Public Health England

Health Protection Report
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Current News

Infection Reports

Vaccine preventable infections

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UK seasonal influenza annual report 2014/15 in summary

Moderate levels of influenza activity were seen in the community in the United Kingdom (UK) in 2014/15, with influenza A(H3N2) the predominant virus circulating for the majority of the season, and influenza B circulating later in the season. The impact of H3N2 was predominantly seen in the elderly, with numerous outbreaks in care homes and levels of excess mortality higher than the last notable H3N2 season of 2008/09. Peak admissions to hospital and intensive care were higher than seen in recent seasons, but lower than the last notable season of 2010/11.

These are among the conclusions of the PHE report on influenza and other respiratory viruses in the UK during the winter of 2014/15 [1]. The annual report is produced by PHE's Respiratory Diseases Department in collaboration with the health protection bodies of the Devolved Administrations, and other national data providers across the UK. It includes summary information for the UK on flu-related mortality and morbidity, and on vaccine uptake data. It also includes updates on the extent of circulation of novel respiratory viruses (including avian-origin influenza) outside of the UK – in the Middle East, Egypt and Eastern China – that are being monitored despite the current low risk to UK residents.

Influenza vaccine uptake and effectiveness

Influenza vaccine uptake in 2014/15 in England was similar to recent seasons in the elderly (72.7%) and in healthcare workers (54.6%), and slightly lower in under 65 year olds in a pre-defined clinical risk group (50.3%). An increase was seen in pregnant women (44.1%) compared to 2013/14 (39.8%).

In 2014 to 2015, the universal childhood influenza vaccine programme with live attenuated influenza vaccine (LAIV) was offered to all 2, 3 and 4 year olds in England, achieving an uptake of 38.5%, 41.3% and 32.9% respectively. A pilot LAIV programme for children of primary and secondary school age (4 to 13 years) in England, achieved an overall uptake of 53.2%.

The UK mid-season overall adjusted vaccine effectiveness (VE) in preventing influenza A confirmed infection in primary care was low, likely reflecting the mismatch between circulating A(H3N2) viruses and the 2014/15 Northern Hemisphere vaccine strain. Work continues to evaluate the impact of the LAIV programme in terms of both direct and indirect protection for the general population across the country. The importance of ensuring high uptake in target groups for the national influenza vaccination programme for the forthcoming influenza season remains.

Other respiratory viruses

Activity from other circulating seasonal respiratory viruses was similar to levels reported in recent years. Two novel respiratory viruses which emerged in 2012/13, Middle East Respiratory Syndrome coronavirus (MERS-CoV) in the Middle East and avian-origin influenza A(H7N9) in Eastern China, have continued to result in human cases in affected countries in 2014/15. There has also been an unprecedented number of human infections with avian influenza A(H5N1) reported in Egypt in 2015. Surveillance and public health measures established in the UK for travellers returning with severe respiratory disease from these regions are on-going while the risk remains.

Reference

1. PHE (2015). Surveillance of influenza and other respiratory viruses in the United Kingdom: winter 2014 to 2015.

Investigation of *M. chimaera* infection associated with cardiopulmonary bypass: an update

As reported on 30 April [1], cases of invasive *Mycobacterium chimaera* infection have been reported in patients who have undergone cardiac surgery in Switzerland and the Netherlands. A Swiss investigation has been published attributing these infections to aerosol generated by contaminated heater cooler units (HCUs) used during cardiopulmonary bypass [2]. A case of similar infection has also been reported in Germany and a rapid risk assessment has been published by the European Centre for Disease Prevention and Control [3]. Of the cases to date in Europe, three fatal outcomes have been reported.

PHE has conducted an investigation in the UK, in partnership with the NHS, the Medicines and Healthcare Products Regulatory Agency (MHRA), Public Health Wales, Health Protection Scotland and the Public Health Agency of Northern Ireland. This included microbiological assessment of HCUs and retrospective case finding.

Microbiological investigation at multiple hospital sites in the UK has indicated that non-tuberculous mycobacteria (common environmental organisms) can be found in the water within HCUs. Non-tuberculous mycobacteria have also been detected in the air around the devices at some of these sites. The investigation to date has focused on the model of HCU which is most commonly used in the UK, which is the same as those described in the Swiss report. It is not clear whether any risk is limited to a particular model or brand of HCU.

Retrospective case finding was conducted to look for patients with similar infections to those reported in Switzerland (*M. chimaera* or other *M. avium* complex endocarditis, surgical site infection or disseminated infection within four years of surgery involving cardiopulmonary bypass). A small number of patients (13) who fulfill these criteria have been found in the UK and are the subject of ongoing investigations. These patients had surgery in many different hospitals in the UK between 2007 and 2014. A definitive link between the heater cooler units and the patient infections has not been established by the UK investigation. Further microbiological investigations are underway.

