countries should also consider starting the second dose in routine.
- Regarding outbreaks of measles among children less than 6 months: if routine MCV1 at 9 months is not implemented well, it is possible outbreaks among children under 9 months of age can occur. If routine MCV1 at 9 months is good, then younger children will be protected by herd immunity.
- Regarding rubella vaccine: not including rubella in measles supplementary immunization activities was a missed opportunity
- Regarding national immunization committee for measles: can modify polio committee and bring on some experts for measles. More specialized persons in measles should be added, however, because the epidemiology of measles and polio are different.
- Regarding the type of measles genotype in the Region: the dominant genotype in the Region is D4 followed by B3. Each country virus needs to be classified, but this is the next step to differentiate D4s for each country.

2.4 Feasibility of eradication of measles

Dr A. Dabbagh, WHO/HQ

In May of 2009 the Executive Board of the World Health Assembly requested that the World Health Organization review the status of global measles control and evaluate the feasibility of global measles elimination (eradication). This report is to be presented to the Executive Board in January of 2010.

The criteria for elimination of a disease include: biological feasibility; impact on health systems; economic analysis; vaccine market analysis; programmatic feasibility; risk analysis for post-measles era; and global context and political feasibility. Each region of the WHO is preparing a report to determine the feasibility of elimination of measles in their region based on these criteria.

Significant progress has been made in measles elimination in the Region. By 2007 (3 years early) the 90% mortality reduction goal was achieved and 18 countries have either reached elimination or are close to elimination. However, key challenges remain including: conflict and insecurity; funding for supplementary immunization activities; inadequate surveillance; polio a competing priority; and stagnating or uneven routine coverage.

In summary, measles eradication is biologically and technically feasible and there is enough vaccine to meet the projected demand. However it is still unclear whether eradication is programmatically feasible by 2020 as only 5 out of 6 regions have elimination goals and India has yet to implement a strong measles immunization programme.

2.5 The Gates Foundation support to measles activities in developing countries

Dr M. Galway, Gates Foundation

The Bill and Melinda Gates Foundation has a strong history in supporting vaccine-preventable disease initiatives. The 2009 budget for vaccine-preventable diseases is US$ 130 million, of which approximately US$ 30 million is used for new grants, $25 million is used for payments on existing grants, and US$ 75 million is for the annual GAVI payments. The new grants portion is used for routine immunization, new vaccines and measles. 2009 Gates Foundation grants and contracts include: US$ 10 million to the Measles Initiative (MI); US$ 1.6 million to WHO on feasibility studies related to measles eradication; measles modelling workshop and global measles vaccine supply analysis through Oliver Wyman; and US$ 300 000 advocacy grant to the Carter Center.

The Gates Foundation engagement strategy for measles advocacy includes political and resource mobilization, technical support, and research. Political mobilization occurs with priority countries such as Nigeria, Ethiopia and India and WHO Regional Directors. Resources are mobilized through GAVI/HSS, matching grants with Lions International, with the Government of the United States and other G8 countries, and through collaboration with the Sabin Institute. Technical support is provided through MI grants, expanded surveillance grants, STOP-like activities with CDC, and for vaccine safety projects. Lastly, research is coordinated with WHO and focused on point of care diagnostics and operational research.

Moving forward, the Gates Foundation will use these strategies to support measles elimination activities. Without significant political mobilization, funding, technical support and innovation, global efforts may falter and undermine regional goals for measles elimination. The Gates Foundation strategy is designed to: a) help head off the projected resurgence of measles; b) create political support for a sustainable global measles effort; and c) build the scientific and technical basis for an evidence-based decision on measles eradication.

Discussion

- Regarding new vaccine/administration routes for measles vaccine: there are limitations with the current vaccine but we do know that it does work. In terms of new vaccines, the aerosol is the closest to being ready for use. It should be ready by next year. There are advantages and disadvantages for aerosol vaccines. These have been included in the analysis for measles elimination.
- Polio eradication should be a prerequisite for moving towards measles eradication:
  - WHO answer – As for polio versus measles – these can be done in tandem – we are trying to sell this as a package by showing that when you are supporting supplementary immunization activities you are supporting the strengthening of systems. Lessons being learnt from the polio and smallpox eradication show these strategies need to be focused on – for example focusing on the weakest link – not leaving until the end.
  - Gates Foundation answer – opinion is that polio is a priority before measles, but not sure how the Gates Foundation would weigh in on the issue if/when an eradication goal is set.
- Regarding whether middle-income countries are on the Gates Foundation's radar: most Gates Foundation money goes to GAVI but GAVI doesn't support middle-income countries very well. One strategy is to advocate for GAVI to work more with middle-income countries. If the decision is made to move towards eradication of measles then the Foundation would have to adjust its budget. Currently most of its vaccine-presventable disease funds go to GAVI though 2015.

3. ACHIEVING AND MAINTAINING HIGH POPULATION IMMUNITY TO MEASLES

3.1 Somalia: Child Health Day: a success story

During 2009 Somalia conducted a child health day (CHD) to distribute measles vaccine along with TT, DPT, OPV, ORS, vitamin A, Aqua Tab, albendazole, health promotion materials and nutrition screening. The strategy used for these CHDs included: fixed posts in all health facilities; temporary selected CHD posts such as schools; and mobile CHD teams for hard to reach areas. CHD campaigns were conducted every six months and each round of the campaign lasted for 5 days. The objectives of the CHDs were to:

- Immunize at least 95% of children aged 9 to 59 months with measles vaccine irrespective of the previous immunization or disease status

- Immunize at least 60% of children aged under one year with routine EPI vaccines
- Immunize at least 95% of children aged 0 to 59 months with one dose of vitamin A according to the age of the child
- De-worm all children aged 12 to 59 months with albendazole
- Screen all children 6–59 months using mid-upper arm circumference tapes and refer acutely malnourished children for further management in selective feeding centers
- Immunize at least 80% of women of child bearing age with protective dose of tetanus toxoid
- Promote the use of oral re-hydration therapy.

Somalia was able to obtain high level political commitments for the CHDs, with ministers administering OPV at the CHD opening ceremony and attending a CHD planning meeting. CHD microplans, social mobilization, supervision, logistics and cold chain, injection safety and waste management were all planned prior to implementing CHDs.

Despite fatigue from the polio vaccination campaign, CHDs were a success in Somalia. Coverages for each of the CHD interventions were as follows:

- Measles – 84%
- DPT 1 – 61%
- OPV – 85%
- Vitamin A – 83%
- De-worming – 83%
- TT – 55%
- ORS – 85%
- Aquatabs – 86%

Strengths of the CHDs were that multiple interventions and delivery strategies were accepted by the public community leaders. An additional strength was the coordination and roles adopted by WHO, UNICEF, Ministry of Health and local nongovernmental organizations.

Weaknesses included: the extensive amount of time needed to complete all the coordination between the different agencies/community; weak social mobilization in some areas; poor training of vaccinators in some areas; money transfer delays in central zone; mismatching vaccine and diluents in one region; and a general delay in reporting results.

Somalia will continue to conduct CHDs for at least 2 more rounds and will continue to work with partners on how to make these vaccines/interventions sustainable beyond CHD delivery. They are working to strengthen routine immunization by implementing the Reaching Every District (RED) approach. Lastly, Somalia plans to conduct an impact assessment of these CHDs at a later date.

3.2 Group work: achieving and maintaining high population immunity to measles in the Region

Group 1: GAVI eligible countries: Afghanistan, Djibouti, Iraq, Pakistan, Somalia, Sudan and Yemen

Countries that presented were Iraq, Pakistan, Somalia and Sudan. The session was broken down by country with a summary and challenges presented for each.

