The World Health Organization has managed cooperation with its Member States and provided technical support in the field of vaccine-preventable diseases since 1975. In 2003, the office carrying out this function was renamed the WHO Department of Immunization, Vaccines and Biologicals.

The Department’s goal is the achievement of a world in which all people at risk are protected against vaccine-preventable diseases. Work towards this goal can be visualized as occurring along a continuum. The range of activities spans from research, development and evaluation of vaccines to implementation and evaluation of immunization programmes in countries.

WHO facilitates and coordinates research and development on new vaccines and immunization-related technologies for viral, bacterial and parasitic diseases. Existing life-saving vaccines are further improved and new vaccines targeted at public health crises, such as HIV/AIDS and SARS, are discovered and tested (Initiative for Vaccine Research).

The quality and safety of vaccines and other biological medicines is ensured through the development and establishment of global norms and standards (Quality Assurance and Safety of Biologicals).

The evaluation of the impact of vaccine-preventable diseases informs decisions to introduce new vaccines. Optimal strategies and activities for reducing morbidity and mortality through the use of vaccines are implemented (Vaccine Assessment and Monitoring).

Efforts are directed towards reducing financial and technical barriers to the introduction of new and established vaccines and immunization-related technologies (Access to Technologies).

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Ad hoc Committee on Maternal and neonatal tetanus

Meeting report

Immunization, Vaccines and Biologicals

World Health Organization

unicef
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Contents

Abbreviations and acronyms ........................................................................................................ iv

1. Validation of maternal and neonatal tetanus elimination as a public health problem: review and advise on proposed methodology for validation, including lot-quality assessment ................................................................. 1
   Recommendations .................................................................................................................. 3

2. Action required to replace tetanus toxoid (TT) with tetanus-diphtheria toxoid (Td) in immunization programmes ............................................................ 3
   Recommendations .................................................................................................................. 4

3. Duration of protection after tetanus toxoid immunization ................................................. 4
   Recommendations .................................................................................................................. 5

4. The burden of tetanus: review of methods for estimating neonatal tetanus burden ....... 5
   Recommendations .................................................................................................................. 5

5. The burden of tetanus: review of methods for estimating maternal tetanus ............... 6
   Recommendations .................................................................................................................. 6

   Recommendations .................................................................................................................. 7

7. Routine monitoring issues: appropriateness of the “protection at birth” method .......... 7
   Recommendations .................................................................................................................. 8

8. Routine monitoring issues: proposed methods to monitor school-based immunization ..................................................................................................................... 9
   Recommendations .................................................................................................................. 9

9. Routine monitoring issues: proposed new case-definition for neonatal tetanus ...... 9
   Recommendations .................................................................................................................. 10

10. Other monitoring issues: indications for serology tetanus antibody testing .......... 10
    Recommendations ................................................................................................................ 11

Closure of the meeting .............................................................................................................. 11
## Abbreviations and acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC</td>
<td>antenatal care</td>
</tr>
<tr>
<td>BCG</td>
<td>bacille Calmette–Guérin (vaccine)</td>
</tr>
<tr>
<td>CFR</td>
<td>case fatality rate</td>
</tr>
<tr>
<td>DALY</td>
<td>disability-adjusted life year</td>
</tr>
<tr>
<td>DTP1</td>
<td>diphtheria–tetanus–pertussis vaccine – first dose</td>
</tr>
<tr>
<td>ELISA</td>
<td>enzyme-linked immunosorbent assay</td>
</tr>
<tr>
<td>EPI</td>
<td>Expanded Programme on Immunization</td>
</tr>
<tr>
<td>ICDDR, B</td>
<td>International Centre for Diarrhoeal Disease and Research, Bangladesh</td>
</tr>
<tr>
<td>LB</td>
<td>live births</td>
</tr>
<tr>
<td>LQA</td>
<td>lot-quality assessment</td>
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<tr>
<td>LQA-CS</td>
<td>lot-quality-assessment cluster survey</td>
</tr>
<tr>
<td>MICS2</td>
<td>Multiple Indicator Cluster Survey – version 2</td>
</tr>
<tr>
<td>MNT</td>
<td>maternal and neonatal tetanus</td>
</tr>
<tr>
<td>MT</td>
<td>maternal tetanus</td>
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<tr>
<td>NT</td>
<td>neonatal tetanus</td>
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<tr>
<td>PAB</td>
<td>protection at birth</td>
</tr>
<tr>
<td>PATH</td>
<td>Program for Appropriate Technology in Health</td>
</tr>
<tr>
<td>PINTMR</td>
<td>pre-immunization neonatal tetanus mortality rate</td>
</tr>
<tr>
<td>SAGE</td>
<td>Strategic Advisory Group of Experts</td>
</tr>
<tr>
<td>SIA</td>
<td>supplemental immunization activities</td>
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<tr>
<td>TBA</td>
<td>traditional birth attendants</td>
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<tr>
<td>TBA</td>
<td>traditional birth attendant</td>
</tr>
<tr>
<td>Td</td>
<td>tetanus-diphtheria toxoid</td>
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<tr>
<td>TT</td>
<td>tetanus toxoid</td>
</tr>
<tr>
<td>TT2+</td>
<td>tetanus-toxoid (second and subsequent doses)</td>
</tr>
<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
</tr>
<tr>
<td>VAB</td>
<td>Vaccines and Biologicals Department <em>(as of November 2003, known as IVB: Immunization, Vaccines and Biologicals)</em></td>
</tr>
<tr>
<td>VR</td>
<td>vital registration</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Maternal and neonatal tetanus
ad hoc Committee
meeting report