PHE and the MHRA continue to investigate this risk and are working with manufacturers, the NHS and the European Centre for Disease Prevention and Control to identify solutions for cardiothoracic centres.

References

1. Investigation of *Mycobacterium chimaera* infection associated with cardiopulmonary bypass, *HPR* **9**(15), 30 April 2015.
2. Sax H, Bloemberg G, Hasse B, Sommerstein R, Kohler P, Achermann Y *et al* (2015). "Prolonged outbreak of *Mycobacterium chimaera* infection after open-chest heart surgery". *Clin Infect Dis* (online, March 11).
3. European Centre for Disease Prevention and Control. "Invasive cardiovascular infection by *Mycobacterium chimaera* potentially associated with heater-cooler units used during cardiac surgery", 30 April 2015.

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Volume 9 Number 18 Published on: **22 May 2015**

Infection Reports

Vaccine preventable infections

- **Laboratory confirmed cases of measles, mumps and rubella, England: January to March 2015**
- **Laboratory confirmed cases of pertussis reported to the enhanced pertussis surveillance programme in England: annual report for 2014**
- **Tetanus in England and Wales: 2014**
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Laboratory confirmed cases of measles, mumps and rubella, England: January to March 2015

Measles, mumps and rubella are notifiable diseases and healthcare professionals suspecting a case are legally required to inform the authorities. Measles and rubella are targeted for elimination in Europe by 2015 and progress towards this target is monitored by the European Centre for Disease Prevention and Control [1]. Oral fluid testing is offered to all notified cases to confirm the diagnosis. This is part of the enhanced surveillance for these vaccine preventable diseases. Recent infection is confirmed by measuring the presence of IgM antibodies or detecting viral RNA (by PCR) in the samples.

Data presented here are for the first quarter of 2015 (ie January to March). Cases include those confirmed by oral fluid testing (IgM antibody tests and/or PCR) at the Virus Reference Department (Colindale) and national routine laboratory reports (mumps infections only) (table 1). Analyses are by date of onset and regional breakdown figures relate to Government Office Regions.

Quarterly figures from 2013 for cases confirmed by oral fluid antibody detection only and annual total numbers of confirmed cases by region and age are available from:

https://www.gov.uk/government/publications/measles-confirmed-cases

https://www.gov.uk/government/publications/mumps-confirmed-cases

https://www.gov.uk/government/publications/rubella-confirmed-cases

Table 1: Total laboratory confirmed cases of measles, mumps and rubella, and oral fluid IgM antibody tests in notified cases: weeks 1-13/2015

Notified and investigated cases						Confirmed cases		
Infecting virus	Cases reported to Health Protection Teams in England*	Oral fluid testing					Other samples	**Total**
		Number Tested	% of reported cases tested	*Total Positive*	*Recently Vaccinated*	Confirmed infections		
Measles	543	394	73%	*26*	*8*	18	2	**20**
Mumps	2057	1406	68%	*152*	*1*	151	76	**227**
Rubella	136	77	57%	*1*	*0*	1	3	**4**

*This represents the number of infections reported as possible cases and investigated by individual PHE centres in England

Measles

Twenty measles infections were laboratory confirmed in England with onset dates in January to March 2015 compared to only four cases in the last quarter of 2014 [1].

Measles cases were reported from four regions with London identifying 15 of the 20 new infections. Scotland and Wales reported no cases this quarter.

All of the new infections were associated with travel abroad; two separate importations from India resulting in a family cluster (two cases) and a school cluster (13 cases), three cases from Germany (two separate importations), and one importation each from China and Thailand. Measles virus was isolated from the samples of the 16 of the 20 cases. The predominant genotype identified was D8 (India, Germany and Thailand), although D4 (India) and H1 (China) were also isolated.

The majority (16/20, 80%) of cases this quarter were in children and adolescents: two (10%) aged 1-4 years; two (10%) aged 5-9 year, eight (40%) aged 10-14 years; four (20%) aged 15-18 years. The remaining four cases (20%) were adults aged 25-61 years. Only one case had a history of vaccination and they reported receiving two doses of a measles-containing vaccine.