- Iraq provides MCV1 at 9 months with MCV and MCV2 at 15 months with MMR. Iraq has seen a drop in MCV1 and MCV2 coverage during 2003–2008 and a large outbreak of measles began in 2008. The way forward in Iraq is to conduct follow-up supplementary immunization activities in October and November of 2009, strengthen routine immunization, and measles case based surveillance.
- Pakistan provides MCV1 at 9 months with MCV2 given between 12 and 23 months (introduced in 2009). National MCV1 coverage is 79%. Pakistan experienced a sharp decline in measles cases following a multi-phase catch-up campaign that took place in 2007–2008. These campaigns were completed successfully and case-based surveillance has been started. The way forward in Pakistan is to fully implement case-based surveillance nationally, to conduct a follow-up campaign in 2011, and to strengthen routine immunization services.
- Northern Sudan has significantly reduced measles cases during 2004–2008 through catch-up and follow-up campaigns. Remaining challenges include the accumulation of susceptible children which requires implementation of follow-up campaigns, difficulty accessing some areas of the country due to conflict and insecurity, difficulty accessing nomadic populations and seasonal migrants, and engaging the private sector in measles vaccination initiatives. Future plans include a follow-up campaign in 2010, expanding collaboration and communication with nongovernmental organizations and community leaders, mapping nomadic population movements to target these groups, using routine and campaign coverage for decision-making, and planning for the introduction of MCV2 in routine immunization programmes.
- Somalia has conducted a catch-up campaign and has seen a drop in measles cases. Follow-up campaigns are being conducted using CHD; however, the number of suspected measles cases is on the rise. The way forward in Somalia is to continue CHDs, to strengthen routine immunization nationally; to strengthen measles case based surveillance in the northeast and northwest zones, and to establish measles case-based surveillance in the south/central zones.

Group 2: Middle income countries: Egypt, Islamic Republic of Iran, Jordan, Lebanon, Libyan Arab Jamahiriya, Morocco, Palestine, Syrian Arab Republic and Tunisia

In general, all middle-income countries have MCV1 and MCV2 routine doses, have case based measles surveillance, and have conducted catch-up campaigns. The primary challenges to achieving measles elimination include limiting importation from neighboring countries, ensuring immunization of migrant groups (nomads, migrant workers, refugees), and maintaining high routine immunization coverage.

Group 3: GCC countries: Bahrain, United Arab Emirates, Kuwait, Oman, Qatar and Saudi Arabia

This group presented collectively by including general themes that cross-cut all countries. In general, these countries have conducted supplementary immunization activities as a response to outbreaks or to control and cover high-risk groups as well as to sustain high immunization coverage. Extensive epidemiological investigations have been conducted in response to outbreaks in Bahrain, Oman, Qatar and Jordan. In all countries case based surveillance and outbreak investigations are conducted. High coverage with two doses of MCV is achieved by most countries in the group; some countries have 3-dose coverage. Most countries have adopted MMR vaccine and conducted regular campaigns to avoid disease shift to the older populations. Challenges include changing demographics in the region, reaching refugees and expatriate laborers with measles vaccine, communication between and within countries, economic limitations and competing priorities (H1N1).

Discussion

Regarding how migrant workers in countries that are close to elimination can catch measles: measles can either be imported to the country by migrant workers and their families or by a non-immunized national. Once transmitted to these under-vaccinated migrant workers, it spreads easily among them because this subgroup does not have herd immunity.

4. INVESTIGATION AND CONTROL OF MEASLES/RUBELLA OUTBREAKS

4.1 Investigation and response to 2008-2009 measles outbreak in Iraq

During the years leading up to 2008–2009, Iraq experienced decreased security and social disruption that limited immunization services, decreased experienced immunization staff, displaced large segments of the population, and eroded immunization/health care infrastructure. These developments ultimately led to low routine immunization coverage and an outbreak of measles during 2008–2009. Prior to this insecurity Iraq had an approximate 20-year history of a 2 dose schedule of measles vaccine and a strong immunization programme.

To investigate this outbreak, enhanced case based surveillance was conducted and all suspected measles cases had a laboratory investigation that included serological confirmation for measles and rubella using IgM ELISA technique. Incidence of measles cases was tracked and demographics (including location) of all measles cases were obtained.

The outbreak extended 89 weeks starting in 2008 and peaked in 2009 with approximately 2000 cases during week 13 of 2009. The highest incidence during the first 36 weeks of 2009 was in the Wassit district (2051–4300 cases) followed by Muthanna, Missan, Diwaniya, Babylon, Kerbala, Baghdad-Karkh, Baghdad-Resafa and Diyala districts, each with between 701 and 2050 cases. The majority of cases were male (52%), 1–4 years of age (45%), and unvaccinated (63%).

Iraq experienced a large-scale outbreak of measles during 2008–2009 affecting largely unvaccinated children aged 1–4 years. In response to this outbreak Iraq initiated outbreak response immunizations that have shown to have decreased measles cases in the latter portion of 2009. Continued campaigns and immunization system strengthening will be needed to maintain the gains achieved in measles incidence reduction and to achieve measles elimination.

4.2 Investigation and control of 2009 measles outbreak in the Libyan Arab Jamahiriya

The national measles/rubella programme in the Libyan Arab Jamahiriya was established to maintain high population immunity for measles and rubella and to ensure quality surveillance to detect any measles or rubella outbreaks. High population immunity to measles and rubella is achieved through routine immunizations and supplementary immunization activities. Despite catch-up, mop-up, and follow-up campaigns during 2005–2009, outbreaks of measles occurred during 2007 and 2009.

Routine and supplementary immunization coverage information was reviewed to evaluate the immunity profile of the Libyan Arab Jamahiriya. In addition, surveillance and laboratory information was reviewed to describe the outbreak by person, place and time.

The 2007 measles outbreak included 59 cases; the majority (69%) was from Sabha. Most cases had recently entered the Libyan Arab Jamahiriya and were not vaccinated against measles. The primary genotype of cases during this outbreak was B3.

The 2009 measles outbreak included 321 laboratory confirmed cases; the area with the highest number of cases (71) was Sabha. Additional characteristics included: most cases (79%) were not vaccinated against measles; 23% of cases were under 12 months of age; cases were mild; the primary genotype during this outbreak was B3; and the outbreak was over in July of 2009.

The measles outbreaks are less in number per year than prior to the catch-up campaign in 2005. The clinical features of the measles cases during the outbreaks described were mild in nature with no reported deaths. Campaigns during 2005 and 2009 markedly decreased the incidence of measles in the target age groups. The measles/rubella surveillance system in Libyan Arab Jamahiriya can detect measles outbreaks. The elimination of measles and rubella can be achieved. A measles follow-up campaign will be conducted during 2010–2011 and will target adults.

Discussion

- Regarding high staff turnover and how to overcome this problem: a lot of former military workers now work in health centres. This creates a knowledge gap. They have limited knowledge of immunization programmes and health care in general and need a lot of training. Challenges of campaigns include travel for supervisors and finding children, as they were kept inside houses. Now that things have gotten better they can be accessed more easily.

- Regarding how to define case mortality: a measles death is defined as a child that dies from pneumonia or gastroenteritis with acute case of measles. The total number of measles deaths may be underestimated, but this is the definition that is reported.
- Regarding the quality of house-to-house supplementary immunization activities and campaigns in general: all districts could not conduct high quality (house-to-house) campaigns, so even though campaigns were conducted they weren't necessarily high quality. 2007 was a difficult year for Iraq. Campaign quality wasn't great as a result. MMR was used in the campaign. In 2009 new vaccine has been distributed to all districts.
- Regarding when to vaccinate in response to an outbreak: previous guidelines were that once an outbreak has occurred there is no need to conduct response. New evidence shows that if an outbreak immunization response is conducted early there is an opportunity to stop transmission. In addition, even before an outbreak is identified as measles, it is recommended to vaccinate children that come to health centres with measles vaccine.
- Vitamin A was given to all cases.
- Regarding what vaccine will be used during the next campaign: the vaccine will be measles.
- No nationwide campaign was conducted in 2008 because of the cholera outbreak, which was competing with measles outbreak.
- MMR vaccine will begin in 2010. Compulsory second or third vaccine. First dose will be given at 15 months. Second dose at school age. First (or zero dose) will be given at 9 months.
- Regarding why so few cases were EPI-linked: not all data is in at this point. This figure may change in the future once all data are in.
- In the Libyan outbreak, most of the cases were Libyans (over 70%).

