Public Health England

Health Protection Report
weekly report

Volume 10 Number 13 Published on: **26 February 2016**

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Volume 10 Number 13 Published on: **1 April 2016**

HSE Annual Science Review 2016

The several components of scientific research activity carried out by the Health and Safety Executive that include a significant public health dimension are illustrated in the Executive's recently published first Annual Science Review [1].

The main part of the new report comprises case studies illustrating the Executive's work in researching the causes of – and the most effective interventions to reduce the risk of – health problems arising from workplace exposures. This encompasses not only medical issues but also research into behavioural, occupational hygiene, engineering control and personal protective equipment aspects of prevention and control.

Four case studies are concerned with work-related respiratory disease, including details of a multidisciplinary project to develop a standard of care to support action on work-related chronic obstructive pulmonary disease (COPD). It is noted that the occupational contribution to COPD prevalence in the UK is 10-15% of the total 900,000 diagnosed cases. The standard of care – comprising practical advice on exposure control, surveillance for early cases and appropriate lung function testing in occupational settings – aims to help reduce, over time, this burden of preventable disease.

Other case studies related to work-related respiratory disease cover: guidance to help the early diagnosis and management of silicosis; understanding the personal cost of occupational lung disease; an investigation into asthma health surveillance in workplaces where there is exposure to flour, wood dust or isocyanate paints; and a study carried out by HSE's Centre for Workplace Health into the physical, financial, psychological and social harm caused to otherwise healthy people by occupational lung disease.

Also covered by case study reports are:

- legal prosecutions that have drawn on expert evidence provided by HSE scientists and engineers
- control of exposure to dust and bioaerosols at materials recycling facilities
- validation of a new lightweight protective system for workers responding to releases of chemical and/or biological agents
- 'nudging' behavioural change in occupational health and safety

Reference

1. Health and Safety Executive (March 2015). Annual Science Review.

NHSBT selective screening for hepatitis E

NHS Blood and Transplant (NHSBT) is responsible for the provision of a safe and secure blood supply for England and North Wales. A range of measures are in place reduce the risk of transfusion-transmitted infections, including donor selection and donation testing.

Recommendations which result in major changes to blood donor selection or screening are usually proposed by the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO).

During 2015 SaBTO reviewed the available data on the epidemiology of hepatitis E virus (HEV) in blood donors and the potential for transfusion-transmission of this infection resulting in harm to an immunosuppressed recipient [1]. Following this review SaBTO recommended, as a precautionary measure, the provision of HEV screened blood components for use in solid organ and stem cell transplant patients. In addition SaBTO wrote to doctors and patient groups to raise awareness of the potential risk from HEV infection in immunosuppressed patients and the possible sources of HEV, including blood and blood products and diet.

All four UK blood services will provide HEV-screen negative components for these susceptible patient groups. In NHSBT only a proportion of donations will be tested for HEV and this will depend on demand. If a donation is found to contain HEV RNA the donor will be suspended, contacted by NHSBT and given appropriate advice. As with other notifiable infections, NHSBT plans to inform the local health protection units of any donors with confirmed hepatitis E infection.

Reference

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Diphtheria in England and Wales: 2015

Tetanus in England and Wales: 2015

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Volume 10 Number 13 Published on: **1 April 2016**

Diphtheria in England and Wales: 2015

Diphtheria is a life-threatening but preventable infection. From January to December 2015 six toxigenic strains of corynebacteria were reported in England: three Corynebacterium diphtheriae *and three* C. ulcerans*. Since April 2014, a PCR service has been available at the national reference laboratory at PHE which confirms the identity of* C. diphtheriae, C. ulcerans *or* C. pseudotuberculosis *and determines whether the gene for the diphtheria toxin (tox) is present. A subsequent Elek test is used to confirm the expression of diphtheria toxin. One additional non-toxigenic tox gene bearing* C. diphtheriae *strain was reported during this period*.

This 2015 review updates a previous annual review of diphtheria cases in England and Wales for 2014 [1]. Data sources for the enhanced surveillance of diphtheria include notifications, reference and NHS laboratory reports, death registrations, and individual case details – such as vaccination history, source of infection and severity of disease – obtained from hospital records and general practitioners.

During 2015, six toxigenic strains of corynebacteria were identified by the Public Heath England (PHE) Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU), which is the National Reference Laboratory for diphtheria. No toxigenic isolates were identified from Wales. Diphtheria is a notifiable disease under the Public Health (Control of Disease) Act 1984 (as amended) and accompanying regulations [2]. Nine official case notifications were received from NOIDS during this period; laboratory investigation identified four as non-toxigenic *C. diphtheriae* infections, one was a toxigenic *C. diphtheriae* infection, two were toxigenic *C. ulcerans* infections, and two were not *Corynebacterium* spp. In the same period, RVPBRU identified a further two toxigenic *C. diphtheriae* strains, one toxigenic *C. ulcerans* strain and one additional non-toxigenic *tox* gene bearing (NTTB) *C. diphtheriae* strain from samples referred from patients who were not formally notified as suspected diphtheria (table 1).