Mumps

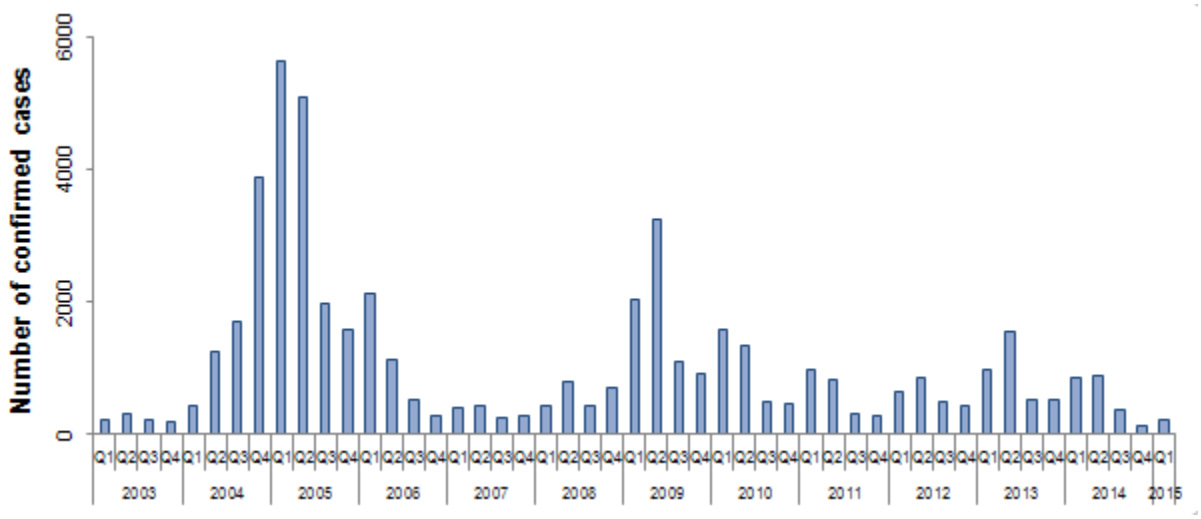
There were 227 laboratory confirmed cases of mumps in England with an onset date in the first quarter of 2015 compared to 140 in the last quarter of 2014, following a trend observed for more than a decade where the first quarter of the year always exceeds the last quarter of the previous year (figure) [2]. Additionally, nine oral fluid samples were confirmed from Wales.

Cases continue to be identified predominantly in young adults between 15 and 30 years of age (194/227 86%, table 2). Over 37% of all cases this quarter have reported receiving at least one dose of MMR vaccination in childhood, suggesting that some waning immunity may be contributing to transmission. Mumps cases were identified in all regions of England although greater numbers were reported in Yorkshire and Humber, and the South East (table 2).

Table 2: Laboratory confirmed cases of mumps by age group and region, England: weeks 1-13/2015

Region	<1	1-4	5-9	10-14	15-19	20-24	25+	Total
North East	–	–	1	1	5	7	10	**24**
North West	–	3	1	2	1	5	16	**28**
Yorkshire & Humber	–	1	3	3	14	11	14	**46**
East Midlands	–	–	–	1	1	–	3	**5**
West Midlands	–	–	–	–	4	2	7	**13**
East of England	–	–	–	1	1	4	15	**21**
London	–	1	4	1	4	4	15	**29**
South East	–	1	–	–	14	7	21	**43**
South West	–	–	–	–	4	9	5	**18**
Total	**0**	**6**	**9**	**9**	**48**	**49**	**106**	**227**

Laboratory confirmed cases of mumps by quarter, England, 2003-2015



Rubella

Four cases of rubella were confirmed this quarter, compared to one in the whole of 2014. Two of the cases were in adults, associated with travel to France, one of them being a pregnant woman. The other two cases were congenital rubella infections.

References

1. ECDC (2015). Measles and rubella monitoring (January).
2. PHE (2015). "Laboratory confirmed cases of measles, mumps and rubella, England: October to December 2014", *HPR* **9**(7): immunisation (27 February).

Laboratory confirmed cases of pertussis reported to the enhanced pertussis surveillance programme in England: annual report for 2014

In England there were 3388 laboratory confirmed cases of pertussis (culture, PCR, serology or oral fluid) reported to the Public Health England pertussis enhanced surveillance programme in 2014. Pertussis is a cyclical disease with increases occurring every 3-4 years. Typically pertussis activity peaks in quarter three within each year, however, there was an unusually high increase in cases in 2012 (figure 1). A third (32%; 1094/3388) of all confirmed cases in England in 2014 were reported in the third quarter (July to September) (table1).

Numbers of confirmed cases in England in 2014 were 27% lower than the 4621 reported in 2013 and 64% lower than the 9367 cases reported in 2012; however the number of confirmed cases in 2014 were three-fold higher than the number of cases reported in 2011 (n=1053). In all those aged four years and older confirmed pertussis cases were higher in 2014 than any year reported prior to 2012 and in the 1-4 year age group total cases were higher than they had been in the 15 years preceding 2012. In infants under a year, however, pertussis cases were slightly higher in 2014 (n=123) than in 2013 (116) but lower than the 508 reported in 2012 and 207 reported in 2011 and was overall in line with annual cases reported prior to 2012.

