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# **Key facts**

To better understand public health terms included in this Disease Tool (e.g. What is a case definition? or What is an infectious agent?), consult our page on <u>Key concepts on epidemiology</u>.

# **Importance**

Before the introduction of vaccines 60 years ago, diphtheria was a leading cause of childhood death around the world. In 2018, countries reported more than 16,000 cases of diphtheria to the World Health Organization (WHO), and there are likely many more cases. The case fatality rate is up to 50 per cent without treatment and even with treatment, case fatality ratios up to 10 per cent have been reported in diphtheria outbreaks.

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## **Case definition**

A **case definition** is a set of uniform criteria used to define a disease for public health surveillance. It enables public health officials to classify and count cases consistently.

The following are standard case definitions to allow national health authorities to interpret data in an international context. However, during an outbreak case definitions may be adapted to the local context and the Red Cross Red Crescent should use those agreed/established by national health authorities. NB: Consider that during community-based surveillance, **volunteers** should use broad (simplified) case definitions (also known as community case definitions) to recognize people exhibiting the signs and symptoms matching diphtheria and encourage them to seek care. Other actors such as **healthcare workers or investigators** studying the cause of a disease, on the other hand, can use more specific case definitions that may require laboratory confirmation.

Globally, diphtheria has become rare and therefore the World Health Organization recommends that surveillance is case-based; that is, providers that identify cases should be required to report those cases immediately, ideally accompanied by laboratory case confirmation. That said, during large outbreaks, case-based surveillance may not be feasible if laboratory testing is logistically challenging and clinical diagnosis may be used to identify associated cases.

**Suspected case definition:** pharyngitis, nasopharyngitis, tonsillitis or laryngitis AND adherent pseudomembrane in the throat or nose. A diphtheria pseudomembrane is an exudate that is greyish, thick and firmly adherent. Dislodging the pseudomembrane is likely to cause profuse bleeding.

**Confirmed case definition:** laboratory-confirmed classic respiratory diphtheria cases meet suspected case definition. Non-respiratory laboratory-confirmed diphtheria cases have a skin lesion or non-

respiratory mucosal infection

WHO, 2018 Diphtheria. Available at:

https://cdn.who.int/media/docs/default-source/immunization/vpd\_surveillance/vpd-surveillance-standar\_ds-publication/who-surveillancevaccinepreventable-04-diphtheria-

r2.pdf?sfvrsn=3840f49a\_10&download=true

WHO case definition: https://www.who.int

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# Alert / epidemic threshold

An **alert threshold** is the pre-defined number of alerts that suggest the beginning of a possible disease outbreak and therefore warrant immediate notification.

**Epidemic thresholds** are the minimum number of cases indicating the beginning of a particular disease's outbreak.

A single laboratory-confirmed case of diphtheria should trigger a public health response. Two temporally and geographically linked cases, of which at least one is laboratory-confirmed, is considered an outbreak of diphtheria.

# **Risk factors**

- Any non-immune person (either not vaccinated or did not develop immunity after vaccination) can become infected.
- Diphtheria outbreaks can be particularly deadly in countries experiencing or recovering from a natural disaster or conflict. Damage to health infrastructure and health services interrupts routine immunization and overcrowding in residential camps greatly increases the risk of infection.
- Overcrowded areas where a person-to-person spread is easily possible.
- Migrants or refugee populations are at increased risk to become infected because of crowded living conditions and missing of routine immunization programmes.
- Lack of proper sanitation and hygiene measures.

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# Attack rate (AR)

The attack rate is the risk of getting a disease during a specific time period (such as during an outbreak).

Attack rates will vary from one outbreak to another. In case of an outbreak, consult the latest information provided by health authorities.

A retrospective study in Bangladesh showed that the attack rate depended on the degree of diphtheria vaccination in a population. The crude attack rate of a large outbreak of diphtheria among the Rohingya population in Cox's Bazar, Bangladesh from 2017 to 2019 was 51.5 cases per 10,000 person-years.

# Groups at increased risk of severe illness (most vulnerable)

- Persons younger than 5 years of age.
- Persons older than 40 years of age.
- People with underlying medical problems like high blood pressure, cardiovascular disease, diabetes, chronic respiratory disease, chronic kidney disease, chronic infectious diseases, cancer and obesity.
- People who are immunosuppressed such as those receiving chemotherapy, transplant recipients or HIV carriers.