5. COUNTRY UPDATES: QUALITY OF MEASLES/RUBELLA CASE-BASED SURVEILLANCE

5.1 Quality of measles/rubella surveillance data reported to EMRO

Mr R. Bekhit, WHO/EMRO

Every country in the Region is held to the same surveillance indicators. The reporting rate indicators for the national and district level include:

- At national level, a rate of 2 non-measles suspected measles cases per 100 000 population.
- Cases investigated and discarded as non-measles cases using laboratory testing in a proficient laboratory and/or epidemiologically-linked to another confirmed disease.

At least 1 non-measles suspected measles case should be reported annually per 100 000 population in at least 80% of the administrative units at the lowest administrative level (for example, a district) or at an administrative level that has an average population of at least 100 000.

Analysis of reporting rate indicators for the Region show that during 2009, eight countries met the measles reporting rate target whereas in 2008 twelve countries met the target. The laboratory confirmation indicator is: specimens adequate for detecting measles IgM should be collected from at least 80% of suspected measles cases and tested in a proficient laboratory. Any cases that are epidemiologically linked to a laboratory-confirmed case of measles or other communicable disease should be excluded from the denominator.

Analysis of laboratory data show that 17 countries met this indicator in 2009 and 14 met the indicator in 2008. Indicators that track the adequacy of a measles case investigation include:

- At least 80% of all reported suspected measles cases should have had an adequate investigation within ≤48 hours of notification.
- The numerator is the number of suspected measles cases for which an adequate investigation[1] was carried out within 48 hours of notification, and the denominator is the total number of suspected measles cases. Laboratory data show that 7 countries met this indicator in 2009, 1 during 2008, and 10 during 2007.

In addition to the indicator above, there are two other indicators that are currently not measurable due to limited data. These include the percentage of outbreaks with samples collected for virus detection (target 80%) and the percentage of suspected cases investigated within 48 hours of notification (target 80%). To meet the criteria for measles elimination, it is necessary to analyse data on all the indicators presented during this presentation. Each country will need to comply with the surveillance quality indicators established for the measles elimination strategy, through time, and by all levels.

Discussion

- Regarding difficulty collecting all the data to ensure meeting the indicators: we are collecting data to assist countries and remind to check districts to make sure there are no problems.
- The indicator on case investigation within 48 hours means to initiate case investigation within 48 hours.
- Meeting the indicator of at least 1 case per district per year may be difficult in some districts with low population. More in-depth analysis of this is needed. If a district is not reporting, there is an issue.
- The Regional Office has a standard investigation form and software to use for reporting.

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[1] An adequate investigation includes at a minimum collection of all of the following data elements from each suspected measles case; name or identifiers, age (or date of birth), sex, date of rash onset, date of specimen collection, vaccination status, date of last vaccination, date of notification and date of investigation and district. In addition, it should include an investigation of all epidemiological links.

5.2 Group work: country status of the performance of measles/rubella surveillance

Group findings

- All countries are using case-based surveillance except Somalia and Afghanistan for certain limits.
- Not all countries reached the target of elimination (<1 case per million population).
- Most of countries did not reach the required non-measles non-rubella case rate and did not meet the indicator of < 48 hours for case investigation.
- Not all countries have a congenital rubella syndrome control plan.
- Some countries have not established a NITAG.

Group recommendations

- Case-based surveillance should be strengthened at the national level in all countries.
- Countries should standardize the forms used for measles and rubella elimination.
- Rubella vaccine should be introduced in countries that have yet to include this vaccine in their routine EPI schedule
- All countries should establish a NITAG
- AFP and measles surveillance should be integrated
- Interim surveillance indicators should be developed
- Measles elimination guidelines should be developed
- Congenital rubella syndrome surveillance should be established.

6. REGIONAL MEASLES ELIMINATION VALIDATION PROCESS

6.1 Progress on development of validation of measles elimination guidelines

Dr B. Naouri, WHO/EMRO

In 1997, Member States of the Eastern Mediterranean Region resolved to eliminate measles from the Region by 2010. In 1999, Regional Office developed a five-year plan for measles elimination based on the WHO–UNICEF joint strategy for measles mortality reduction. This plan evolved over time and includes the following strategy.

- Achieving wide scale population-based immunity through catch-up campaigns as needed
- Sustaining high measles immunity through high vaccination coverage (> 95% coverage) of all cohorts born after the campaign with two measles vaccine doses provided through the routine programme (MCV1 and MCV 2) or routine MCV1 and periodic follow-up campaigns every 3 to 4 years
- Strengthening an integrated surveillance system for measles by establishing case-based surveillance with investigation and laboratory testing of all suspect cases of measles

Considerable progress has been made toward measles elimination in the Region. By the end of 2008, all countries conducted catch-up campaigns. As result of increased coverage and

vaccination campaigns, case-reports of measles decreased from 38 592 in 2000 to 15 670 in 2007.

WHO estimates that measles mortality in the Region decreased from 96 000 deaths in 2000 to < 10 000 deaths in 2007, indicating that countries achieved the 2010 GIVS goal of 90% reduction in measles deaths by 2010 (compared with measles mortality in 2000) 3 years ahead of schedule. Currently, nationwide case-based surveillance for measles is conducted in 19 coutnries. Pakistan, Morocco and Somalia conduct case-based surveillance in sentinel surveillance networks and are planning to implement nationwide measles surveillance by end of 2009.

While some countries face challenges in achieving high population-based immunity and high quality measles surveillance, others are approaching measles elimination. In 2008, eight countries (Bahrain, Islamic Republic of Iran, Jordan, Libyan Arab Jamahiriya, Oman, Palestine, Syrian Arab Republic and Tunisia) reported an incidence rate of confirmed measles of less than 1 case per 1 million population in the presence of good measles surveillance. Many of these countries would like to validate their measles elimination status.

In anticipation of the need to validate measles elimination, the Regional Office hosted a technical consultation to elaborate the process in September 2008. Recommendations made during this consultation included the need to define the criteria, parameters, and process for documenting and confirming measles elimination. This protocol outlines criteria for elimination, indicators to be monitored, data to be collected, as well as the methodology and process to validate measles elimination in the Region. Through verification and analysis of the documentation for each country, it will be established whether the Region has reached the elimination goal.

Objectives

- Describe epidemiological and virologic evidence required to document the absence of measles caused by endemic measles virus transmission.
- Define performance indicators and quality criteria for measles surveillance activities to document the absence of endemic measles virus circulation.
- Outline methods for countries to determine whether population-based immunity is high enough to sustain interruption of transmission and to prevent, in the presence of measles virus, the reestablishment of endemic circulation.
- Describe methods to determine if national immunization programmes are capable of maintaining the achievement of measles elimination.
- Outline process to assess the quality of information; determine whether the data are complete, valid, representative, and consistent among the different sources of information.

Field testing

During 2009 the measles elimination guidelines were tested in the Islamic Republic of Iran, Jordan and Syrian Arab Republic. The duration of each test was 5 days. Data were

collected using in-depth key informant interviews (EPI, surveillance, laboratory), desk reviews, field visits to health centres (rural and urban), and questionnaires. The 5 essential components of these reviews included: 1) country background information on measles/rubella vaccination programme; 2) measles/rubella and congenital rubella syndrome epidemiology; 3) performance of surveillance activities; 4) laboratory activities; and 5) population immunity.