A national outbreak of pertussis (level 3 incident [1]) was declared by the HPA in April 2012 and, as a response to the ongoing outbreak, the Department of Health (DH) announced the introduction of a temporary immunisation programme for pregnant women on 28 September 2012 [2]. In June 2014 the Joint Committee on Vaccination and Immunisation (JCVI) recommended that the programme should continue for a further five years [3]. The most recent PHE figures report that the proportion of mothers due to give birth between January 2014 and December 2014 who had been immunised with a pertussis containing vaccine in pregnancy in England ranged from 52.7% - 62.3% [4].

The national incidence for all age groups, based on laboratory confirmations in England and 2011 population estimates [5], was two cases of pertussis per 100,000 population in 2011, 18 per 100,000 in 2012, nine per 100,000 in 2013 and six per 100,000 in 2014 (figure 2). As was seen in 2012 and 2013, the majority (81%; 2738/3388) of laboratory confirmed cases in England in 2014 occurred in individuals aged 15 years and older. The number of confirmed cases in this age group continued to decrease from a peak of 7775 in 2012 (incidence of 18/100,000) to 3912 in 2013 (incidence of 9/100,000) and 2738 (incidence 6/100,000) in 2014 (figure 2).

As expected, the incidence of laboratory confirmed cases continued to be highest in infants less than three months, who are at most risk of serious disease and too young to be fully vaccinated.

Confirmed pertussis incidence in this age group was 58 per 100,000 in 2014, compared to 50 per 100,000 in 2013 and 240 per 100,000 in 2012 (figure 2). Accordingly, the number of confirmed cases in infants <3 months increased by 15% in 2014 (98 cases) compared to 2013 (85 cases), but was 76% lower than 2012 (407 cases) and 41% lower than 2011 (166). In England, 14 deaths were reported for infants with pertussis confirmed in 2012. Following the introduction of pertussis vaccination in pregnancy; three babies died following pertussis confirmed in 2013 and seven in 2014. In Wales one baby with pertussis certified as an underlying cause of death was reported in 2014. All cases were too young to be protected by infant vaccination and only one of the infants born after the introduction of the maternal programme had a mother who had been vaccinated during pregnancy.

These surveillance data in young infants following the introduction of a programme to immunise pregnant women are encouraging as a relatively low incidence has been maintained, with expected seasonal increases. It is important to be aware, however, that raised levels of pertussis persist in older age groups and women should, therefore, continue to be encouraged to be immunised against pertussis during pregnancy in order to protect their babies from birth. The pertussis immunisation in pregnancy programme in England has shown high levels of protection against pertussis in babies born to vaccinated mothers [6,7]. The Medicines and Healthcare Products Regulatory Agency also found no safety concerns relating to pertussis vaccination in pregnancy based on a large study of nearly 18,000 vaccinated women with similar rates of normal, healthy births in vaccinated and in unvaccinated women [8].

Since mid-2006 there has been greater use of serology testing compared to previous years due to increasing clinical awareness of pertussis in older children and adults [9] and increased awareness of the availability of this diagnostic method [10]. In 2014, serology confirmed cases accounted for the greatest proportion (92%; 3110/3388) of total laboratory confirmations, and accounted for 98% (2683/2738) of all confirmed cases of pertussis in older age groups (table 2). All but three infants under one year of age with confirmed pertussis in 2014 were tested using culture and PCR methods. Oral fluid (OF) testing was introduced in 2013 for testing children aged five to <17 years and in 2014, 90 of 577 cases (16%) in this age group tested positive for a recent pertussis infection by OF testing only.

The choice of laboratory testing method is dependent on the age of the patient and the stage of the illness; this is reflected in the distribution of testing methods summarised in table 2. Culture is the gold standard for diagnosis but loses sensitivity with increasing time from the onset of illness and is unlikely to be positive after two weeks from the onset of symptoms. The Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU) at PHE Microbiology

Services Division (Colindale) encourages submission of all *Bordetella pertussis* isolates for confirmation and national surveillance purposes.

Bordetella pertussis PCR testing for hospitalised cases <1 year [11] old has been offered by the RVPBRU since 2002 and from July 2014, PCR testing for all ages has been deployed via lead PHE laboratories in a phased approach [12]. This form of testing is particularly encouraged in all children aged 1-4 years, who present within three weeks of onset, for whom recent vaccination may confound serology results.