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# Infectious agent

**Infectious agents** are bacteria, viruses, fungi, prions and parasites. A disease caused by an infectious agent or its toxic products is defined as an infectious disease.

Toxin (poison)-producing *Corynebacterium diphtheriae (C. diphtheriae)* 

Two other Corynebacterium species (*C. ulcerans and C. pseudotuberculosis*) may produce diphtheria toxin; both species are zoonotic but no person-to-person spread has been documented.

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## Reservoir / host

A **reservoir of infection** is a living organism or material in or on which an infectious agent lives and/or usually multiplies. Reservoirs include humans, animals and the environment.

A **susceptible host** is a person at risk of being infected. The level of susceptibility depends on age, sex, ethnicity and genetic factors, specific immunity also depends on other factors that affect an individual's ability to resist infection or to limit its ability to cause infection.

A **zoonotic disease** or **zoonosis** is an infectious disease that has jumped from a non-human animal to humans.

Humans.

Only for *C. ulcerans* and *C. pseudotuberculosis* zoonotic disease: animals.

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# How disease is spread (modes of transmission)

Categorisation of **modes of transmission** varies from one agency to another. In addition, some infectious agents can be transmitted by more than one mode. A list of modes of transmission can be found in the key concepts to serve as guidance to better understand the diseases included in this website.

- **Airborne and droplet spread:** sneezing, coughing, talking and droplet nuclei in the air transmit *C. diphtheriae*. Sharing eating and drinking utensils can increase droplet spread. Objects like contaminated bedding can also lead to transmission.
- **Contact transmission:** People can also get sick from touching infected open sores or ulcers from someone with cutaneous diphtheria.

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# **Incubation period**

This time from when infection occurs to the onset of symptoms is called the **incubation period**. It is a range of days and it can be different for each disease.

Two to five days (range 1–10 days).

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## **Period of infectiousness**

**Period of infectiousness** is the time interval during which an infected person can transmit the infection to other susceptible persons.

A person is infectious as long as virulent bacteria are present in respiratory secretions, usually two weeks without antibiotics, seldom more than six weeks. In rare cases, chronic carriers may shed organisms for six months or more.

# Clinical signs and symptoms

**Respiratory diphtheria:** The most common and most severe type of diphtheria, whereby the exotoxin produced causes the formation of a membrane of dead tissue in the throat and over the tonsils, making breathing and swallowing difficult. It can cause weakness, sore throat, mild fever, swollen glands in the neck. The exotoxin damages other organs as well when getting into the blood stream, often resulting in complications such as heart failure, nerve damage, loss of the ability to move (paralysis), kidney damage and death, even with treatment. Without treatment, up to half of patients can die from the disease.

**Cutaneous diphtheria:** More rarely (up to 2 per cent of all diphtheria cases), it can affect mucous membranes at other non-respiratory sites, such as genitals and conjunctiva (membrane covering the eye and the inside of eyelids), causing open sores or ulcers. However, cutaneous diphtheria rarely results in any other severe disease.

# Other diseases with similar clinical signs and symptoms

Influenza, parotitis due to other causes, COVID-19 disease, pertussis, measles, other infections of the respiratory tract. Non-infectious diseases like exacerbated chronic respiratory diseases or allergies.

# **Diagnosis**

Swabbing the back of the throat or nose or an open ulcer and laboratory testing for *C. diphtheriae*. It is important to start treatment right away if there is suspicion of diphtheria as laboratory findings can take some time.

## Vaccine or treatment

Please refer to the appropriate local or international guidelines for clinical management. All clinical management including the administration of a treatment or vaccine should be conducted by a health professional.

All suspect diphtheria cases require isolation, collection of nasal and pharyngeal swabs and culture, Diphtheria Antitoxin Treatment (DAT) and antibiotic treatment.

Diphtheria toxoid, the vaccine to prevent diphtheria, should be given to infants as a primary series of three doses, followed by three appropriately spaced booster doses to ensure long-term protection. Diphtheria vaccines are commonly available in combination with other vaccines such as pertussis and tetanus.

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# **Immunity**

There are two types of immunity:

- **Active immunity** results when exposure to an agent triggers the immune system to produce antibodies to that disease.
- **Passive immunity** is provided when a person is given antibodies to a disease rather than producing them through his or her own immune system.

