Neonatal Tetanus

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The World Health Organization (WHO) estimated that there were 34,000 neonatal tetanus (NT) deaths worldwide in 2015 (1). This 96% reduction from an estimated 787,000 NT deaths since 1988 represents significant progress towards the maternal and neonatal tetanus elimination (MNTE) goal. However, the disease remains an important global public health problem, particularly in settings with high neonatal mortality and among some of the poorest and most marginalized subpopulations worldwide.

Tetanus is caused by toxigenic strains of Clostridium tetani, a gram-positive bacterium. C. tetani spores are ubiquitous in the environment. NT most often occurs through cutting of the umbilical cord using non-sterile techniques or applying non-sterile traditional remedies to the umbilical cord stump, but infection of the umbilical stump is not always evident. Deliveries carried out by persons with unclean hands or on a contaminated surface are also risk factors for maternal and neonatal tetanus (MNT). Tetanus is not transmissible from person to person.

C. tetani produces a toxin which acts on the central nervous system to cause the muscular rigidity and spasms typical of tetanus. In NT, symptoms appear 3 to 28 days after birth, averaging 7 days. The first sign of tetanus in a neonate is usually an inability to suck or breastfeed and excessive crying. Characteristic features of tetanus are trismus (lockjaw, or inability to open the mouth), risus sardonicus (forced grin and raised eyebrows) and opisthotonus (backward arching of the spine). See Figures 1 and 2. Autonomic nervous system dysfunction (hypertension, abnormal pulse) and spasm of respiratory muscles and larynx can lead to respiratory failure. The case-fatality rate of NT without treatment approaches 100%, though with intensive care this can be decreased to 10–20% (1).

The WHO-recommended schedule for tetanus toxoid containing vaccines (TTCV) includes six doses: a three-dose primary infant series and three booster doses given at ages 12–23 months, 4–7 years, and 9–15 years. Pregnant women and their newborn infants are protected from tetanus if the mother received six TTCV...
doses during childhood, or five doses if a catch-up vaccination schedule was initiated after 1 year of age. In countries where MNT remains a public health problem, pregnant women without reliable documentation of vaccination should receive at least two TTCV doses, preferably Td (vaccine containing tetanus toxoid and low-dose diphtheria toxoid for older ages), with an interval of at least four weeks between doses. At each subsequent pregnancy, one TTCV dose should be given as indicated to achieve long-term protection until the series is completed.

The strategy for achieving MNTE includes high TTCV coverage of pregnant women and supplemental immunization activities (SIAs) of women of reproductive age in high-risk areas, as well as promoting clean delivery services and cord care practices. High quality NT surveillance is a key component of the MNTE strategy.

### RATIONALE AND OBJECTIVES OF SURVEILLANCE

Every NT case is an event that marks the failure of multiple levels of the health system. The key objective of NT surveillance is to detect cases of NT towards monitoring achievement and maintenance of MNTE, defined as less than one NT case per 1,000 live births annually in every district. NT surveillance data (or a lack thereof) are used to identify areas and subpopulations at high-risk for NT and guide effective public health response for MNTE. High-quality surveillance data and other key program indicators should be used at the national and subnational (district) levels to monitor the impact of interventions and achievement and maintenance of MNTE.

### BOX 1 Maternal tetanus and relationship to neonatal tetanus surveillance for MNTE

Maternal tetanus is defined as tetanus occurring during pregnancy or within 6 weeks after pregnancy ends (with birth, miscarriage or abortion), and has the same risk factors and means of prevention as neonatal tetanus. For this reason, NT elimination (<1 case per 1,000 live births) is considered a proxy for maternal tetanus elimination. Surveillance for non-neonatal tetanus should detect cases of maternal tetanus, but in most countries, occurs through aggregate reporting that lacks the required information on age, sex and pregnancy status to distinguish maternal tetanus. See Non-Neonatal Tetanus chapter for more information.
TYPES OF SURVEILLANCE RECOMMENDED

The minimal recommended standard for NT surveillance is nationwide, case-based surveillance, meaning that every suspected NT case should be investigated and classified as confirmed or discarded. NT surveillance is population-based and includes all neonates aged 0–28 days. Laboratory confirmation is not an aspect of NT surveillance, as the basis of tetanus diagnosis is clinical rather than laboratory-based.