A meeting of an ad hoc Committee for Maternal and Neonatal Tetanus (MNT) was held at the John Knox Centre, Geneva, Switzerland on 25 and 26 March 2003. The meeting was co-hosted by WHO and UNICEF.

The meeting was opened by Dr Maureen Birmingham who welcomed participants and summarized the objectives of the meeting, which were: (i) to discuss a series of technical issues related to maternal and neonatal tetanus (MNT); and (ii) to provide guidance to WHO and UNICEF on these topics. The use of a combined lot-quality assessment and cluster survey (LQA-CS) method to validate elimination of MNT as a public health problem was proposed as the main technical issue for discussion.

Mr Lwanga was nominated to chair the meeting, with Dr Stevenson as rapporteur. Various technical topics were introduced by one or several participants, and then extensively discussed by the group.

1. Validation of maternal and neonatal tetanus elimination as a public health problem: review and advise on proposed methodology for validation, including lot-quality assessment

Mr Stroh presented an overview of the LQA-CS hybrid method. The method combines the methodology of lot quality assessment (LQA) sampling and that of the cluster surveys of the Expanded Programme on Immunization (EPI) in order to measure neonatal tetanus (NT) incidence. It is applied in countries that claim to have achieved MNT elimination status, and where a review of the available district level data needs to be complemented by information on NT incidence. Experiences with the application of EPI-type cluster surveys to assess disease incidence and prevalence and with the use of LQA to assess records and immunization coverage were briefly reviewed to describe the rationale for, and the development and testing of, the combination of the two methods.

The proposed methodology investigates the outcome of 1000 live births (LBs) in those district(s) that, on the basis of available information, are most likely to have the highest incidence of NT. NT is considered to be eliminated as a public health problem when no NT deaths can be identified, and not eliminated in the surveyed area if 4 or more NT deaths are found. If 1, 2, or 3 NT deaths are found among the 1000 LBs, another 2000 LBs are to be surveyed. In such case, NT is considered as eliminated if 3 or less NT deaths are found in the two samples of 3000 LBs combined, and not eliminated if 4 or more NT deaths are detected among the total of 3000 LBs.
Dr Msambichaka and Dr Kamal Fouad Fahmy shared their experiences with the implementation of the survey methodology in Zimbabwe and Morocco respectively.

In Zimbabwe, the method was implemented in November 2000. Prior to the LQA-CS, districts at higher risk were identified through a review of data using core and surrogate indicators. Districts to be surveyed in the LQA-CS were then selected from a short list, taking into account logistic constraints. Double sampling of 50 clusters in the first sample and 100 clusters in the second sample was used. In the first sample one neonatal death was attributable to tetanus. No such death was found in the second sample. A total of 3000 LBs were surveyed for the two samples ($n_1=1000$ and $n_2=2000$). The experience seemed to indicate the need for better notification and advocacy about the LQA-CS so as to improve the country’s ownership of the exercise. The implementation of the LQA-CS was prolonged because of a number of logistic and administrative issues, resulting in a substantial cost increase. Better supervision during the second sample could have improved the quality of the findings. The LQA-CS confirmed Zimbabwe’s claim to have eliminated NT as a public health problem.