In contrast, serology investigation by estimation of anti-pertussis toxin (PT) IgG antibody levels for older children and adults is routinely offered for older children/adults who have been unwell with a cough for at least two weeks. The RVPBRU is also offering an OF testing service for clinically suspected cases reported to local Health Protection Teams, who are aged between 5-16 years (<17yrs) and have been coughing for at least two weeks and have not been immunised against pertussis in the previous year. However, as recent pertussis vaccination (primary and pre-school booster vaccination) can confound the serology and OF results, these investigations are not usually recommended for infants or children within one year of receiving the pertussis vaccine (primary or pre-school booster).

Further information is available in the PHE Microbiology Services Colindale Bacteriology Reference Department User Manual at:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/340615/BRDW0078.01_Bacteriology_Reference_Dept_User_Manual_.pdf

Figure 1. Total laboratory-confirmed pertussis cases per evaluation quarter in England: 2005-2014

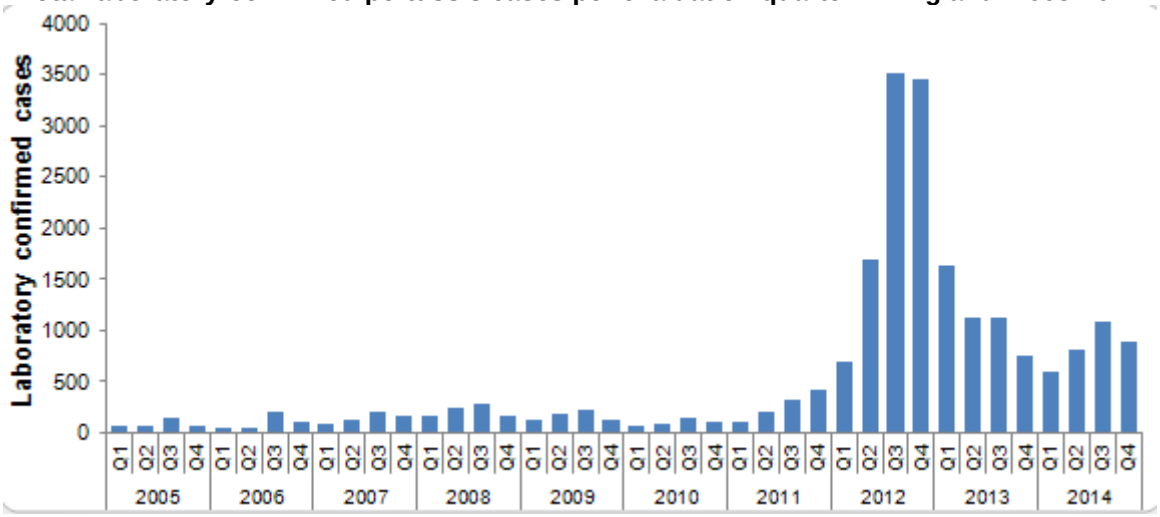


Table 1. Laboratory-confirmed cases of pertussis by quarter and test method in England: 2014

Quarter	Culture*	PCR	Serology	OF only	Total
Jan - Mar	15	13	552	22	602
Apr - Jun	21	25	743	21	810
Jul - Sep	32	39	991	32	1094
Oct - Dec	17	9	824	32	882
Total	**85**	**86**	**3110**	**107**	**3388**

* Culture confirmed cases may additionally have tested positive using other methods. Submission of all presumptive B. pertussis isolates is encouraged for confirmation of identity and to allow further characterisation for epidemiological purposes.

Figure 2. Incidence of laboratory-confirmed pertussis cases by age group in England: 1998-2014

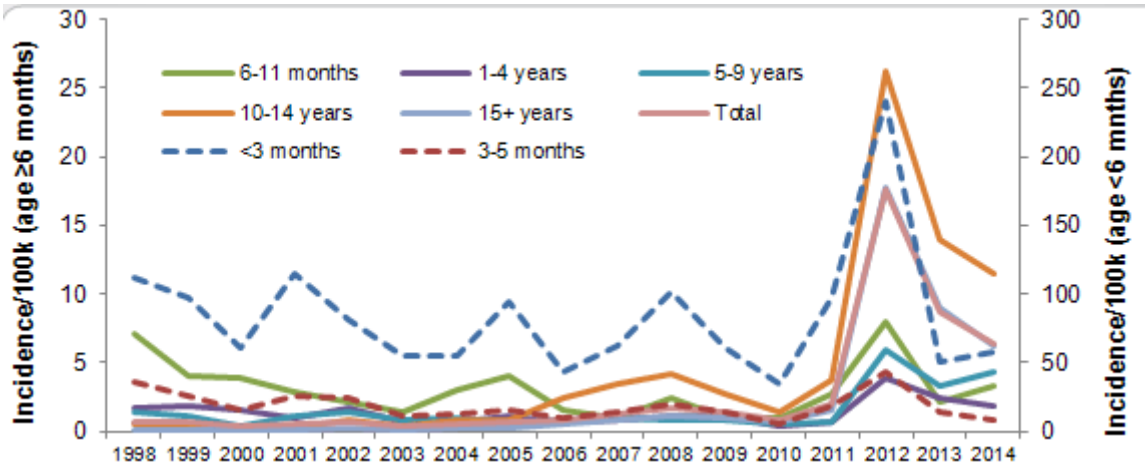


Table 2. Age distribution of laboratory-confirmed cases of pertussis in England: 2014