CASE DETECTION

- Facility-based. Conduct facility-based surveillance by sensitizing surveillance focal points and key clinical staff (such as pediatric ward and special care nursery staff) at designated reporting sites to immediately report every NT case to the designated surveillance staff. The network of reporting sites should include both public and private facilities.

- Passive surveillance. Report the number of NT cases seen at designated reporting sites at a specified frequency (weekly or monthly) to the next higher level, even if there are zero cases (referred to as “zero reporting”). Health facility reports should be regularly monitored and verified by surveillance staff.

- Active surveillance. Make regular visits to reporting sites that are most likely to admit NT patients (weekly at major health facilities), or as part of active search for acute flaccid paralysis (AFP) and measles-rubella. During visits, review facility registers for unreported NT cases and ask key clinical staff whether any new NT case has been identified since the previous visit. At minimum, every facility should review registers for NT cases annually. Active surveillance can also be conducted in the community during outreach visits, SIAs or case investigations.

- Community-based surveillance. Community-based surveillance should be done in high-risk areas through a network of traditional birth attendants, community leaders, traditional healers or other community members that are sensitized to report NT cases and deaths to health authorities.

LINKAGES TO OTHER SURVEILLANCE

Ideally, NT surveillance is linked with active surveillance for AFP and measles-rubella and routine aggregate surveillance with zero reporting as part of Integrated Disease Surveillance and Response (IDSR). Linkage to vital events surveillance and neonatal death surveillance (2) may be useful for increasing NT surveillance sensitivity and helping to conserve resources.

CASE DEFINITIONS AND FINAL CLASSIFICATION

All suspected NT cases should be investigated. The basis for case classification is entirely clinical and does not depend on laboratory confirmation.

SUSPECTED CASE DEFINITION FOR CASE FINDING

A suspected case for NT is a case that meets either of these two criteria:

- any neonate who could suck and cry normally during the first two days of life and developed tetanus-like illness or death between 3 and 28 days of age

OR

- any neonate who died of an unknown cause during the first month of life.
Ideally, every NT case should be investigated. However, before achieving MNTE, the emphasis should be on implementing SIAs and community interventions to reduce NT burden in known high-risk areas.

Once MNTE has been achieved, each suspected NT case or death should be investigated by trained staff to confirm or discard the case, ideally within seven days of notification. The sooner the mother and persons who attended the birth are visited, the more likely they are to be available and remember relevant details.

All reported cases or deaths should be investigated using a standard case investigation form to confirm the NT diagnosis based on case history and symptoms. The investigation should determine why the infant contracted tetanus, such as lack of maternal vaccination, birth unattended or attended by unskilled staff, use of unhygienic cutting tools or application of substances to the umbilical stump. A simplified algorithm can be used to determine if the mother and infant were protected at birth (PAB) against tetanus, based on maternal vaccination history (see Box 2 below).

As NT diagnosis is entirely clinical, misdiagnosis can occur due to lack of training or lack of exposure to NT cases in low-incidence settings. Misdiagnosed cases of NT are most commonly meningitis, sepsis (including umbilical sepsis) or birth defects. Trismus (lockjaw) is absent in these illnesses. In addition, there is no bulging of the fontanelle in NT. During tetanus spasms, the child is conscious, and the spasm is often brought on by stimuli such as light and sound, unlike convulsions from other causes such as high fever where the child is unconscious. In addition to clinical presentation, details from the case investigation (such as lack of maternal vaccination, unskilled birth attendant or application of unhygienic substances to the cord) may support the NT diagnosis.