In Morocco, the implementation of the survey was used to train consultants in the operational aspects of the LQA-CS. Morocco’s claim of NT elimination as a public health problem was validated in March 2002 by a desk review followed by a double sample LQA-CS survey. Data on cases, coverage and other indicators from all 68 districts were reviewed by two independent groups of experts, and the review resulted in the selection of three districts in which the LQA-CS would be implemented. After a 2–day training of interviewers, which included field exercises, 50 clusters were surveyed over 2 days in the 3 districts altogether. The experience showed the importance of good channels of communication between the teams and the supervisors, particularly to consolidate the results of the teams and to quickly inform the teams about the need to start a second sample. In the case of Morocco, no NT deaths were identified among the first sample and the exercise was terminated after completion of the survey of the 50 clusters (1000 children). The result confirmed Morocco’s claim to have eliminated NT as a public health problem.

In the ensuing discussion, the group exchanged information and ideas related to the use of the LQA-CS versus alternative methods. Of particular importance to the Committee was the need to define in an objective way the indications for a LQA-CS versus the use of coverage surveys or sero-prevalence surveys. The issue of reliability of data used to identify high-risk districts was raised, including the fact that tetanus toxoid (TT) coverage may not translate directly into levels of protection, and the fact that clean-delivery rates may not adequately capture the levels of risk of exposure to unclean delivery or high-risk cord-care practices. The group accepted an algorithm, proposed by a subgroup, on indications for the use of LQA-CS versus coverage or serological surveys (see Figure 1).

As for ensuring the quality of LQA-CS, the Committee stressed the need for careful training and supervision to ensure that neonatal deaths were properly identified by the surveyors. A comparison of observed number of neonatal deaths to the expected number could be used as a quality-control indicator for the LQA-CS. Further improvement is required in presenting the LQA-CS methods simply and clearly; the statistical basis of LQA-CS is still perceived to be complex, with only limited understanding by key stakeholders. National ownership should be promoted.

The group further discussed the consequences of a country being validated as having achieved elimination status, and the costs of false positive versus false negative results. It was agreed that validation constitutes a snapshot of the situation at the moment of validation. Validation also signals a switch towards maintenance strategies. The group also discussed
how different validation methods can provide different types, or levels, of information that are needed for sustaining low mortality rates.

**Recommendations**

− LQA-CS validation surveys can be used to validate NT elimination as a public health problem. The algorithm accepted by the meeting (Figure 1) gives guidance as to the best circumstances for the use of LQA-CS. Coverage surveys may have a role in situations where there is doubt about reported TT coverage levels, but further validation of coverage surveys with serological surveys may be required. Serological surveys can have a role in areas where supplemental immunization activities (SIA) and other interventions have been implemented. In any case, the issue of the optimal number of districts to assess should be addressed as a trade-off between a focus on a single high-risk district and the possibility of not correctly identifying the highest risk district(s).

− The focus of the LQA-CS protocol on NT deaths instead of NT cases is an acceptable limitation.

− WHO should develop guidance for using finite population corrections to use LQA-CS in district(s) with small populations (<750 000), so that small districts can be sampled individually rather than as a group.

2. **Action required to replace tetanus toxoid (TT) with tetanus-diphtheria toxoid (Td) in immunization programmes**

For several years, the Strategic Advisory Group of Experts (SAGE) has recommended a switch from TT to Td vaccine in all vaccination programmes. Thus far, very few countries, with the exception of countries in the American Region, have followed the SAGE recommendation. In its 2002 meeting, the SAGE requested WHO to ask the MNT ad hoc Committee to address the question of what was required so that the switch from TT to Td could effectively take place.

Dr Dellepiane explained the supply-and-demand implications related to a possible switch from TT to Td, and stressed the need to share information with manufacturers and to involve vaccine producers from the very beginning of the programme. She stressed the importance of working with them on potential capacity constraints and on means to overcome constraints so that any possible switch would not cause a vaccine shortage. Increasing the number of WHO pre-qualified vaccine producers and accurate forecasts of vaccine needs were among the main issues to be addressed. The need for work on the demand side in an effort to make the best possible estimates was also emphasized.

In the subsequent discussion, the Committee expressed concerns about how an adequate supply of Td (and even TT) could be assured given the low profit margin for these vaccines. Lack of a full understanding of the risks of diphtheria epidemics was seen as contributing to the limited demand for Td vaccine. School-based programmes were considered as particularly suitable to introduce the replacement of TT by Td, in terms of boosting diphtheria immunity among potentially susceptible youngsters and addressing the current limited-supply issue.
Recommendations

- Replacing TT by Td should be done in a phased manner, with an initial focus on school-based programmes. Other target groups, including pregnant women, would be added at later stages.