Main findings

The main findings of the field testing for each essential component of the evaluation were:

- Country background information
  - Sub-group population size unknown: refugees, foreign workers, nomads, others
  - No population density country map (only tables)
- Measles/rubella and congenital rubella syndrome epidemiology:
  - No reports on investigation/control of measles outbreaks
  - Very limited data on rubella/congenital rubella syndrome
- Performance of surveillance activities:
  - Reporting rate of 1 measles suspected case is not met in all districts
  - No regular EPI, surveillance and laboratory meetings
  - Data management: “missing data” or “unknown”
  - No uniform case investigation and conducting investigation within 48 hours not tracked
  - Data not used for action
- Laboratory activities: no quality control programme set for private laboratories that are testing for measles
- Population immunity
  - Low coverage among some sub-populations: refugees, mobile population, foreign workers, others
  - Strategies to improve vaccination coverage and other control measures are not well identified among high-risk groups/areas
  - Outbreaks still occurring in some countries that seem close to elimination

Next steps and conclusion

Next steps toward measles elimination validation in the Region include completing additional field testing in 2010 and finalizing the validation tool. Additional activities to be completed during 2010–2011 will be to develop a comprehensive rubella/congenital rubella syndrome elimination plan for the Region, and for the development of national and regional committees for the validation of measles elimination. The same committee responsible for polio eradication might be modified to address validation of measles elimination. Outside experts should be added to the committee to address specific areas keeping in mind the need to avoid conflict of interest.

In conclusion, no significant gaps were found in data to document measles elimination during field tests. Countries are encouraged to review the measles elimination and

surveillance quality indicators and to evaluate their progress toward achieving these indicators in preparation for elimination validation. Validation of measles may start as early as 2011 for countries that have met these indicators.

6.2 Experience of PAHO in the development of guidelines for validation of measles elimination

Dr P. Rota, CDC Atlanta

The measles elimination goal for the Region of the Americas was the year 2000. The Pan American Health Organization defined measles elimination as the interruption of endemic measles virus transmission in all the countries of the Americas for a period greater than or equal to 12 months, in the presence of high quality surveillance. Strategies employed to achieve this goal include vaccination campaigns ("catch-up" – children 1–14 years; "keep-up" – maintain coverage of ≥ 95 % in the routine programme for children aged 1 year; "follow-up" – children aged 1–4 years and introduction of MMR or MR in routine programme; and "speed-up" – target adolescents and adults) and high-quality integrated measles/rubella surveillance.

Criteria essential to the documentation and verification of measles elimination includes: implementation and maintenance of high quality surveillance; verification of the interruption of endemic measles, rubella and congenital rubella syndrome cases in all countries of the Americas for a period of at least 3 years from the last known endemic case, in the presence of high quality surveillance; verification of absence of virus transmission through viral laboratory detection; and demonstration that all population cohorts aged less than 40 years have reached coverage of >95% with measles/rubella containing vaccine.

Once elimination is verified, major challenges remain to maintaining measles, rubella, and congenital rubella syndrome elimination in the Americas. These challenges must be addressed by each country in the region to ensure the measles virus does not become re-established in the region. Some challenges include:

- The risk of virus importations from other regions
- Preventing cases secondary to importation (in some countries)
- Preventing and responding to outbreaks
- Reaching susceptibles through a second opportunity/high-quality follow-up campaigns
- Strengthening integrated measles/rubella and congenital rubella syndrome surveillance
- The low PPV of IgM detection and limited number of samples for virus detection/isolation

Since the introduction of catch-up campaigns in the 1990s, measles cases drastically decreased from approximately 250 000 cases in 1990 to approximately 3000 cases in 1999. Follow-up campaigns during the 2000's maintained this reduction and during 2002 endemic transmission of measles was interrupted in the Americas. As a result of these efforts, a total of 3.2 million measles cases and 16 000 deaths will have been averted during 2000–2020. This will ultimately result in a savings of US$ 208 million in treatment costs.

6.3 Testing of validation of measles elimination guidelines: lessons learned

Islamic Republic of Iran

- The Islamic Republic of Iran has achieved >95% coverage in almost all districts; however there may be some immunity gaps in lower levels such as in slums and among nomadic populations, gypsies and refugees.
- Potential threats to achieving elimination include: competing public health/political priorities; high prevalence of measles in border areas; adverse events following immunization may limit public acceptance to immunization; human resource limitation; and financial shortage.
- Regarding surveillance indicators: the case detection rate should be improved by motivating health care workers, collaboration with private sectors, and communication by the medical society.
- Regarding the measles validation guidelines:
  - Are structured the same way as the polio eradication initiative
  - Provide better data analysis at the national level
  - Demonstrate weaknesses of the national programme
  - Are needed for the countries which are near the elimination goal
  - Provide a uniform template for the Region
  - Amount of data requested is appropriate for initial review but is too much for an annual report.

Jordan

- An outreach programme for reaching high risk groups (gypsies, nomads, refugees, etc) is needed.
- Monitoring the measles indicators at district level 7 is needed.
- The private sector needs to be engaged to be involved in reporting.
- The national validation committee is comprised of three paediatric infectious disease physicians, two epidemiologists, a virologist, and representatives from paediatric and public health associations. All members are from outside the Ministry of Health.
- The technical committee for measles and rubella elimination is comprised of three pediatricians from the Ministry of Health, the director of communicable diseases, the EPI manager, and representatives from the pediatric association, private sector, Royal Medical Services, and the national laboratory.

Discussion

- Regarding surveillance indicators at subnational (district or provincial) level: it may be useful to look at subnational indicators to identify areas that aren't meeting the indicators and also to find areas that are performing well and to see why.
- It is important to maintain focus on sensitivity of surveillance system, the quality of data reported, quality of laboratory sample processing and the immunity profile of the country.

- The amount of data collected ruing the initial elimination validation is appropriate. However, it would be too much to complete for annual updates. An annual update guideline should be created similar to the polio eradication annual update to use for measles.
- Jordan has included a neonatologist on its national validation committee.

6.4 Panel discussion: use of indicators to monitor measles surveillance quality and measles elimination at country level

Dr A. Dabbagh, Dr A. Uzicanin, Dr P. Rota, Dr F. Mahoney, Dr N. Teleb

Below are listed the indicators discussed during this session, the major themes discussed per indicator, and the points and counterpoints presented during the discussion session. These discussion points/counterpoints do not constitute final decisions regarding the indicators but are presented to summarize the points discussed per indicator.

Reporting rate. At national level, a rate of 2 non-measles suspected measles cases per 100 000 population should be considered a minimum. These cases must have been investigated and discarded as non-measles cases using laboratory testing in a proficient laboratory[2] and/or epidemiological-linkage to another confirmed disease.

In addition, at least 1 non-measles suspected measles case should be reported annually per 100 000 population in at least 80% of the administrative units at the lowest administrative level (for example, a district) or at an administrative level that has an average population of at least 100 000.

Main points raised with regard to this indicator are as follows.

Case definition: should it be fever/rash or non-measles non-rubella?

- Point: Countries without rubella immunization programmes will easily meet this indicator because they will have rubella cases. Some countries with rubella immunization programmes may have difficulty meeting this indicator and those that are near measles and rubella elimination may consider switching to fever rash illness as the case definition.
  - Panel counterpoint: Countries like Brazil in the Americas, even though they had rubella immunization, were able to meet this indicator – experiences from other regions show that this can be met.
  - Panel counterpoint: These are the exact points discussed 2 years ago. Countries were asked to go back and review this topic to see if they could do fever/rash illness. Iraq thought that doing this would have had a huge burden on the

[2] A proficient laboratory is a WHO network laboratory that uses a validated assay and has passed the annual WHO proficiency test.

laboratory. Perhaps a decision should be taken whether the whole Region switches to fever/rash, or at least those countries that are approaching elimination.

- Point: Countries like Pakistan may have enough non-measles rubella cases and will be able to meet this indicator easily. As for the districts, there are a number of districts that are sparsely populated – it will be difficult for some countries to get this indicator. Perhaps population proportion should be calculated.
- Point: At the national level there is no problem but perhaps the second administrative level should be used rather than district (instead of saying first administrative level say 'second admin level') where there will be more than 100 000 population.
- Point: Population and type of populations living in districts are variable, in some they are foreigners, others national – however Bahrain is able to reach the indicator in all areas.
- Point: Egypt will work on surveillance and wants to integrate AFP surveillance with measles surveillance. Egypt is going to use fever/rash case definition.
- Point: Going to global elimination will require a standard case definition.
- Point: Why would rash/fever illness and non-measles suspected measles have the same rate?
- Point: Why is rubella not included? Why not non-measles non-rubella suspected measles?