Ensure that the filled case investigation form includes the findings and actions taken or recommended, and is sent to the next level. Also give written feedback to the reporting facility and community.

PUBLIC HEALTH RESPONSE
The mother of the suspected NT case and any other unprotected woman of reproductive age in the community should receive TTCV as indicated (two doses separated by four weeks) to protect her and her infants during future births. If possible, the mother should be provided a TTCV dose before leaving the hospital, as part of outreach vaccination organized in conjunction with case investigation, or within six months of confirming the NT case.
Identification of a confirmed NT case may indicate a more systematic problem. A rapid community assessment should be conducted to determine the need for interventions.

- Starting from the house where the confirmed NT case occurred, move house to house to interview 10–15 other mothers in the community who delivered in the last two years about their vaccination status, delivery place and attendant, application of substances to the umbilical cord, and the survival and vaccination status of their last born child.

- If at least 80% of mothers are protected (either through clean delivery and hygienic cord practices, or PAB immunization status), the response can be limited to vaccination of the mother of the NT case and promotion of clean birth and hygienic cord care practices.

- If less than 80% of mothers are protected, determine the cause of non-protection and formulate an appropriate intervention. If less than 80% of mothers are protected through vaccination, assure that this community is added to the microplan for routine immunization sessions, including outreach sessions that should include vaccination of pregnant women with TTCV. Make a return visit with a basket of interventions, including providing TTCV to pregnant women.

- If less than 90% of last-born children received DTP3, strengthen routine immunization services in the area (for example, incorporate community in outreach microplans, reduce missed opportunities at outreach sessions, antenatal care visits and sick child visits).

- Complete corrective actions based on the factors that placed the infant at risk for NT. Corrective actions may include maternal immunization, education on hygienic delivery or cord care practices and better coordination with maternal and child health services.

**Simplified protection at birth (PAB) method**

During case investigations, surveillance staff can use a simplified PAB method to determine whether a birth is protected against tetanus based on written maternal immunization records and questioning the mother about the number TTCV doses she received during the last pregnancy and the number of doses she received during school-age, previous pregnancies, or campaigns/outreach occurring any time before the last pregnancy. A birth is protected if the mother received:

- two TTCV doses during the last pregnancy (with second dose given at least two weeks before birth)
  OR
- one TTCV dose during the last pregnancy (given at least two weeks before birth) and one or more doses at any time before that pregnancy
  OR
- no dose during the last pregnancy and three or more adolescent/adult doses at any time before that pregnancy (3).
LABORATORY TESTING

Tetanus diagnosis is entirely based on clinical features and does not depend on laboratory confirmation. *C. tetani* is recovered from microbiologic culture of wounds in only about 30% of cases, and the organism is sometimes isolated from patients who do not have tetanus. As non-toxigenic strains of *C. tetani* also exist, definitive laboratory diagnosis is not currently possible.

DATA COLLECTION, REPORTING AND USE

RECOMMENDED DATA ELEMENTS

» Case notification
  » Name (if confidentiality is a concern the name can be omitted so long as a unique identifier exists)
  » Unique case identifier*
  » Date of notification*
  » Source of notification (health facility location, name of person)
  » Date of case investigation*

» Geographic information
  » Place of residence (city, district, and province)
  » Reporting health facility

» Demographics
  » Date of birth*
  » Sex*

» Clinical
  » Age of baby in days at onset of symptoms
  » Date of onset (date of onset of lockjaw or inability to suck)*

» Date of hospitalization

» Signs and symptoms, including at minimum:
  • Ability to suck and cry during the first 2 days of life*
  • Between 3 and 28 days of age, cannot suck normally*
  • Muscle stiffness and/or spasms (jerking)*

» Neonatal outcome
  » Final outcome of child’s illness: alive, dead, unknown*
  » Final classification: confirmed, discarded, not investigated
  » Date of discharge/death