- WHO should prepare a situational analysis of countries using Td in their immunization schedule for adolescents and/or women of childbearing age, based on the data available in the Joint Reporting Form.

- WHO and the UNICEF Supply Division should jointly prepare a position paper outlining responsibilities and actions required for switching to Td.

- WHO should conduct an analysis of the build-up of pools of susceptible people. Such an analysis would increase awareness of the risk of diphtheria outbreaks and contribute to the creation of demand for Td.

3. Duration of protection after tetanus toxoid immunization

Dr Hoshaw-Woodard presented a summary of a meta-analysis of published literature that she conducted to estimate the duration of immunity (length of protection) after tetanus immunization (antitoxin titre > 0.01 IU/ml). She evaluated various factors (number of doses, interval between doses, type of vaccine, and age at primary vaccination) that may affect this duration. Survival analysis was used to estimate the length of protection, after accounting for censoring (i.e. the fact that not all subjects were followed until they lost protection). Data were analysed separately by age group and number of doses. Overall (i.e. averaging over differing intervals between vaccinations as well as type of vaccine), protection was greater than 80% at three years, five years, and at least nine years for adults who received two, three and four doses respectively. Protection was greater than 80% at 6, 20, 25, 22 and 45 years for children who received 2, 3, 4, 5 and 6 doses respectively.

Interpretation of these results is limited due to large amounts of missing data and limited long-term follow-up. Furthermore, in many instances it was not known exactly when subjects had lost protection, and data on women of child-bearing age and school-aged children, the two most important groups from a vaccination point of view, were limited. The fact that the data from the publications may not have been uniformly collected further complicates interpretation.

During the discussion it was highlighted that the findings of the meta-analysis could have far-reaching implications, particularly regarding policy in the following fields:

- Whether the currently recommended minimal interval of 6 months between TT doses 2 and 3 could be shortened. Shorter intervals would facilitate the organization and social mobilization of TT SIAs.

- Whether a 5-dose TT schedule implemented by the age of 8 years, as is currently the case in Indonesia, would provide sufficient protection against tetanus throughout childbearing years. If so, immunization of adult (pregnant) women could be ceased.

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1. On the WHO/UNICEF Joint Reporting Form a series of country-level immunization-related data and indicators are collected annually. A summary of those data is published annually by WHO as the WHO Vaccine Preventable Diseases Monitoring System - Global Summary.
• Whether the current 3-dose schedule for SIAs could be changed to a 2-dose schedule. A reduction of the number of doses in SIAs would result in large cost savings and easier SIA implementation.

The discussion then focused on a number of technical issues related to the quality and comparability of the published data used in the meta-analysis: vaccine formulation/potency (toxoid content, adjuvants), type of assay used (particular concern about studies using indirect assays and the sensitivity of tests using low titres), accuracy of histories of past vaccination (number and spacing of doses, differential misclassification of dose history for males versus females), etc. The variance of Kaplan-Meyer estimates, particularly at longer follow-up times, was also questioned. It was suggested that the quality of a meta-analysis could be improved if only data from studies with higher-quality data were analysed rather than using data from all available publications.

Recommendations

− Specific policy questions regarding duration of protection need to be identified and gaps in knowledge assessed. A decision is then needed as to whether a meta-analysis of relevant published data would be the most appropriate way to address these issues, given the options and the limitations of such an analysis, or whether a study to collect new data would be indicated.

4. The burden of tetanus: review of methods for estimating neonatal tetanus burden

Dr Birmingham presented a summary of the method being proposed by WHO/Vaccines and Biologicals (VAB) to estimate the disease burden (mortality and morbidity) of NT in 2000. The presentation included an overview and justification for the current method, a summary of the data sources, a discussion of how disability-adjusted life years (DALYs) are accounted for, and a sensitivity analysis of the model.

There were, generally, no objections to the methodology used; most of the discussion focused around certain parameters and how they were derived. In particular, the issue of “skilled delivery” versus “clean delivery”, and the role of traditional birth attendants (TBAs) in reducing NT deaths, generated discussion. The use of TT2+ coverage in the model was also discussed, with the suggestion made that in reality the model uses “protection at birth” (PAB) rather than actual annual coverage. The Committee discussed whether the current estimates of PAB, based on expert opinion and known data, should be compared with those that can be generated through a cohort model. It was suggested that there should also be a table of estimates for PAB and pre-immunization NT mortality rate (PINTMR) used for each country since the model is most sensitive to these parameters. The uncertainty around PAB/TT2+ coverage should be factored into the sensitivity analysis component of the model. Other points raised were the issue of dissemination and advocacy, and the need for countries to “use” the data and the model in some meaningful way. The use of DALYs was seen as a way to engage advocacy for MNT elimination as a public health problem but, for this to be meaningful, they should be used in combination with other data rather than as stand-alone figures.