Age group	Culture*	PCR	Serology	OF only	Total
<3 months	48	49	1	-	98
3-5 months	3	10	1	-	14
6-11 months	7	3	1	-	11
1-4 years	6	5	34	3	48
5-9 years	3	2	96	27	128
10-14 years	2	2	294	53	351
15+ years	16	15	2683	24	2738
Total	**85**	**86**	**3110**	**107**	**3388**

* Culture confirmed cases may additionally have tested positive using other methods. Submission of all presumptive B. pertussis isolates is encouraged for confirmation of identity and to allow further characterisation for epidemiological purposes.

References

1. "Confirmed pertussis in England and Wales continues to rise", *HPR* **6**(15), 13 April 2012.

2. "Pregnant women to be offered whooping cough vaccination" (28 September 2012). Department of Health website.

3. Joint committee of Vaccination and Immunisation minutes.

4. Pertussis Vaccination Programme for Pregnant Women: vaccine coverage estimates in England, October 2012 to March 2014 (PHE statistics).

5. Office for National Statistics – 2011 Census population estimates.

6. Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, Donegan K, *et al* (2014). Effectiveness of maternal pertussis vaccination in England: an observational study, *Lancet*.

7. Dabrera G, Amirthalingam G, Andrews N *et al* (2014). A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn Infants in England and Wales, 2012–2013, *Clinical Infectious Diseases* (online), 19 October.

8. Donegan K, King B, Bryan P (2014). Safety of pertussis vaccination in pregnant women in UK: observational study. *BMJ* **349** g4219.

9. Harnden A, Grant C, Harrison TG, Perera R, Brueggemann AB, Mayon-White R, *et al* (2006). Whooping cough in school age children with persistent cough: prospective cohort study in primary care. *BMJ* **333**: 174-7.

10. Fry NK, Tzivra O, Li YT, McNiff A, Doshi N, Maple PA, *et al* (2004). Laboratory diagnosis of pertussis infections: the role of PCR and serology. *J Med Microbiol* **53**: 519-25.

11. Fry NK, Duncan J, Wagner K, Tzivra O, Doshi N, Litt DJ, *et al* (2008). Role of PCR in the diagnosis of pertussis infection in infants: 5 years' experience of provision of a same-day real-time PCR service in England and Wales from 2002 to 2007; *J Med Microbiol* **58**: 1023-29.

12. PHE (2014). Internal PHE communication: Briefing note 2014/07 (29 September).

Tetanus in England and Wales: 2014

Tetanus is a life-threatening but preventable infection. From January to December 2014 only seven cases were reported in England; and one tetanus-related death was recorded during this period. This report updates the HPR annual report for 2013 [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.

Seven cases of tetanus were identified in England between January and December 2014; no cases were reported from Wales. Tetanus is a notifiable disease under the Public Health (Control of Disease) Act 1984 (as amended) and accompanying regulations [2]. During 2014, notifications were only received for four cases, one of which was subsequently reclassified as not being due to tetanus. The other four tetanus cases reported here were identified due to local clinicians contacting PHE for advice on a suspected case.

The seven cases were aged 15 to 87 years old. Two cases, one male and one female, were born after 1961 and therefore eligible for routine childhood vaccination [3]. Of the five cases born prior to 1961, two (one male and one female) were identified among 45-64 year olds and three (two female and one male) were aged over 64 years, the age group which historically has been the most affected by tetanus [4].

Five of the cases occurred during June and July. All of the cases had a history of injury. Four cases sustained lacerations in the home or garden, the other three sustained injuries in the street, at a horse stable, and in a woodland. Only one of the cases sought treatment at the time of exposure; their wound was dressed but there was no record of post-exposure prophylaxis being offered. No cases were identified among people who inject drugs (PWIDs) [5].

Among the two cases born after 1961, one was fully immunised having received five doses of tetanus-containing vaccine and one was age appropriately immunised having received four doses of vaccine. Among the five cases born prior to 1961; one was partially immunised having received four doses of vaccine, two were known to be unimmunised. No vaccination history was available for the remaining two cases, however, given their age (75+ years old) they were unlikely to have been immunised.