» Maternal and perinatal risk factors
  » Age of mother
  » Ethnic group
  » Migrant status (mother’s length of residency in locality where delivery took place)
  » Number of live births delivered (including this most recent one) by the mother
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- Number of previous births with similar symptoms and whether child(ren) survived
- Number of antenatal care (ANC) contacts the mother had with a trained healthcare worker during this last pregnancy
- Location of ANC (for follow-up regarding missed vaccination opportunity)
- PAB status of last birth (see Box 2)*
- Place of birth: hospital, health centre, home, other, or unknown*
- Assistance during childbirth: health staff (skilled birth attendant), traditional birth attendant, family member/alone, other, or unknown*
  - If not health staff, ask if clean surface and hands were used for delivery
- Tool(s) used to cut umbilical cord and sterilization of tool (cleaned and boiled)*
- Substance put on umbilical cord*
- Maternal outcome (dead, alive; cause of death)

▷ Public health response
- Mother given TTCV (such as Td) dose(s) at the time of case detection/investigation, or as soon as possible afterwards (yes, no, not needed/already protected, unknown/unavailable)
  - If given protective dose, record date that TTCV dose was given

* Designated core variable required to be completed as part of an adequate case investigation.

REPORTING REQUIREMENTS AND RECOMMENDATIONS
The number of NT cases should be reported separately from non-NT cases by designated reporting sites weekly, monthly or at another specified frequency, even if there are zero cases (zero reporting). Copies of case investigation forms or electronic data from these forms should be forwarded to the national level.

Cases of NT should be reported annually to WHO-UNICEF, and separately from non-NT, through the Joint Reporting Form. Reporting of NT is not required by International Health Regulations (IHR).

RECOMMENDED DATA ANALYSES
▷ Number and incidence of confirmed NT cases per 1,000 live births, by month, year, sex, and district
▷ Percentage of confirmed NT cases that were PAB by maternal vaccination (see Box 2)
▷ Percentage of confirmed NT cases whose mother received ANC, and among those who received ANC, were not vaccinated (for analysis of missed opportunities)
▷ Percentage distribution of confirmed NT cases by
  - Place of birth (health facility or home delivery)
  - Type of birth assistance
  - Type of cord-cutting tools used
  - Type of umbilical cord dressing used
  - Mother’s age
  - Mother’s parity (first birth vs. multiple births)
▷ Distribution of outcomes (death, survived, unknown) among confirmed NT cases
▷ Percentage of confirmed NT cases whose mother received a TTCV dose(s) after the NT case occurred, as a result of the case detection/investigation or soon after
▷ Percentage of neonatal deaths attributable to NT (if part of neonatal death surveillance)
▷ Risk assessments (see below, Using data for decision-making)

As with other diseases, surveillance data should be triangulated with data from the immunization program, such as vaccination coverage, history of SIAs, ANC coverage, and skilled birth attendance (SBA) coverage to understand the entire picture of disease when formulating conclusions and new policies or strategies.
USING DATA FOR DECISION-MAKING

- Monitor achievement and maintenance of MNTE ($< 1$ NT case per 1,000 live births in every district) and document evidence towards validation of elimination.
- Input data into annual risk assessments to identify high-risk geographical areas for targeting improvements in antenatal, obstetric, and vaccination services and conducting targeted SIAs for women of reproductive age.
- Identify NT risk factors such as place/type of delivery, cord care, age and parity of mother, migrant status and ethnicity, in order to design appropriate messaging and interventions.
- Monitor impact of interventions, including SIAs.
- Identify missed opportunities for maternal immunization with TTCV, such as ANC visits, child visits and outreach.
- Document evidence needed for immunization policy or strategy change (for example, introduction of WHO-recommended booster doses and school-based immunization if first-time mothers are not being reached with vaccination at ANC visits).
- Rapidly identify cases for appropriate case management (refer NT cases for medical care and provide TTCV dose to mother).
- Monitor surveillance performance indicators and identify areas that need targeted surveillance reviews or strengthening (this may be needed when surveillance data appears unreliable when compared with NT risk).