Recommendations

− The proposed methodology should be described in the scientific literature.
The description of the model to estimate NT cases and deaths should provide the following modifications and clarifications:

- A clearer definition of what skilled delivery is, and how it relates to clean delivery, should be included in the paper.
- The coverage estimate should be labelled as a “best estimate of protection at birth” instead of “TT2+ coverage”.
- A table, summarizing the PAB and PINTMR estimates for each country, should be included in the description.
- The sensitivity analysis component of the model should factor in the uncertainty around PAB/TT2+ coverage.

Advocacy and efforts to explore ways to encourage countries to use and analyse their own data should be increased.

5. The burden of tetanus: review of methods for estimating maternal tetanus

Dr Wolfson presented a summary of the method being proposed by WHO/VAB to estimate the disease burden of maternal tetanus (MT) in 2000. The method is based on proportionally relating MT burden to NT burden after adjustment for factors that would impact differential incidence.

Some of the discussion on MT burden (such as the difference between skilled and clean delivery) raised issues similar to those concerning NT burden. Several other issues were also raised, such as whether or not estimating MT burden is important (given that the estimates of total burden are fairly low), and the implications of averaging data across published studies to obtain estimates of key model parameters rather than focusing on just one high-quality study. The fact that four studies used in the analysis had been conducted in one country raised concerns about the over-representation of that country’s situation in the analysis. Considerable attention was devoted to the controversy that may be generated if the country-specific estimates also reveal information about estimates of terminated pregnancies, particularly in countries where termination of pregnancy is illegal. This matter needs to be looked into further, and handled appropriately. The group also discussed how case-fatality rates (CFRs) were calculated, how to make them more country-specific and how to incorporate estimates of skilled delivery.

Recommendations:

- Efforts to model MT incidence and mortality should continue, as MT is an integral part of the effort to eliminate MNT as a public health problem.
- MT modelling results can be used as an advocacy tool to promote school-based TT or Td booster programmes.
- Consideration should be given to modifying the model to account for variation in CFRs across countries as well as variations in access to care.

6. The burden of tetanus: review of methods for estimating non-neonatal tetanus

Dr Stein introduced the methodology developed by WHO to estimate non-neonatal tetanus incidence and mortality. The non-neonatal tetanus estimations are based on two distinct methods, depending on the setting. For developing countries, cases are based on NT
incidence, assuming that NT cases comprise 80% of all cases under five years of age. Subsequently an age-distribution by region, according to a 1995 publication by Galazka\(^2\), is used to allocate tetanus cases to older age groups. For developed countries, reported cases with a notification efficiency of 75% are the basis for the estimation of incidents.

Non-neonatal tetanus deaths are estimated using case-fatality ratios from the literature; for developed countries these estimates are triangulated with vital registration (VR) data where VR coverage is high. For 2000, the method computed that, globally, 309,000 people had died of tetanus (neonatal and non-neonatal).

The subsequent discussion centred mainly on the quality of data and possible alternative information sources. ICDDR, B in Bangladesh was mentioned as a good source for data. Other data were said to be possibly available from a 20-sentinel site study published in the *Weekly Epidemiological Record* in the 1980s.

**Recommendations**

- Participants were invited to follow-up with further suggestions of data sources to help with modelling.

7. **Routine monitoring issues: appropriateness of the “protection at birth” method**

Dr Deming explained that the PAB method for monitoring TT coverage avoids major problems associated with the TT2+ method. The TT2+ denominator is the total number of LBs during a defined period; the numerator is all doses of TT2-5 given to pregnant women during the period. The main problem with this method is that the numerator excludes protected mothers who do not receive TT during their pregnancy, either because they do not attend antenatal care (ANC) clinics or because no vaccine is given during ANC. The PAB denominator consists of all children assessed at the DTP1 contact, or alternatively all LBs; the numerator is all children receiving DTP1 who were protected at birth according to the vaccination history of the mother. The PAB method thus includes protected mothers in the numerator, regardless of whether they received TT in their last pregnancy, but leaves out protected mothers whose children do not receive DTP1. The PAB method can also be used to reduce missed opportunities for TT vaccination.