Protective immunity does not always develop after recovery from disease. Therefore, individuals recovering from diphtheria should complete the diphtheria toxoid vaccination during convalescence.

Vaccination schedule needs booster doses to ensure long-term protection.

# Which interventions are most effective for prevention and control?

The following is a list of activities considered for Red Cross Red Crescent volunteers to take part in. It is not an exhaustive list of all prevention and control activities for the specific disease.

• Communicate risks about the disease or epidemic, not only to share information on prevention and mitigation measures, but also to encourage informed decision-making, positive behaviour change and maintenance of trust in the Red Cross Red Crescent response. This includes the identification of rumours and misinformation around disease—frequent during health emergencies—to manage them appropriately.

Volunteers should use the most context-appropriate communication techniques (ranging from social media to face-to-face interactions).

- Community education and engagement activities to encourage the adoption of protective behaviours:
  - Isolation of those who are sick. In the case of children, the caregiver may receive prophylaxis for diphtheria.
  - Coughing etiquette (cover mouth when coughing or sneezing; tissues should be disposed of immediately). People should keep a distance of about one metre, if possible, from those who present symptoms such as coughing or sneezing.
  - Regular handwashing with soap
  - Correct use of antibiotics. Ensure that community members understand that antibiotics should only be taken if prescribed by a health professional and should carefully follow instructions on the duration of the antibiotic's administration. This includes completing the antibiotics course even when people are already feeling well.
- Social mobilization for mass vaccination, including extensive Information, Education and Communication (IEC) activities on the benefits of the diphtheria vaccine, the routine vaccination schedule in-country and/or Supplementary Immunization Activity (SIA) campaign dates and locations, and the importance of completing the WHO-recommended three initial doses (during infancy) plus the three booster doses (prior to adolescence). As some people may miss out on completing the recommended schedule, volunteers should remind community members that those who are unvaccinated or who have not completed the full vaccination recommended doses should receive the doses needed to complete vaccination at any age to gain protection.
- Rapid detection of suspect cases and encouragement of early health-seeking behaviours at healthcare centres.
- Contact tracing and follow-up for seven days. All contact tracing activities must be done in close coordination with health authorities.

### Which interventions have NO evidence and therefore are NOT recommended?

In some countries there is a myth that the Diphtheria, Pertussis and Tetanus (DPT) vaccine may lead to sudden infant death syndrome. As a result, people may avoid the vaccine altogether. There is no evidence of a causal link between the administration of the vaccine and sudden infant death. It should be noted however, that vaccines such as DPT vaccine are administered during infancy, which is also a time when babies may suffer sudden infant death syndrome. That is, reported cases of sudden infant death syndrome would have happened even if the vaccine had not been administered and are co-incidental to vaccination.

# **Epidemic characteristics and RCRC indicators and targets**

The first table below includes data that should be gathered from health authorities and relevant non-governmental actors to understand the progress and characteristics of the epidemic in the specific country and area of intervention. The second table includes a list of suggested indicators that can be used for monitoring and evaluating Red Cross Red Crescent activities; wording of indicators may be adapted to specific contexts. Target values for a specific indicator can vary widely from one context to another and therefore managers should define them based on the specific population, area of intervention and programmatic capacity. Exceptionally, some indicators in this website may include target values when a globally agreed standard exists; e.g. 80 per cent of individuals who slept under an insecticide-treated net (ITN) the previous night—the normative World Health Organization benchmark for universal coverage with ITNs.

### **Epidemic characteristics and progression**

Suspected cases per week (disaggregate by age, sex)

Probable cases per week (disaggregate by age, sex)

Confirmed cases per week (disaggregate by age, sex)

Number of deaths per week (disaggregate by age, sex)

Annual percentage of children who have age-appropriate vaccination coverage for DTP3 in settings with humanitarian crises or emergencies

#### **Indicators for Red Cross Red Crescent activities**

Number of volunteers trained on a specific topic (e.g. Epidemic Control for Volunteers (ECV); Community-based surveillance (CBS); WASH training; CBHFA training, etc.)