All seven cases received tetanus immunoglobulin (TIG) or human normal immunoglobulin (HNIG) during their admission to hospital. Three presented with mild symptoms (grade 1), one presented with moderate symptoms (grade 2), and three had severe symptoms (grade

3) including one fatality. The two age-appropriately immunised cases had mild symptoms, which is consistent with previous reports [1]. A partially immunised case had moderate symptoms (grade 2).

Samples from six of the cases were sent to the Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU). Three of the cases had protective levels of antibodies against tetanus (>0.1 IU/ml) at the time the sample was taken; however, the attending clinician considered these cases to be clinical tetanus. The remaining three cases did not have protective levels of antibodies; *C. tetani* was cultured from wound swabs for two of these cases.

One death due to tetanus was reported during this period (case fatality rate 14.3%; 1/7) in an 80+ year old female. The immunisation status of the case was not known and there was no record of the case having received prophylaxis at the time of exposure. The case was admitted into hospital and received immunoglobulin based on clinical presentation of severe tetanus.

During 2014, a further nine suspected cases of tetanus were investigated by PHE; all (five men and four women) were adults aged between 27 to 81 years old. Samples from six of the cases were sent to RVPBRU; five 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 [7].

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

1. PHE (2014). Tetanus (England and Wales): 2013. *HPR* **8**(12): immunisation. Available online at: https://www.gov.uk/government/publications/tetanus-in-england-and-wales-2013/tetanus-in-england-and-wales-2013

2. Notifications of Infectious Diseases (NOIDs) (October 2012).

3. Department of Health (2006). Immunisation against infectious disease. Chapter 30. Tetanus. Available at

4. Rushdy AA, White JM , Ramsay ME, Crowcroft NS (2003). Tetanus in England and Wales 1984-2000. *Epidemiol Infect* 130: 71-7.

5. Hahne SJM, White JM , Brett M, George R, Beeching NJ, Roy K, et al (2006). Tetanus emerges in injecting drug users in the UK [letter]. *Emerg Infect Dis* **12**(4): 709-10.

6. PHE website (March 2013). Information for Health Professionals.

7. PHE website (March 2013). HPA recommendation on the treatment and prophylaxis of tetanus.

Diphtheria in England and Wales: 2014

Diphtheria is a life-threatening but preventable infection. From January to December 2014 only one toxigenic strain of Corynebacterium ulcerans *was reported in England. (Five non-toxigenic tox gene bearing* C. diphtheriae *strains were reported during the period.) This report updates the previous three-year review of diphtheria cases in England and Wales for 2011-13 [1] and highlights newly published recommendations for public health control and management of of the infection [2]. 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.*

This 2014 review updates a previous three-year review of diphtheria cases in England and Wales for 2011-2013 [1] and highlights the newly published recommendations for the public health control and management of diphtheria [2]. 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 2014, one toxigenic strain of corynebacteria, from a cutaneous case of *C. ulcerans*, was 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.

Fourteen case notifications were received during this period; three were non-toxigenic *tox* gene bearing (NTTB) *C. diphtheriae,* 10 were non-toxigenic *C. diphtheriae* infections, and one was a non-toxigenic *Corynebacterium* spp*.* infection. In the same period, RVPBRU identified one toxigenic *C. ulcerans* strain and two additional NTTB *C. diphtheriae* strains 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: 2014

Total notifications	**14***
Number due to non-toxigenic *C. diphtheriae*	10
Number due to toxigenic *C. diphtheriae*	0
NTTB *C. diphtheriae*	3
Number due to toxigenic *C. ulcerans*	0
All toxigenic *corynebacteria isolates*	**1**
Toxigenic *C. diphtheriae*	0
NTTB *C. diphtheriae*	5
Toxigenic *C. ulcerans*	1

* *Corynebacterium* spp. isolated from a one sample

C. diphtheriae

No toxigenic *C. diphtheriae* strains were isolated in 2014.

There were five NTTB *C. diphtheriae* var. mitis strains isolated, three were isolated from tissue samples from patients with skin lesions and two were isolated from nasopharyngeal samples from patients with sore throats (table 2). The patients were aged 24 to 41 years, three were female and two were male. Two patients were reported as have complete primary immunisations; one was reported as immunised but a full vaccination history was not available; one was unimmunised; the immunisation history of the fifth was unknown.

None of the patients reported contact with anyone who had symptoms suggestive of respiratory or cutaneous diphtheria or travel to an endemic country. The three patients with skin lesions all had a similar underlying medical condition which increased their susceptibility to bacterial infections. Neither of the patients with mild respiratory symptoms; had any identifiable risk factors.