Dr Deming said that the PAB method is currently used in several countries. In Tunisia, where it has been used since 1993, PAB and TT2+ coverage in 1997 were 80% and 50% respectively, and the TT2+ method was discontinued. In 1999, the PAB estimate was 83%, while TT coverage from the MICS2 survey the same year was 77%. In Syria, the TT2+ result for 2001 was 20%, while the PAB result was 90%.

Dr Van Cuong presented the results of a study validating PAB criteria in Viet Nam where PAB monitoring uses the total number of “protected” infants as the numerator and the total number of newborn infants in a given area as the denominator. An infant in Viet Nam is considered to be protected at birth against NT if the mother has received two doses of TT during the last pregnancy or at least three doses of TT at any time in previous years. To determine the validity of these criteria, an analysis of 646 NT cases reported in the country from 1994 to 1998 was carried out. Ninety-three per cent (602) of the 646 NT cases did not fit the criteria set for “protection at birth”. The presenter concluded, however, that the criteria

used to define PAB are valid and reliable enough to be used by health workers as a simple management tool to monitor the progress towards eliminating MNT as a public health problem and to assess the eligibility of women for further TT doses according to the EPI schedule.

In the subsequent discussion several issues were raised, including which would be the better contact for PAB: DTP1 or BCG? Although BCG coverage is usually higher than DTP1 coverage, the BCG contact was not considered ideal to assess PAB because BCG is often given by maternity staff or health workers vaccinating infants after the neonatal period. Hence record-keeping would be more complicated and training of maternity staff would be needed.

The issue of which denominator should be used was another major topic of discussion. In some countries the number of children assessed at the DTP1 contact is used, while in others the number of LBs serves as denominator. The use of LBs as a denominator has the advantages of being conservative and consistent with calculations of coverage for other (childhood) antigens. The drawback is that, at health facility level, the number of LBs in the catchment area is often not known; hence the usefulness of the method is limited. In the African Region, PAB had been recommended only in countries with DTP1 coverage of 80% or above, hence making the denominator less of an issue. The Committee recognized that different situations can justify the use of either denominator, but agreed that the standardization of the denominator for international reporting was also desirable.

Prevalence of clean delivery is traditionally not part of monitoring the PAB method but, if added (as in Tunisia), it would allow for a more complete assessment of the PAB. The group recognized that such an addition would constitute additional work and skills and could complicate the determination of the PAB indicator.

PAB determination was said to be an opportunity to assess the mother’s TT eligibility, although a full TT eligibility assessment would require that questions be added or adjusted to the PAB assessment. If implemented, it would help to reduce the number of missed opportunities to vaccinate the mother with TT.

The Committee saw data quality as essential, requiring both training and supervision. It was noted that WHO has not yet developed a PAB training manual or supervisory aids. Evaluations of adherence by health workers to PAB guidelines and validation of mothers’ answers were seen as useful. The group felt that countries should adopt PAB only when resources are available to ensure data quality and when the use of these resources is considered to be justified in the context of other health priorities.

The demand by countries for introduction of PAB was said to increase after SIAs had been implemented.

Recommendations

- PAB should not be universally recommended.
- WHO should continue to refine the PAB method and make it available to countries. Continued refinement should include simplification, and optimization of simplicity versus data quality. Guidance should be provided for countries as to the situation in which PAB can be considered as a good choice.
- WHO should do an inventory of how PAB status is determined in countries using the PAB method: whether records, maternal history or both are used and, when maternal history is used, what questions are asked.
WHO should standardize the denominator for international PAB reporting.

8. Routine monitoring issues: proposed methods to monitor school-based immunization

Dr Vandelaer explained that in recent years some countries have started to take advantage of high primary school enrolment rates to provide TT primary or booster doses in schools to primary school children and non-enrolled school-aged children. While this strategy has clear advantages in terms of long-term protection and ease of implementation, the monitoring of the performance of this strategy has not been standardized. He suggested two possible ways to monitor school-based tetanus immunization which differ in the denominator: one uses all children enrolled in school; the other uses all LBs in the school’s catchment area. A tally sheet was suggested which would allow for a breakdown of vaccination given by sex, grade, school and district.

Dr Hariadi briefed the Committee on the practical implementation in Indonesia. In Indonesia, school-based immunization is part of the strategy to immunize all children with sufficient doses to ensure high protection levels during adulthood. He explained that the method to monitor school-based immunization had not been standardized. The participation of different kinds of schools (government, private, etc.) complicated the compilation of the number of schools that had been included in the strategy. The number of enrolled children was used to calculate coverage rates. Record-keeping at school level was seen as poor. He said that issuing individual vaccination records for each child was essential to ensure quality of the strategy.