SURVEILLANCE PERFORMANCE INDICATORS

NT surveillance should be evaluated through periodic national reviews approximately every five years, by integrating with other VPDs and including triangulation of aggregate and case-based NT reports as well as a review of facility records for missed cases. Retrospective review of facility registers should be conducted in hospitals and large health clinics at least annually to identify previously unreported NT cases alongside other VPDs and other diseases. As part of the quarterly EPI data review meetings, surveillance, coverage, and programme performance data should be reviewed at the national and subnational level to help identify potential areas where surveillance gaps might exist or surveillance needs to be strengthened. At least annually, review the indicators listed in Table 1.
## TABLE 1 Neonatal Tetanus Surveillance Performance Indicators

<table>
<thead>
<tr>
<th>SURVEILLANCE INDICATOR</th>
<th>DESCRIPTION</th>
<th>TARGET</th>
<th>FORMULA</th>
<th>NOTES</th>
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<tbody>
<tr>
<td><strong>COMPLETENESS OF REPORTING</strong></td>
<td>Percentage of designated sites reporting NT data, even in the absence of cases (zero reporting)</td>
<td>≥ 90%</td>
<td># sites reporting NT / # designated reporting sites for NT surveillance x 100 (for a given time period)</td>
<td>At each level reports should be received on or before the requested date.</td>
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<tr>
<td><strong>TIMELINESS OF REPORTING</strong></td>
<td>Percentage of designated sites reporting NT data on time, even in the absence of cases (zero reporting)</td>
<td>≥ 80%</td>
<td># of surveillance units in the country reporting by the deadline / # of designated reporting sites for NT surveillance x 100</td>
<td></td>
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<tr>
<td><strong>COMPLETENESS OF INVESTIGATION</strong></td>
<td>Proportion of NT suspected cases that have been investigated (only among cases reported from health facilities)</td>
<td>≥ 90%</td>
<td># of NT case investigations / # of suspected NT cases reported x 100</td>
<td>If case-based database only includes data on case investigations performed, this indicator can be calculated as: # suspected cases in the case-based dataset / # suspected cases in the aggregate report x 100. This indicator will reflect the representativeness of case-based surveillance and efficiency of case investigations.</td>
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<tr>
<td><strong>TIMELINESS OF INVESTIGATION</strong></td>
<td>Percentage of all suspected cases investigated within 7 days of notification</td>
<td>≥ 80%</td>
<td># suspected NT cases investigated within 7 days of notification / # suspected NT cases investigated x 100</td>
<td>Note 1: The core variables are: case identification, date of birth, sex, place of usual residence, date of illness onset, date of notification, date of investigation, symptoms in case definition, outcome (alive/dead), maternal vaccination history, place/type of delivery, tool for cutting cord, and material applied to cord. Note 2: For any case, if information on any of the core variables is missing, the investigation is inadequate.</td>
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<tr>
<td><strong>ADEQUACY OF INVESTIGATION</strong></td>
<td>Percentage of investigated suspected cases with complete information for all core variables</td>
<td>≥ 80%</td>
<td># of suspected NT cases for which an adequate investigation was completed with collection of 12 core variables / # of suspected NT cases investigated x 100</td>
<td></td>
</tr>
<tr>
<td><strong>ACHIEVEMENT AND MAINTENANCE OF MNTE</strong></td>
<td>Percentage of districts with &lt; 1 NT case per 1 000 live births</td>
<td>100%</td>
<td># districts with &lt; 1 NT case per 1 000 live births / total # districts x 100</td>
<td>Ideally, this indicator should be calculated using confirmed NT cases. If the completeness of investigating suspected cases is &lt; 90%, the indicator can be calculated using suspected cases to highlight districts needing further investigation, targeted interventions and program strengthening.</td>
</tr>
<tr>
<td><strong>ADEQUATE CASE RESPONSE</strong></td>
<td>Percentage of confirmed NT cases for which the mother received a TTCV dose in conjunction with case detection or investigation</td>
<td>100%</td>
<td># of mothers of NT cases that received a TTCV dose in conjunction with case detection or investigation / total # of NT case investigations x 100</td>
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WHO Vaccine-Preventable Diseases Surveillance Standards
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SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