Definition of lowest administrative unit: Should lowest administrative unit apply to province or district?

- Point: The transmission of measles in not same in rural versus urban. It is not normal to have the same minimum rate for all districts rural/urban and for all districts with different number of population. It is important to have a fixed number for the lowest level fixed area. In Tunisia there are rural districts in the desert with small dispersed populations; it is not expected to find the same number in districts with urban area compared to rural.
  - Panel counterpoint: Even though this is a low indicator most districts are not able to meet it. They need to be able to meet this indicator before we change.
- Point: In Qatar, most cases are being reported at the national level and aren't necessarily reported to the district level.

Laboratory confirmation. Specimens adequate for detecting measles IgM should be collected from at least 80% of suspected measles cases and tested in a proficient laboratory. Any cases that are epidemiologically linked to a laboratory-confirmed case of measles or other communicable disease should be excluded from the denominator.

Main points discussed about this indicator were as follows.

Indicator level: should it be 80% or higher?

- Point: should this be raised to 100%. If we use 80% collection, then 20% of cases are excluded from the reporting rate. The issue is that they are measles cases but are not used in the reporting rate.

  - Panel counterpoint: These percentage cutoffs are set arbitrarily –80% is set as the minimum but we are still having trouble meeting it.
- Point: Iraq –the 20% not tested can be classified as clinically diagnosed and then they can be in the rate. "Adequate sample" needs to be defined, along with when to collect sample.
  - Panel counterpoint: If you are testing more then you will meet your first indicator.

How many specimens to collect during an outbreak?

- Panel point: Samples should be collected for virus detection from 80% of identified transmission chains and tested in an accredited laboratory.
  - Member counterpoint: Iraq – 80% is too high – usually they are all the same genotype of virus.
- Panel counterpoint: Sometimes you can tell how many outbreaks/chains based on laboratory. Not asking for 80% of samples during an outbreak.
- Panel counterpoint: Each situation is unique for each country. In countries that are close to elimination, every case is an outbreak and specimens should be collected on all cases.

Adequacy of investigation. At least 80% of all reported suspected measles cases should have had an adequate investigation within ≤48 hours of notification. The numerator is the number of suspected measles cases for which an adequate[3] investigation was carried out within 48 hours of notification, and the denominator is the total number of suspected measles cases.

Main points discussed about this indicator were as follows.

Should we consider collecting all vaccination history rather than just last date of vaccination?

- Point: Pakistan – elements of adequate investigation, important one, date of last vaccination. Propose instead of asking date of last vaccination – ask if child has vaccination in last 6 weeks rather than last date.
  - Panel counterpoint: This is a good way to distinguish between vaccine-related rash and real measles. Another way may be to collect data on all vaccinations – this will help to determine vaccine effectiveness during an outbreak.

Scope of indicator

- Point: Is this indicator for suspected cases or just cases with an adequate sample?

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[3] An adequate investigation includes at a minimum collection of all of the following data elements from each suspected measles case; name or identifiers, age (or date of birth), sex, date of rash onset, date of specimen collection, vaccination status, date of last vaccination, and district. In addition, it should include an investigation of all epidemiological links (as defined at the country/regional level).

- Panel counterpoint: indicator is for all cases.

Regarding when investigation is initiated and when it is adequate

- Point: Initiate investigation and adequate investigation are two different things.
  - Panel counterpoint: Perhaps another indicator should be considered for completeness of investigation among confirmed cases. Then there would be 2 indicators – 1) investigation within 48 hours, 2) adequate investigation of confirmed cases.

Viral detection. Samples[4] should be collected for virus detection from 80% of identified transmission chains (outbreaks) and tested in an accredited laboratory. The numerator is the number of transmission chains with sufficient samples for viral detection and the denominator is the number of transmission chains identified.

Main points discussed about this indicator were as follows.

Genotyping during an outbreak

- Point: why bother genotyping if it is always D4?
  - Panel counterpoint: all D4 genotypes are not identical. We can tell the differences between viruses within each genotype and can help tell us the chain of transmission.

Difference between chain of transmission and an outbreak

- Point: Pakistan – use either chain of transmission or outbreak to avoid confusing things.
  - Panel counterpoint: you can have chain of transmission (2) without an outbreak.

7. RECOMMENDATIONS

To Member States

1. Use data for action.
2. For outbreaks, develop specific strategies to bridge the immunity gap among high-risk groups.
3. Improve the quality of supplementary immunization activities (GCC coutnries).
4. With regard to measles surveillance and elimination indicators:
   4.1 Collect and analyse data at subnational and district level

[4] Where possible, samples should be collected from 5–10 cases early in the outbreak and every 2–3 months thereafter if transmission continues. For virus isolation, throat or urine samples should be collected within 5 days after rash onset. For virus detection using molecular techniques, throat samples can be collected up to 14 days and for oral fluid samples up to 21 days after rash onset.

4.2 Investigate the root cause of low performance and implement corrective actions
4.3 Develop interim level of indicators for countries with measles control goal.

To the Regional Office

5. Improve/expand advocacy and funds raising for measles elimination activities.
   - Develop advocacy materials
   - Improve visibility of measles elimination and messaging
   - Provide update on progress towards measles elimination to the Regional Committee
   - Regional advocacy: reach out to the Islamic Development Bank, Arab Women's Organization, etc.
   - Conduct immunization weeks along with Child Health Days
   - Complete updates and messages using the EMRO measles website
   - Expand social mobilization

8. SUBMEETING ON MEASLES AND RUBELLA LABORATORY NETWORK

8.1 Introduction

A submeeting on the measles and rubella laboratory network was held on 1 October 2009. The objectives of the submeeting were to:

- Review progress made on laboratory surveillance of measles/rubella in the Region
- Provide update technical information on laboratory issues related to measles elimination goals in the Region
- Discuss further strengthening and way forward on measles and rubella laboratory network in the Region.

The meeting was attended by national focal points for measles and rubella laboratory and surveillance officers from countries in the Region. Dr Hinda Ahmed welcomed the participants and inaugurated the session. During the course of the meeting four sessions were dealt each addressing specific topics where amble time was given for discussion and exchange of information among the LabNet.

8.2 Progress and challenges in global and regional measles and rubella laboratory surveillance

8.2.1 Global measles and rubella laboratories network
Mr D Featherstone, WHO/HQ

The measles and rubella laboratory network (LabNet) consists of 679 laboratories serving 164 countries. As of August 2009, almost 320 000 serum samples were tested globally for measles IgM with China contributing a large proportion of the numbers of tests. Timeliness and quality of the testing is high with more than 80% of laboratories reporting at least 80% of their results within 7 days. The quality of the LabNet is high as indicated in

passing score of the global proficiency test, almost 99% of the national laboratories achieved a pass and most achieved 100%. Most of the remaining subnational laboratories participated in national proficiency testing programmes with a similar high level of performance.

The tracking of virus globally can help determine whether outbreaks are caused by endemic or imported virus strains and can monitor progress with achieving measles control goals. There has been a marked increase in the collection of measles molecular epidemiological data since 2003 as more laboratories develop capacity for molecular techniques and the programmatic value in tracking viruses has been recognized. In 2007 a WHO genotype database was established to track measles viruses detected by the LabNet. 3425 measles viruses had been submitted to the database comprising 18 of the 23 genotypes from 113 countries out of these 14 were from countries of the Region. Marked improvement was noted in molecular surveillance but could do better especially for the silent countries and for rubella

In 2007–2008 training workshops were held in 5 WHO regions to meet the needs of laboratories experiencing staff turnover. Since 2007, training workshops have also involved strengthening the capacity of laboratories for virus detection.