The Committee discussed the issue of denominators and agreed that the choice of denominator depends on the purpose of monitoring: to evaluate population-level impact or to monitor and improve implementation of school-based immunization. It was said that both routine monitoring and periodic sampling could have a role in monitoring school-based immunization. In any case, the Committee members agreed that immunizations should always be recorded on an individual’s immunization record.

Recommendations

- Immunization in schools should be recorded on an immunization card.
- Monitoring indicators would be different, depending on whether monitoring focused on school-based immunization programme performance or on the overall number of doses administered.
- Routine monitoring and regular sampling can both have a role in monitoring school-based immunization.

9. Routine monitoring issues: proposed new case-definition for neonatal tetanus

Dr Gasse presented a revised case-definition for confirmed cases of NT which had been proposed to improve the specificity of the diagnosis, particularly in LQA-CS.

Currently, the following case-definition is recommended by WHO:

Any neonate with a normal ability to suck and cry during the first 2 days of life, and who, between three and 28 days of age cannot suck normally, and becomes stiff or has convulsions (i.e. jerking of the muscles), or both.

The proposed new case-definition is:
Any neonate with normal ability to suck and cry during the first 2 days and who, between 3 and 28 days of age, cannot suck normally and who has convulsions or spasms triggered by minimal stimuli such as light, noise or touch OR who has signs of stiffness and rigidity which include any of the following: trismus, clenched fists or feet, continuously pursed lips, curved back (opisthotonus).

A review of the diagnostic criteria in nine textbooks was not conclusive and revealed confusion on the definitions of some of the symptoms (e.g. spasm versus convulsion). A study by WHO on the specificity and sensitivity of the current NT case definition was also presented. Although the newly proposed case definition would be more specific, it would also lose some sensitivity. Furthermore, it was seen as more complex and hard to use at field investigation level.

Following the discussions, the Committee concluded that routine reporting requires a sensitive case definition, and the current one seems to meet the need. However, a more specific definition could be developed and proposed to confirm suspected NT cases in situations where false positive results should be avoided. The example of polio, which also has two definitions (one clinical and one virological), was cited.

**Recommendations**

- For the purpose of reporting cases (in countries without elimination of MNT as a public health problem) the current case definition is adequate. However, confusing wording such as convulsions versus spasms needs to be modified.

- For validation of MNT elimination as a public health programme a more specific case definition is needed. Such a case definition needs to be tested before being widely implemented.

10. **Other monitoring issues: indications for serology tetanus antibody testing**

The last agenda item was intended as an information item for the Committee.

Dr Vandelaer summarized the present situation on serological testing for tetanus antibodies and he briefed the Committee on a meeting on tetanus serology held in New York in July 2002. While the double-antigen ELISA provides precise results, it is currently performed by only one laboratory. PATH is developing a simple-to-use dipstick test, capable of detecting antibody levels of 0.1 IU/ml. The test is ready for laboratory testing. The meeting in New York concluded that the development of such a test would serve merely as an addition to existing monitoring methods (e.g. surveys) and not as a replacement of such methods.

During the discussion, further clarification was given on the technical details of the PATH test. Concerns were raised about the sensitivity at a level of 0.1 IU/ml, as it is likely to create problems in assessing actual protection levels. A study in the Central African Republic was cited where 15% of protected women had levels between 0.01 IU/ml and 0.1 IU/ml. The fact that the test will take 20–30 minutes was seen by some as a drawback compared to laboratory tests that use samples collected on filter paper.

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**Recommendations**

No recommendations were put forward.

**Closure of the meeting**

Dr Gasse, on behalf of UNICEF, and Dr Vandelaer, on behalf of WHO, thanked the participants, the chair and the rapporteur for their contributions and the meeting was closed.
Figure 1. Decision tree for validation methods

Assessment team applies following algorithm:

Independent desk review

\[ \downarrow \]

Surrogate indicators taken into account

\[ \downarrow \]

Field visit

\[ \downarrow \]

Team may decide to increase TT coverage requirement (TT2 > 80%) if risk factors for exposure are highly prevalent\(^a\)

At least 1 of 3\(^b\) criteria met in each of the districts

\[ \downarrow \]

None of criteria met in one or some of the districts

\[ \downarrow \]

Possible elimination, but cannot confirm

Confirm elimination

\[ \downarrow \]