Tetanus is not considered an outbreak-prone disease. In general, NT outbreaks do not occur, but clusters linked to a single source of substandard clinical care have been observed. For disease clusters occurring in countries where MNTE has already been achieved, every case should still be investigated, and there should be, no change in the surveillance process. Before achieving MNTE, disease clusters should be investigated to determine risk factors, but the primary emphasis should be on implementing SIAs in known high-risk areas to reduce NT burden.

CLINICAL CASE MANAGEMENT

NT is a medical emergency requiring hospitalization, immediate treatment with human tetanus immune globulin (TIG), agents to control muscle spasm (preferred: benzodiazepines), and antibiotics (preferred: metronidazole or penicillin G). A single intramuscular dose of human TIG is recommended as soon as possible to prevent further progression of the disease. If TIG is not available, equine-derived antitoxin tetanus serum (ATS), can be given in a single intravenous dose, after testing for hypersensitivity. Alternatively, intravenous immune globulin (IVIG) may be used. Supportive care should be provided including keeping patients in a dark and quiet environment to reduce the risk of reflex spasms, and nasogastric feeding for newborn infants. If muscle spasms are occurring, it is critical to maintain a safe airway. If mechanical ventilation is not available, patients should be carefully monitored in order to minimize spasm and autonomic dysfunction while avoiding respiratory failure.

CONTACT TRACING AND MANAGEMENT

As tetanus is not contagious, no contract tracing is needed.

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NEONATAL TETANUS SURVEILLANCE

RISK ASSESSMENTS
NT risk assessments are used to identify high-risk areas for targeted SIAs, programme improvement, and field evaluation during MNTE validation. For countries yet to achieve MNTE, NT risk assessments should be performed at least every one to three years, triangulating district-level data on NT incidence, skilled birth attendance (SBA), TT/PAB coverage from routine and SIAs, and other proxy indicators. For countries that have already achieved MNTE, regular risk assessments using the same inputs should be done, details of which will be outlined in the forthcoming WHO document, Protecting all: sustaining maternal and neonatal tetanus elimination guide (3).

ETHICAL AND EQUITY ISSUES
Discussion of neonatal deaths may be a sensitive topic, especially among some cultures and ethnic groups. NT may occur most frequently among marginalized groups missed by the immunization programme, such as migrants, the homeless and residents in urban slums, who may be sensitive to questioning by outside government officials. Use guidance from local health staff on how best to address these challenges.

NEONATAL DEATH SURVEYS
The relative contribution of NT to neonatal mortality can be assessed through audits of neonatal deaths at health facilities or in community settings, as described in the document called Making every baby count: audit and review of stillbirths and neonatal deaths (2) and implemented in some countries as part of the Every Newborn: an action plan to end preventable deaths. (Available here: http://www.who.int/maternal_child_adolescent/newborns/every-newborn/en/). In some countries, activities in sentinel communities may approach or achieve real-time reporting of neonatal deaths and attempts should be made to link NT case detection to investigation through case-based surveillance. Of note, neonatal mortality cluster surveys (with verbal autopsies) are also conducted in the districts determined to be of highest risk for NT during MNTE validation exercises (4).

SEROLOGICAL SURVEYS OR SEROSURVEILLANCE
Where feasible, serosurveys of tetanus IgG among adult women should be considered as a complementary tool for monitoring MNT risk and guiding vaccination strategies. Because immunity does not result from natural infection, tetanus seroprotection reflects population immunity from vaccination. Close attention should be paid to the survey objective, sampling strategies and laboratory methods to ensure that results are valid and interpretable (Annex 2). Serosurveillance should not replace NT surveillance.
REFERENCES

REFERENCES CITED

ADDITIONAL REFERENCES