8.2.2 Regional measles and rubella laboratory network
Dr H Ahmed, WHO/EMRO

Recommendations outlined in last year's (October 2008) laboratory network sub-meeting were reported to be fully implemented. These included individual country training for measles/rubella molecular techniques for virus, such as in Afghanistan, Iraq and Syrian Arab Republic. National measles/rubella laboratories that had difficulties in shipment of liquid serum samples to RRLs for validation have implemented dried serum on filter paper techniques. In addition, innovative techniques were used for genotype detection by the RRL. Surveillance officers participated in the regional laboratory network meeting to facilitate sharing experiences and resolving challenges.

Up to September 2009, 19 812 measles suspected cases were reported, of which 10 124 were tested for IgM resulting IgM positive 4695 and 569 rubella IgM positives. Fifty per cent of laboratory confirmed measles cases came from from the Iraq measles outbreak which started in late 2008 and continued to April 2009. Issues like accreditation and enhancing collection of clinical specimen for measles and rubella virus detection and genotyping are ongoing processes. 20 countries have passed accreditation review. Attempts at using screening kits which have not been independently validated were carried out in Jordan before introducing to the laboratory test kit.

Surveillance of measles virus molecular epidemiology is becoming more and more important towards measles elimination goal. Genotyping is increasingly being used in measles surveillance programme to monitor the success of elimination programme. Countries in the Region have made remarkable progress in identifying circulating measles virus strains. In the Region, identified measles genotypes are: C2, B3, D4, D5, D6, D7 D8 and H1. The predominant genotype is D4, with 14 countries in the Region having detected D4. However,

the baseline information of measles genotype is not yet known in Palestine, Saudi Arabia or the United Arab Emirates; Palestine has not had measles cases in the past three years. Bahrain, Islamic Republic of Iran, Iraq, Libyan Arab Jamahiriya, Morocco, Oman, Pakistan and Syrian Arab Republic are countries that efficiently monitor circulating measles virus.

There has been some improvement in submitting viruses sequence information to the WHO genotype database on timely basis, however, require additional effort.

Challenges include the following.

- Measles validation process, increased laboratory workload on H1N1 activities
- Keep assuring quality of non-validated IgM assays improving virological surveillance
- Validating procedures dry serum and extract RNA/dry measles infected Vero/SLAM cells for shipment
- Continuity cost of laboratory supplies and training from external resource
- High cost of serological and molecular laboratory testing of measles and rubella

8.2.3 Progress in measles/rubella laboratory surveillance in Pakistan

In 2009 up to July the national measles and rubella laboratory tested 389 serum samples of which 104 were IgM positive for measles. For rubella, 284 serum samples were tested and 81 were IgM positive for rubella. The laboratory has passed and scored 100% on the 2009 proficiency panel for both measles and rubella as well as for external quality control. The adequacy rate of received samples at the laboratory is 99.4% and 100% of specimen results are send by laboratory to EPI within 7 days. Information on last date of vaccination is still very poor for 18.5% of cases.

Specimens for measles virus detection: 7 throat swabs were received at the laboratory, inoculation of cell cultures failed to yield isolated virus. However when all were run by PCR, measles virus was detected in all of the 7 samples. These were subjected to sequencing analysis and measles genotype D4 was identified.

One measles outbreak was investigated in North Waziristan in 2009. Of 8 blood samples, 7 were IgM positive and 1 equivocal. No throat swabs were collected. Efforts should be made to collect clinical specimens for virus detection in all outbreaks.

8.2.4 Progress in measles/rubella laboratory surveillance in Oman

Up to September 2009, the national measles and rubella laboratory tested 471 serum samples of which 26 were IgM positive for measles and 6 were positive for rubella IgM. The laboratory has passed and scored 100% on the 2009 proficiency panel for both measles and rubella as well as for external quality control.

The adequacy rate of received samples at the laboratory is 98.7% and 99.8% of specimen results are sent by the laboratory to EPI within 7 days. Information on last date of vaccination has improved and reached 73%.

17 specimens (11 throat swabs and 6 urine samples) were tested for measles virus and genotyped; 15 were found to be measles virus genotype B3 and the remaining 2 were D8. An outbreak of measles genotype B3 was found in Dhofar region, Oman. They were imported cases from Yemen.

Constraints and challenges include the following.

- Retesting of equivocal cases is a challenge as it is difficult to get a second sample from patients.
- Gaps due to movement of experienced senior staff for various reasons result in the need for training new young staff and in shortages of human resources.
- Awareness of elimination is not present at all levels.

8.2.5 Evaluation of diagnostic automation measles IgM ELISA kits in Jordan

Validation of non-validated kits was carried out. Four serological test kits for measles IgM (DAD-Behring, Serion Verion, Adaltis, Diagnostic Automation) were tested in parallel using 24 serum samples. All samples produced the same test results in all kits except the Diagnostic Automation, which gave 10 negative samples as false positive. The laboratory has passed and scored 100% on the 2009 proficiency panel for both measles and rubella.

The laboratory sent a complaint of poor testing results to Diagnostic Automation. The company then sent another kit with another antigen indicating that the price would increase due to high cost of raw materials. The second kit produced concordant results of the other three kits. The company has two production lines for the same parameter, which is alarming. Thus companies with two production lines for the same parameter with quality performance differences should be rejected, and exchange of documented information between regional laboratories is essential.

8.2.6 Discussion

- A recommendation is needed for standardizing validation procedures for received kits.
- Missing information on immunization status (immunization in last 3–4 weeks after rash onset) is not uncommon in investigation forms. It should be complete as possible.
- Training new young staff is an ongoing challenge.

8.3 Progress in measles/rubella virological surveillance in the Region

8.3.1 Measles virus surveillance in the Region
Dr H. Triki, RRL, Pasteur Institute

The RRL Tunisia received during 2008–2009 a total of 89 specimens from Djibouti, Egypt, Kuwait, Libyan Arab Jamahiriya, Morocco, Sudan, Syrian Arab Republic and Tunisia for detection and genotyping measles virus. The tested samples were throat swabs, urine, PCR products, RNA extracts and virus isolates referred from NMLs for genotyping. Serum samples selected among those sent for ELISA serology validation were also tested. 33 measles

genotypes could be identified from 65 PCR positive samples from the 8 referring countries. The identified B3 genotypes were 6 from Djibouti, 8 from Libyan Arab Jamahiriya and 5 from Tunisia. Measles virus D4 genotypes were 1 from Sudan and 4 from the Syrian Arab Republic; 3 and 2 identified measles virus genotype D8 belonged Kuwait and Morocco, respectively.

It allows determining the origin of imported viruses and tracking virus circulation throughout the world. At present, many measles sequences from the Region are not yet published in Genbank. Laboratory directors were encouraged to submit sequence data to the international Genbank database.

New techniques being introduced in the laboratory include amplification and sequence analysis in the H gene on measles viruses and amplification in the E1 gene for rubella genotyping. There were difficulties in amplifying isolates from Sudan and Tunisia in 2008. New primers are recommended by CDC Atlanta. Other isolates from Tunisia (late 2008 and 2009) and Sudan are under investigation.

8.3.2 Referral of specimen for measles and rubella test validation
Dr Suleiman Al-Busaid, RRL Oman

In 2008 and 2009, a total of 65 and 243 serum samples for validation, respectively were send to the RRL in Muscat. In 2008 referral countries were Bahrain, Islamic Republic of Iran, Qatar and Yemen, while in 2009 more countries engaged in sending serum samples: Afghanistan, Bahrain, Islamic Republic of Iran, Lebanon, Pakistan, Syrian Arab Republic and United Arab Emirates. Concordance of results was excellent: over 94% for measles in both years for all countries except Yemen (which claimed by mistake sending mixed serum samples for measles and other pathogens); and obtaining 55%, 69% and 77% for rubella for Qatar, Bahrain and United Arab Emirates, respectively. These countries are using Biotest or Vidas for rubella. However, there is lack of regular specimen referral, incompleteness of data sent for samples to be genotyped, e.g. date of onset/collection, province etc. Absence of OD values makes determination of concordance difficult; not all laboratories are using uniform kits e.g. Dade-Behring Enzygnost kits.