Table 1. Diphtheria notifications and isolates of toxigenic corynebacteria, England: 2015

Total notifications	**9***
Number due to non-toxigenic *C. diphtheriae*	4
Number due to toxigenic *C. diphtheriae*	1
NTTB *C. diphtheriae*	0
Number due to toxigenic *C. ulcerans*	2
All toxigenic *corynebacteria isolates*	**7**
Toxigenic *C. diphtheriae*	3
NTTB *C. diphtheriae*	1
Toxigenic *C. ulcerans*	3

* *Corynebacterium* spp. isolated from two samples

C. diphtheriae

Three toxigenic *C. diphtheriae* var. mitis strains were identified in 2015; all were isolated from wound swabs (cutaneous diphtheria). All three patients had recently travelled to a country which was endemic for *C. diphtheriae,* were treated with antibiotics and offered vaccination as appropriate; one also received diphtheria anti-toxiin. None of the patient's experienced systemic complications and all recovered from their infection. Contact tracing identified over 80 close contacts including household contacts, relatives, and health care workers. All were offered chemoprophylaxis and vaccination as appropriate. Throat swabs taken from the close contacts of the patients were all negative for corynebacteria.

An additional NTTB *C. diphtheriae* var. mitis strain was isolated from a tissue sample (cutaneous diphtheria) from a patient with skin lesions due to an underlying medical condition which increased susceptibility to bacterial infections (table 2). The patient was treated with antibiotics and offered vaccination, and recovered without experiencing systemic complications. In total, four close contacts of this patient, including household contacts and healthcare workers, were identified. All were offered chemoprophylaxis, vaccination as appropriate, and were swabbed. None of the close contacts exhibited cutaneous or respiratory symptoms and no swabs yielded *C. diphtheriae*.

C. ulcerans

Three toxigenic *C. ulcerans* strains were isolated in 2015; one from a wound swab (cutaneous diphtheria), swab (cutaneous diphtheria), one a throat swab (mild respiratory diphtheria), and one from pus drained from a lymph node (other presentation). The patients were treated with antibiotics and offered vaccination as appropriate; none experienced systemic complications, and all recovered from their infection.

Contact tracing identified 13 close contacts of the three patients. All of the close contacts were offered chemoprophylaxis, vaccination as appropriate, and were swabbed. None of the close contacts exhibited cutaneous or respiratory symptoms and no swabs yielded *C. ulcerans*.

Risk factors for *C. ulcerans* include contact with companion animals (2-4) and all of the patients reported contact with dogs. Pharyngeal swabs were taken from six dogs belonging to two of the patients; none tested positive for toxigenic *C. ulcerans*. Two of the patients also had underlying conditions which increased their susceptibility to bacterial infections.

Table 2: Clinical presentation of diphtheria cases and causative organism, England 2015

	Causative organism			
Clinical presentation of cases	Toxigenic *C. diphtheriae*	NTTB *C. diphtheriae*	Toxigenic *C. ulcerans*	**Total**
Classic respiratory diphtheria (with pseudomembrane)	0	0	0	**0**
Mild respiratory diphtheria (sore throat/pharyngitis)	0	0	1	**1**
Cutaneous diphtheria	3	1	1	**5**
Other	0	0	1	**1**

Microbiological laboratories are encouraged to submit all suspect isolates of *C. diphtheriae* and other potentially toxigenic corynebacteria to PHE RVPBRU using the form R3 [3]. From 1 April 2014, the test result which helps inform public health action is a PCR which confirms the identity *of C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis* and determines whether the gene for the diphtheria toxin (tox) is present. If the tox gene is detected, the isolate goes on to have an Elek test to detect expression of toxin [3]. RVPBRU also provides advice on all aspects of laboratory diagnostics and testing for diphtheria and related infections. Advice on immunisation against diphtheria, provision of vaccine and provision of diphtheria antitoxin for therapeutic use is available from the PHE Colindale Immunisation Department and in the recently published revised guidance for public health control and management of diphtheria [3].