**Numerator:** Number of volunteers trained

Source of information: Training attendance sheets

Suspect cases detected by volunteers who were encouraged to seek healthcare and who arrived at a health facility (NB. This indicator requires the implementation of a system in collaboration with the health facility, whereby health workers specifically asked the patient how they heard about the service)

**Numerator:** Suspect cases detected by volunteers in a determined period preceding this survey (e.g. two weeks) for whom advice or treatment was sought from a health facility

**Denominator:** Total number of suspect cases in the same period preceding the survey

Source of information: Survey

Percentage of people recognizing at least one transmission route and at least one measure for preventing it

**Numerator:** Total number of people who recognized at least one transmission route and at least one measure for preventing it during the survey

**Denominator:** Total number of people surveyed

Source of information: Survey

If supporting vaccination campaigns:

Number of households covered during the Supplementary Immunization Activity (SIA)

Number of volunteers participating in the SIA

Number of vaccinations realized during the SIA among children aged 6 months – 15 years Source of information: Vaccination activity records

## See also:

• For Community Engagement and Accountability (CEA) indicators for activities accompanying ECV actions, please refer to the IFRC CEA toolkit (Tool 7.1: Template CEA logframe, activities and indicators) at: <a href="https://www.ifrc.org/document/cea-toolkit">https://www.ifrc.org/document/cea-toolkit</a>

• For vaccination activities, see the IFRC Social Mobilization Guide for Vaccination Campaign and Routine Immunization at: <a href="https://oldmedia.ifrc.org/ifrc/wp-content/uploads/2020/01/1\_SM-Guide-RC\_version-1.pdf">https://oldmedia.ifrc.org/ifrc/wp-content/uploads/2020/01/1\_SM-Guide-RC\_version-1.pdf</a>

# Impact on other sectors

Sector	Link to the disease
WASH	The spread of droplets is reduced by proper hygiene and sanitation. Sharing eating and drinking utensils can increase droplet spread.
Nutrition	Malnutrition increases the risk for severe diphtheria.
Shelter and settlements (including household items)	Outbreaks are of particular concern in crowded settings when hygiene and sanitation is poor and vaccination rates are low.
Psychosocial support and mental health	Diphtheria can have several negative impacts on psychological, social and emotional aspects of a person's life, apart from its physical effects only. Psychological reactions may include anxiety and worry about the outcome, social withdrawal, among others. Long-term complications like heart or kidney failure and nerve damage worsen mental health. Isolation and contact tracing in communities are highly stressful situations especially for children and very challenging on a psychological level.
Sex and Gender	Gender roles influence exposure. Women and girls may face increased risk of diphtheria especially through caregiving roles, which can delay their own treatment.  Men and boys may be exposed in crowded living or work environments. Gender norms can influence health-seeking behaviour, with men often less likely to seek early care.  Pregnant women with low vaccination coverage may face higher risk of complications, highlighting the importance of preventive care, including immunization and timely access to treatment and health services. Girls, compared with boys, usually show less access to overall vaccination including vaccines targeting diphtheria.
Education	Diphtheria is an infectious disease which occurs mainly in unvaccinated children. Outbreaks in schools can happen as children stay close to each other. Children may then be at risk of getting the disease if attending classes, or at risk of losing on education if staying at home because of isolation or illness.
Livelihoods	Illness and isolation lead to reduction in productivity as people may not be able to work due to disease. This can lead to a loss of income due to the reduction in work activity and to the diversion of resources to seek medical treatment.

#### **Resources:**

- Polonsky JA, Ivey M, Mazhar MKA, Rahman Z, le Polain de Waroux O, et al. (2021) Epidemiological, clinical, and public health response characteristics of a large outbreak of diphtheria among the Rohingya population in Cox's Bazar, Bangladesh, 2017 to 2019: A retrospective study. PLOS Medicine 18(4): e1003587. https://doi.org/10.1371/journal.pmed.1003587
- WHO (2017) *Myths and facts about immunization*. Available at : https://www.euro.who.int/\_\_data/assets/pdf\_file/0005/339620/Myths-and-facts.pdf
- WHO (2018) *Diphtheria*. Available at: https://www.who.int/immunization/monitoring\_surveillance/burden/vpd/WHO\_SurveillanceVaccinePreventa ble\_04\_Diphtheria\_R2.pdf?ua=1
- WHO. (2017). *Myths and facts about immunization*. Available at: <a href="https://www.euro.who.int/\_data/assets/pdf\_file/0005/339620/Myths-and-facts.pdf">https://www.euro.who.int/\_data/assets/pdf\_file/0005/339620/Myths-and-facts.pdf</a>