Clinical specimens for measles virus genotypes were received in 2008 and 2009 from NML in Bahrain, Islamic Republic of Iran, Iraq, Oman and Syrian Arab Republic. The tested samples were throat swabs, urines, infected Vero/SLAM cells or PCR products on filter paper. Identified measles virus genotypes were D4, D8 and B3 cases in Oman, D4 from Bahrain, Islamic Republic of Iran, Iraq and Syrian Arab Republic in addition for the first time in Region. Measles virus genotype H1 was identified from Islamic Republic of Iran, isolated in 2009, indicating an imported case.

In conclusion, excellent progress has been made in specimen referral in 2009 as compared to 2008. Validation was carried at Oman RRL from 47 filter papers absorbed with the serum from the Islamic Republic of Iran. The reproducibility of results was excellent with 100% concordance. RNA extraction and genotyping was carried out from one filter paper absorbed with infected cells from the Islamic Republic of Iran and Syrian Arab Republic. The

genotypes found were D4 and H1 respectively. Transferring samples using filter papers seems to be a convenient method. In 2009 the RRL conducted training programmes for candidates from Afghanistan, Iraq, Lebanon and the Syrian Arab Republic.

8.3.3 Experience of PAHO in the development of guidelines for validation of measles elimination
Dr P. Rota, CDC

The Region of the Americas eliminated measles in 2000; however, imported cases occur every year. The region has set definitions of measles and rubella elimination. For measles, elimination is defined as interruption of endemic measles virus transmission in all the countries of the Americas for a period greater than or equal to 12 months, in the presence of high-quality surveillance. For rubella, it is defined as interruption of endemic rubella virus transmission in all the countries of the Americas for a period greater than or equal to 12 months without the occurrence of congenital rubella syndrome cases associated with endemic transmission, in the presence of high-quality surveillance.

During 2009 a total of 57 (87%) confirmed cases which were imported and importation-related cases. 18 of these cases were imported from nine countries: Cape Verde, China, France, India, Italy, Philippines, South Africa, United Kingdom and Viet Nam. This shows the importance of virological surveillance, which has been extensively expanded in the Americas by collecting samples for virus detection. The goal is to obtain genetic information from every chain of transmission and sporadic case. Sequence analysis is still the only way to distinguish between a vaccine reaction and imported and importation-related spread.

Challenges include the following.

- Frequent importation of virus from endemic areas
- Cases occuring in unimmunized or under-immunized individuals (personal belief or religious exemptions)
- Cases of primary and secondary vaccine failure
- Detection of vaccine reactions and confusion with disease
- Difficulty in obtaining samples from remote areas
- Collection of appropriate samples for virological surveillance

A recent PAHO meeting on measles elimination developed core recommendations.

Quality control

- To document the elimination of measles and rubella, every country is urged to report results from a fully accredited national laboratory. For this reason, the laboratories should seek accreditation according to the WHO's current standards for the laboratory network, using the verification list adapted by PAHO.

Virological surveillance

- Countries should establish priorities to obtain samples for virus detection, with emphasis on, for example, frontier zones, industrial zones, tourists areas, and in contacts with a high probability of exposure.
- The laboratories should try to establish a genetic baseline by characterizing endemic cases or archive samples (serum, nasopharyngeal fluid, urine or tissue samples).

Case classification and laboratory testing for sporadic cases

In an elimination setting, accurate case classification depends on careful review of all laboratory results and EPI data

- Laboratory and epidemiologic teams from each country should use the new PAHO laboratory testing guidelines for classification of sporadic measles and rubella cases according to their needs
- Since additional testing requirements will depend in part on epidemiologic, clinical and demographic data, communication between laboratory and epidemiologic teams is essential
- It is also important to strengthen virological surveillance. An adequate sample for virus detection can improve the ability to confirm cases and can provide valuable information about the transmission pathways of the virus.

Congenital rubella syndrome (CRS)

- To support the regional CRS elimination goal, countries and laboratories should establish the means to confirm CRS cases and monitoring of virus shedding by CRS cases

8.3.4 Monitoring and identifying measles and rubella viruses circulation in the Islamic Republic of Iran

1072 blood samples were tested for measles IgM antibody. Of these, 115 samples were measles IgM positive; 12 of them were due to vaccination. In 2009, the Islamic Republic of Iran experienced a measles outbreak which was confined. 18 clinical specimens were collected for virus isolation/detection. In three specimens, virus was isolated and in 15 measles virus was identified by RT-PCR. Sequence analysis was performed 16 of of the detected measles virus was found to be genotype D4. For 2 cases, the genotype identified was H1.

This is the first time the measles virus H1 genotype was identified in the Islamic Republic of Iran and in the Region. This genotype is common in South-East Asia. Since there is increasing population movement between the Islamic Republic of Iran and South-East Asia, it is assumed that H1 is an imported case. The indigenous measles virus D4 has been circulating in Islamic Republic of Iran since 1988.

8.3.5 Discussion

- Progress has been made by the regional laboratory network in virological surveillance. There has been improvement in the strength of laboratory, surveillance and EPI communication and coordination to enhance clinical specimen collection for virus detection.
- Documentation of imported virus strains is due to extensive efforts in expanding and collecting samples from all outbreaks.
- There is need to continue improving the quality of virological surveillance for measles and rubella in obtaining more samples for viral detection and isolation by improving methods of collecting samples.
- Virus isolation and RT-PCR capacity needs to be expanded in the network using oral fluid.
- Timely and accurate reporting of genotype and sequence is necessary to share genetic information.
- Successful surveillance is a result of coordination between epidemiological and laboratory surveillance.
- Countries requested means of identifying measles virus genotype D4 linking to country-specific transmission.

8.4 Reporting data and measles elimination laboratory indicators

8.4.1 Measles and rubella data reporting issues
Mr R. Bekhit, WHO/EMRO

The main objective of this presentation was to highlight the importance of the laboratory elements of data in completing the line list to assist surveillance analysis and allow the monitoring of progress towards measles elimination, and to encourage countries to collect the elements of data needed for the process of validation. The importance of completion and timeliness of data elements was highlighted in order for countries to calculate the target indicators which need close collaboration and coordination of the laboratory focal points and the surveillance focal points. As well, it is important to report to the RRL for quality assurance and genotyping, using the Excel sheet data exchange template provided. The data exchange formats with countries information were presented and reviewed, with participants stressing missing data elements to be considered in the future. Regional feedback presented on the monthly measles/rubella bulletin is to be used for action to improve meeting indicators for measles elimination target.

8.4.2 Discussion

- Countries noted the need to streamline and standardize data systems between laboratory and surveillance.
- Completeness of data information on measles cases is not optimum; countries recognized the need to invest more efforts.
- Laboratories were requested to use the data exchange format when sending specimens for validation or genotyping to the RRL.

8.5 Group work: troubleshooting and tips on measles/rubella diagnostic techniques

Serological key points

Serology. Parameters that need to be looked at for ELISA assay (serum, oral fluid and dry serum) were discussed at length. The requirement of every laboratory to have documented graphically internal quality control to maintain good assay was discussed. Key parameters for assay performance checks were pointed out and include the following.

- Manufacturer's instruction: the kit instruction should be read for every new batch
- Filters of ELISA reader: correct filter, light path and power stability
- ELISA washer: channels clear, clean and programmed number of washings
- Pipette calibration: do frequently, correct volume dispensed
- Tubes that are used for dilutions: clean but not treated with any chemicals
- Distilled water: to be used for reconstitution of reagents
- Incubator temperature: right temperature and to be monitored
- Procedure time: time interval of assay should be observed
- Internal quality control: monitor OD values kit to kit, do graphics

Virus isolation. With regard to failure to isolate virus from clinical specimen (sensitivity of Vero/SLAM cells), the following points were raised.