Background

Diphtheria became rare in England following the introduction of mass immunisation in 1942, when the average annual number of cases was about 60,000 with 4,000 deaths. Primary vaccine coverage (three doses) in the United Kingdom (UK) for children aged two has been at least 94% since 2001 and is currently 96%, above the World Health Organisation (WHO) target of 95% [4]. Diphtheria vaccine is made from inactivated diphtheria toxin and protects individuals from the effects of toxin-producing corynebacteria. Three *Corynebacterium* spp. can potentially

produce toxin; *C. diphtheriae* (associated with epidemic person-to-person spread via respiratory droplets and close contact)*, C. ulcerans* and *C. pseudotuberculosis* (both less common globally and traditionally associated with farm animal contact and dairy products) [5,6].

Laboratory confirmation of diphtheria can be made by isolation of *C. diphtheriae, C. ulcerans or C. pseudotuberculosis* or detection of its DNA by, eg, PCR, The determination of toxigenicity requires submission of the isolate to the national reference laboratory, PHE RVPBRU. Identification and the presence of the *tox* gene are tested for by qPCR. If the *tox* gene is detected, the isolate is tested for expression of diphtheria toxin using the Elek test [7]. Non-toxigenic *C. diphtheriae* usually lack the entire *tox* operon, however, a small proportion of non-toxigenic strains carry incomplete *tox* variants, but do not express the diphtheria toxin protein. These strains are designated non-toxigenic toxin gene bearing (NTTB).

Classic respiratory diphtheria is characterised by a swollen ‘bull neck’ and strongly adherent pseudomembrane which obstructs the airways; a milder respiratory form of the disease where patients present with sore throat or pharyngitis is reported in immunised or partially immunised individuals [6]. Cutaneous presentations, characterised by ‘rolled edge’ ulcers, are usually associated with travel to tropical areas of the world. A recent review of diphtheria in the UK between 1986 and 2008 emphasises the changing epidemiology of the disease with the majority of toxigenic isolates in recent years associated more often with *C. ulcerans* than *C. diphtheria* [6].

The normal reservoir of *C. ulcerans* is cattle and human cases traditionally have been associated with the consumption of raw dairy products, however, recent studies have suggested that cats and dogs could also be potential reservoirs for this organism [8,9]. Travel and close contact with cattle, other farm animals and horses are other potential risk factors for infection. Although there is no direct evidence of person-to-person transmission of *C. ulcerans* infection there have been incidents that suggest this mode of transmission is possible. The guidelines for consultants in health protection on the control of diphtheria recommend that anyone who has been in close contact in the previous seven days with a case of infection caused by toxigenic *C. diphtheriae* or *C. ulcerans* should be considered at risk [10]. These guidelines were updated in 2015; however, the above recommendation remains largely unchanged. Additionally, although NTTB corynebacteria are not known to cause diphtheria it is recommended that they are eliminated using antibiotics in the same way as fully toxigenic (ie Elek-positive, toxin-expressing) strains.

As a disease becomes rare, the completeness and accuracy of surveillance information become more important and each clinical diagnosis (ie notification) needs to be confirmed by laboratory diagnosis. In addition to notifications, enhanced surveillance for diphtheria incorporates data from reference and NHS laboratories, death registration, and individual case details such as vaccination history, source of infection and severity of disease obtained from hospital records, general practitioners and local incident team reports. Linkage of notified cases of suspected diphtheria and confirmatory laboratory data shows that most notifications are cases of pharyngitis associated with isolation of non-toxigenic or non-toxigenic *tox* gene bearing strains of *C. diphtheriae,* and therefore interpretation of notification data should be undertaken with caution.

References

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Volume 10 Number 13 Published on: 1 April 2016

Tetanus in England and Wales: 2015

Tetanus is a life-threatening but preventable infection. From January to December 2015 only six cases were reported in England and Wales; one tetanus-related death was recorded during this period. This report updates the HPR annual report for 2014 [1] and reiterates current recommendations on diagnosis and clinical management of cases. Data sources for the enhanced surveillance of tetanus include notifications, reference and NHS laboratory reports, death registrations, and individual case details – such as vaccination history, source of infection and severity of disease – obtained from hospital records and general practitioners.

Five cases of tetanus were identified in England between January and December 2015; one case was reported from Wales. Tetanus is a notifiable disease under the Public Health (Control of Disease) Act 1984 (as amended) and accompanying regulations [2]. During 2015, notifications were only received for three cases, one of which was subsequently reclassified as not being due to tetanus. The other four cases of clinical tetanus reported here were all identified due to local clinicians contacting PHE for advice on suspected cases.

The six cases were aged 50 to 85 years old. One case, a female, was born after 1961 and therefore had been eligible for routine childhood vaccination [3]. Of the five cases born prior to 1961, one male was aged between 45 and 64 years of age and four (three female and one male) were aged over 64 years, the age group which historically has been the most affected by tetanus [4].

Unlike the previous year, where five of seven cases occurred in June and July, two of the cases occurred in April, two occurred between June and August, and two occurred in October. All of the cases had a history of injury. Five cases sustained lacerations or puncture wounds in the home or garden, and one sustained injuries in a park.