In total, 34 close contacts of the patients were identified, including household contacts, social contacts, and healthcare workers. Where possible the contacts were offered chemoprophylaxis, vaccination as appropriate, and swabbed. One contact exhibited symptoms consistent with a mild respiratory infection; however, swabs taken from this contact did not yield *C. diphtheriae*. None of the remaining 33 close contacts exhibited cutaneous or respiratory symptoms and no swabs yielded *C. diphtheriae*.

All five patients were treated with antibiotics and offered vaccination as appropriate, none experienced systemic complications, and all recovered from their infection with a corynebacterium strain.

C. ulcerans

One toxigenic *C. ulcerans* strain was isolated from a wound swab (cutaneous diphtheria) in 2014. The patient was an adult male who had an unknown immunisation history who presented with a post-surgical wound which had become infected; earlier samples taken from the wound did not yield *C. ulcerans*. The patient was treated with antibiotics and received a dose of diphtheria containing vaccine; there were no systemic complications and he recovered from his illness.

Risk factors for *C. ulcerans* include contact with companion animals [2-4] and the patient reported contact with a dog but no other risk factors were identified. Pharyngeal swabs taken from the dog tested positive for toxigenic *C. ulcerans*. The animal was treated with antibiotics under veterinary guidance and clearance swabs taken once treatment was complete did not yield *C. ulcerans.* Throat swabs from four close contacts of the patient were all negative for corynebacteria.

Table 2: Clinical presentation of diphtheria cases and causative organism, England 2014

	Causative organism			
Clinical presentation of cases	Toxigenic *C. diphtheriae*	NTTB *C. diphtheriae*	Toxigenic *C. ulcerans*	**Total**
Classic respiratory diphtheria (with pseudomembrane)	–	–	–	**0**
Mild respiratory diphtheria (sore throat/pharyngitis)	–	2	–	**2**
Cutaneous diphtheria	–	3	1	**4**

Since April 2014, a new PCR service has been available at the national reference laboratory at PHE which confirms the identity of *Corynebacterium 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.

Five non-toxigenic tox gene bearing *Corynebacterium diphtheriae* strains were reported during this period.

Microbiological laboratories are encouraged to submit all suspect isolates of *C. diphtheriae* and other potentially toxigenic corynebacteria to PHE RVPBRU using the form R3 [2]. From 1 April 2014, the test result which helps inform public health action is a PCR which confirms the identity *of Corynebacterium 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 [2]. 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 [2].

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% [3]. 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) [4,5].

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 [6]. 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 [5]. 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* [5].

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 [7,8]. 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 communicable disease control (CCDCs) 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 [9]. These guidelines have recently been updated; 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 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

1. "Diphtheria in England and Wales: 2011-2013", *HPR* **8**(14), 28 March 2014.

2. PHE (2015). Public health control and management of diphtheria (in England and Wales): 2015 guidelines.

3. PHE (2014). NHS Immunisation Statistics. England: 2013-14.

4. Bostock AD, Gilbert FR, Lewis D, Smith DC (1984). Corynebacterium ulcerans infection associated with untreated milk. *J Infect*. **9**(3), 286-8.

5. Wagner KS, White JM, Crowcroft NS, De Martin S, Mann G, Efstratiou A (2010). Diphtheria in the United Kingdom, 1986-2008: the increasing role of *Corynebacterium ulcerans*. *Epidemiol Infect.* **138**(11): 1519-30.

6. De Zoysa A, Fry NK, Efstratiou A, Harrison T (2014). Detection of diphtheria toxin gene-bearing and non-toxin gene-bearing Corynebacterium diphtheriae and Corynebacterium ulcerans/ Corynebacterium pseudotuberculosis using a quadruplex Rotor-Gene Q PCR assay. European Scientific Conference on Applied Infectious Diseases Epidemiology (ESCAIDE); 5-7 November 2014 (Stockholm).

7. De Zoysa A, Hawkey PM, Engler K, George R, Mann G, Reilly W, *et al*.(2005). Characterization of toxigenic Corynebacterium ulcerans strains isolated from humans and domestic cats in the United Kingdom. *J Clin Microbiol.* **43**(9): 4377-81.

8. Lartigue M-F, Monnet X, Le Flèche A, Grimont PA, Benet J-J, Durrbach A, *et al* (2005). Corynebacterium ulcerans in an immunocompromised patient with diphtheria and her dog. *Journal of clinical microbiology* **43**(2): 999-1001.

9. Bonnet JM, Begg NT (1999). Control of diphtheria: guidance for consultants in communicable disease control. World Health Organization. *Commun Dis Public Health* **2**(4): 242-9.