- Efficiency of Vero/hSLAM is equivalent to that of B95a, but is much safer because Vero/hSLAM do not secrete Epstein Barr Virus
- Lack of virus isolation on Vero/hSLAM has been reported by laboratory, this needs further investigation to identify the problem.

RT-PCR troubleshooting

Problem: low yield or no amplification product

Solutions

- Template was degraded. Verify the integrity of the template by electrophoresis.
- Too much or too little template was used. Verify template concentration.
- Inhibitor was present in sample. Reduce the volume of template in the reaction. Use ethanol precipitate to remove inhibitors.
- Primer concentration was too low. Verify primer concentration in the reaction.
- Reaction component was missing. Always perform a positive control reaction with a template.
- Thermal cycler was programmed incorrectly. Verify that times and temperatures are correct.

Problem: nonspecific amplification products (PCR or RT-PCR)

Solutions

- Reaction conditions were suboptimal.
- Primer concentration was too high. Verify primer concentration in the reaction.
- Reaction was contaminated by another RNA or DNA.

Problem: low yield or no first-strand product (RT-PCR)

Solutions

- RNA was degraded. Verify RNA integrity by denaturing agarose gel electrophoresis.
- Primer annealing was poor.
- RNA template was impure. Carryover from some RNA purification methods can interfere with RT-PCR.
- Target RNA was not present in the sample or was present at low levels.

8.6 Recommendations

Regional reference laboratories

1. Distribute a pamphlet with different measles kits evaluated as a reference for countries that lack institutions for evaluating such kits.

National measles and rubella laboratory network

2. Store aliquots of serum samples with identified reactivity and isolates for a long period at −70 °C or in liquid nitrogen for internal quality control, and maintain their data record.
3. Pilot validation of stability procedures for dry serum and extract RNA/dry measles infected Vero/SLAM cells for shipment.
4. Continue efforts to strengthen collaboration with LabNet and EPI.
5. Collect specimens from each chain of transmission for measles virus detection and genotyping
6. Ensure timely and accurate reporting of genotype and sequence information.

Regional Office

7. Conduct training to improve data quality.
8. Continue maintaining LabNet core capacity to meet the requirements of the programme.

Annex 1

PROGRAMME

Sunday, 27 September 2009

08:00–08:30	Registration	
08:30–09:00	Opening Session Message from Regional Director, WHO/EMRO Introduction of participants Election of officers Adoption of agenda, programme and proposed working groups	*Dr N. Teleb, WHO/EMRO*

Session 1: Global and regional updates on measles/rubella control/elimination

09:00–09:30	Measles elimination: global overview	*Dr E. Hoekstra, UNICEF/HQ*
09:30–10:00	Regional measles elimination progress	*Dr B. Naouri, WHO/EMRO*
10:00–10:15	Regional measles/rubella laboratory progress and challenges	*Dr H. Ahmed, WHO/EMRO*
10:15–10:30	Discussion	
11:00–11:15	Feasibility of eradication of measles	*Dr A. Dabbagh*
11:15–11:45	The Gates Foundation support to measles activities in developing countries	*Dr M. Galway, Bill and Melinda Gates Foundation*
11:45–12:00	Discussion	

Session 2: Achieving and maintaining high population immunity to measles

01:00–01:30	Somalia: Child Health Day: a Success Story	*Dr Assegid WHO/Somalia*
01:30–01:45	Discussion	
01:45–03:45	Group Work: Achieving and maintaining high population immunity to measles in the Region	
04:15–05:00	Group presentations and discussion	

Monday, 28 September 2009

Session 4: Investigation and control of measles/rubella outbreaks

08:30–09:00	Investigation and response to 2008-09 measles outbreak In Iraq
09:00–09:30	Investigation and control of 2009 measles outbreak in Libyan Arab Jamahiriya
09:30–09:45	Discussion
10:15–12:00	Group work: Case study: investigation of a measles outbreak
01:00–03:00	Group work: Case study: investigation of a measles outbreak (continuous)

03:30–04:00	Poster presentation: session 1	

Tuesday, 29 September 2009

Session 4: Country updates: quality of measles/rubella case-based surveillance

08:30–09:00	Quality of reported measles/rubella surveillance data to EMRO	*Mr R. Bekhit, WHO/EMRO*
09:00–09:30	Discussion	
09:30–10:30	Group Work: countries status of the performance of measles/rubella surveillance	
11:00–01:00	Group Work: countries status of the performance of measles/rubella surveillance (cont'd)	
02:00–03:00	Group presentations and discussion	
03:00–04:00	Poster presentation: session 2	

Wednesday, 30 September 2009

Session 5: Measles elimination validation process

08:30–09:00	Progress on development of measles elimination validation guidelines	*Dr B. Naouri, WHO/EMRO*
09:30–10:00	Experience of PAHO in the development of guidelines for validation of measles elimination	*Dr P. Rota/CDC*
10:00–10:15	Discussion	
10:45–11:30	Testing of validation of measles elimination guidelines in countries: Lessons learned: Jordan, Syrian Arab Republic, Islamic Republic of Iran 15 minutes per country	
11:30–11:45	Discussion	
11:45–12:45	Panel discussion: Use of indicators to monitor measles surveillance quality and measles elimination at country level	*Dr P. A. Dabbagh,WHO/HQ Dr A. Uzicanin, CDC Atlanta Dr C. Castillo-Solozano, WHO/PAHO, Dr Paul Rota, CDC Atlanta, Dr E. Mohsni WHO/EMRO*
01:45–02:45	Final recommendations	
02:45–03:15	Prizes presentation for the best 3 posters	
03:15–03:45	Closing	

Thursday, 1 October 2009 Submeeting on the measles and rubella laboratory network

08:30–09:00	Welcome note Introduction Adoption of the agenda

Session 1. Update on progress and challenges of the global and regional measles/rubella laboratory surveillance

09:00–09:15	Global laboratory network	*Mr D. Featherstone, WHO/HQ*
09:15–09:30	Regional laboratory network	*Dr H. Ahmed WHO/EMRO*
09:30–09:40	Discussion	
09:40–10:10	Laboratory activities on measles and rubella case-based surveillance	
	Oman	*Dr S. Al-Baqlani*
	Pakistan	*Mr S. Zaidi*
	Jordan	*Dr R. Abdel Rahman Saleh*
10:10–10:20	Discussion	

Session 2. Progress on measles/rubella virological surveillance in the Region

10:50–11:20	Reports of measles virus genotypes in the Region and importance of timely reporting to RRL and to WHO genotype database	*Dr Suleiman and Dr H. Triki, RRLs Oman andTunisia*
11:20–12:00	Measles elimination tracing chain of transmission and epidemiological pathways	
	PAHO experience	*Dr P. Rota, CDC Dr T. Mokhtari*
	Islamic Republic of Iran	
12:00–13:00	Lesson learned in strengthening of laboratory, surveillance and EPI communication and coordination to enhance clinical specimen for virus detection	*Roundtable discussion*

Session 3. Reporting data and measles elimination laboratory indicators

14:00–14:15	Measles and rubella data reporting issues	*Mr R. Bekhit, WHO/EMRO*
14:15–14:45	Measles elimination laboratory surveillance indicators	

Session 4. Trouble shooting and tips on measles/rubella diagnostic techniques

14:45–15:15	Serology: parameters that need to be look at for ELISA assay (serum, oral fluid and dry serum)
15:35–15:50	Virus isolation: failing to isolate virus from clinical specimen (Sensitivity of Vero/SLAM cells)
15:50–16:20	RT–PCR: unspecific bands in the detection of measles and rubella and follow-up countries received training and not implemented
16:20–16:45	Conclusions and recommendations
16:45–17:00	Distribution of proficiency test panels and other laboratory supplies

Annex 2

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