Three of the cases sought treatment at the time of exposure; all had their wounds dressed and two were given antibiotics, but there was no record of post-exposure prophylaxis being offered to any of the cases. No cases were identified among people who inject drugs (PWIDs) [5].

The case born after 1961 had received four of the recommended five doses of a tetanus containing vaccine for an adult; however, the most recent dose was more than 20 years ago. Among the five cases born prior to 1961 four were known to be unimmunised. No vaccination history was available for the remaining case, however, given they were over 75 years of age they were unlikely to have been immunised.

All six cases received tetanus immunoglobulin (TIG) or human normal immunoglobulin (HNIG) during their admission to hospital. One presented with mild symptoms (grade 1), two presented with moderate symptoms (grade 2), and three had severe symptoms (one grade 3a and two grade 3b) including one fatality. The partially immunised case had moderate symptoms (grade 2).

Pre-immunoglobulin blood samples from four of the cases were sent to the Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU) for anti-tetanus antibody testing. Two of the cases had levels of antibodies against tetanus that may be considered to confer protection (>0.1 IU/ml) at the time the sample was taken. However, in both cases the attending clinician still considered these cases to be clinical tetanus. The remaining two cases did not have ‘protective’ levels of antibodies.

One death due to tetanus in an unimmunised female in her mid-eighties was reported during this period (case fatality rate 16.7%; 1/6). There was no record of her having received prophylaxis at the time of injury and was admitted into hospital four days after exposure where she received immunoglobulin based on clinical presentation of severe tetanus.

During 2015, a further seven suspected cases of tetanus were investigated by PHE; all (four men and three women) were adults aged between 20 to 72 years old. Blood samples from three of the cases were sent to RVPBRU; all were found to have ‘protective’ levels of antibodies against tetanus (>0.1IU/ml) [6]. In each case tetanus was excluded from the diagnosis by the attending clinician.

Background, diagnosis and clinical management

Tetanus is a life-threatening but preventable disease caused by a neurotoxin (tetanospasmin, TS) produced by *Clostridium tetani*, an anaerobic spore-forming bacterium. Tetanus spores are widespread in the environment, including in soil, and can survive hostile conditions for long periods of time. Transmission occurs when spores are introduced into the body, often through a puncture wound but also through trivial, unnoticed wounds, chronic ulcers, injecting drug use, and occasionally through abdominal surgery. Neonatal tetanus is still common in the developing world where the portal of entry is usually the

umbilical stump, particularly if there is a cultural practice of applying animal dung to the umbilicus. Tetanus is not transmitted from person to person. The incubation period of the disease is usually between three and 21 days, although it may range from one day to several months, depending on the character, extent and localisation of the wound.

Tetanus immunisation was introduced in the 1950s and became part of the national routine childhood programme in 1961. Since then, vaccine coverage at two years of age has always exceeded 70% in England and Wales and since 2001 has been around or above 95%, the target coverage set by the World Health Organization (WHO). The objective of the immunisation programme in the UK is to provide a minimum of five doses of tetanus-containing vaccine at appropriate intervals for all individuals. As there is no herd immunity effect, individual protection through vaccination is essential. In most circumstances, a total of five doses of vaccine at the appropriate intervals are considered to give satisfactory long-term protection, and routine boosters every 10 years are no longer recommended [2].

Tetanus is usually confirmed by a clinical diagnosis alone, although three diagnostic laboratory tests are available: detection of tetanus toxin in a serum sample, isolation of *C. tetani* from the infection site, and demonstrating low levels or undetectable antibody to tetanus toxoid in serum. The first two tests provide microbiological confirmation, whereas the third can only support the diagnosis [6].

Clinical management of tetanus includes administration of TIG, wound debridement, antimicrobials including agents reliably active against anaerobes such as metronidazole, and vaccination with tetanus toxoid following recovery. Early treatment with TIG can be lifesaving. As the supply of TIG is limited to the use of TIG is restricted to patients requiring treatment for suspected tetanus. Where a suitable TIG stock cannot be sourced, Public Health England recommends that HNIG for intravenous use may be used as an alternative for treatment of clinical tetanus. For tetanus prone wounds requiring prophylactic TIG, HNIG for subcutaneous use may be given intramuscularly as an alternative to TIG [7]. It is most important that a blood sample for the detection of tetanus toxin or the determination of anti-tetanus antibodies is collected BEFORE the administration of TIG or normal human immunoglobulin [7] and to maximise toxin detection is collected as close to onset of neurological symptoms as possible, preferably within two days. This is because toxin binds rapidly to the active site and is removed from the circulatory system.

References/notes

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