Not eliminated

<table>
<thead>
<tr>
<th>LQA-CS</th>
<th>Coverage survey</th>
<th>Serosurvey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pass LQA-CS =</td>
<td>Coverage surveys need to be further validated by</td>
<td>Particularly useful when there have been SIAs</td>
</tr>
<tr>
<td>NT elimination</td>
<td>sero-surveys, to ensure appropriate role in validation</td>
<td>If protection levels are &gt;80% : NT elimination achieved</td>
</tr>
<tr>
<td>achieved</td>
<td>Measure both TT and clean delivery coverage</td>
<td></td>
</tr>
<tr>
<td>Fail LQA-CS =</td>
<td>Births considered protected if mother’s TT history or</td>
<td></td>
</tr>
<tr>
<td>Review</td>
<td>history of clean delivery indicate protection</td>
<td></td>
</tr>
<tr>
<td>finished. Need</td>
<td>If PAB &gt;80%: NT elimination achieved</td>
<td></td>
</tr>
</tbody>
</table>
| to review options /strategies to achieve elimination | If PAB <80%: Either review is finished OR consider conducting LQA-CS if requested? | }

\(^a\) The minimum requirement may be increased even in the absence of highly prevalent risk factors.

\(^b\) The three criteria for MNT elimination are:

- NT rate of < 1/1000 LBs in presence of sensitive surveillance, or
- Clean delivery rate of ≥70%, or
- TT2+ immunization coverage of ≥80%.
Annex 1: Agenda

Joint WHO-UNICEF ad hoc Committee Meeting on MNT Elimination as a Public Health Problem
25–26 March 2003

Tuesday, 25 March

08:30   Registration
08:45   Opening of the meeting
        Introductory remarks and objectives (Dr Maureen Birmingham)
09:00   Validation of MNT elimination as a public health problem: review and advise on proposed methodology for validation, including LQA.
        Briefing on proposed methodology (Dr George Stroh)
        Experiences with field implementation (Dr Khadija Msambichaka; Dr Kamal Fouad Fahmy)
        Discussion on appropriateness of proposed methodology to validate elimination of MNT as a public health problem

10:30   Coffee break
11:00   Discussion on appropriateness of proposed methodology to validate elimination of MNT as a public health problem (continued)
        Recommendations
12:30   Lunch break
14:00   (1) Immunization issues: action required to replace TT with Td in immunization programmes
        Summary of supply and demand issues (Dr N. Dellepiane de Rey Tolve)
        Discussion
        Recommendations
15:00   Coffee break
15:30   (2) Duration of protection after TT immunization
        Summary of review of literature (Dr Stacy Hoshaw-Woodard)
        Discussion
        Recommendations
17:00   End of Day 1
Wednesday, 26 March

08:30  The Burden of Tetanus:
   (1) Review of methods for estimating NT burden *(Dr Maureen Birmingham)*
   Brief introduction on proposed methodology *(Dr Lara Wolfson)*
   Discussion
   Recommendations

10:00  *Coffee Break*

10:30  (2) Review of methods for estimating maternal tetanus
   Brief introduction on proposed methodology *(Dr Lara Wolfson)*
   Discussion
   Recommendations

   (3) Review of methods for estimating non-neonatal tetanus
   Brief introduction on proposed methodology *(Dr Claudia Stein)*
   Discussion
   Recommendations

12:00  *Lunch Break*

13:00  Routine monitoring issues: appropriateness of the
   “Protection at Birth” (PAB) method as monitoring tool
   Brief introduction on PAB method *(Dr Michael Deming)*
   Experiences from country level *(Dr Nguyen Van Cuong)*
   Discussion
   Recommendations

14:00  Proposed methods to monitor school-based immunization
   Brief introduction on monitoring issues related to
   School immunization *(Dr Jos Vandelaer)*
   Experiences from country level *(Dr Wibisono Hariadi)*
   Discussion
   Recommendations

15:00  *Coffee Break*

15:30  Proposed new case definition for neonatal tetanus.
   Issues with current case definition and proposed revised case definition
   *(Dr François Gasse)*
   Discussion
   Recommendations

   Other monitoring issues: indications for serology tetanus antibody testing
   Issues and current status of tetanus serology testing *(Dr Jos Vandelaer)*
   Discussion
   Recommendations

17:00  Wrap-up and final recommendations

17:30  Closure
Annex 2: List of participants
Joint WHO-UNICEF ad hoc Committee Meeting
on MNT Elimination as a Public Health Problem
25–26 March 2003

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