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Guidelines for the Public Health Management of Pertussis in England

Produced by the Pertussis Guidelines Group

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V01.4	Updated PHE Guidelines for the Public Health Management of Pertussis in England	October 2016
V02.0	PHE guidelines amended following extension of the availability of oral fluid testing.	May 2018

Introduction

These guidelines, which update the 2012 Health Protection Agency (HPA) Guidelines for the public health management of pertussis (1), are based on a recent review of all currently available scientific evidence and consultation with experts where required.

The key changes in the October 2016 guidance include:

- updated epidemiology of pertussis in England since the introduction of the pertussis immunisation programme for pregnant women in October 2012
- updated information on, and interpretation of, the available laboratory methods to confirm clinically suspected cases of pertussis at regional Public Health England (PHE) laboratories and the national reference laboratory at the Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU), PHE Colindale
- revised definitions of the priority groups for public health action, in particular the definition of a vulnerable infant which takes into account the latest evidence of the effectiveness of the immunisation programme for pregnant women
- revised definition of the recommended exclusion period, which has been reduced from 5 days to 48 hours
- updated information on the available pertussis vaccines for post exposure management and outbreak control
- updated flow diagrams for management of cases and close contacts (Appendix 1).

In version 2:0 (May 2018) the guidelines were further amended following extension of the availability of oral fluid testing. The main changes were:

- from May 2018, oral fluid testing available for children aged 2 to <17 years
- use of days rather than weeks in guidance for appropriate pertussis testing in order to add clarity
- clarification that cases of parapertussis do not require public health action
- hexavalent (DTaP/IPV/Hib/HepB) vaccine added to the primary schedule for infants born from 1 August 2017
- the addition of appendix 6 which summarises testing for pertussis in Primary Care

The information presented by this guidance is intended to supplement, not substitute for, the expertise and judgement of healthcare professionals.

These guidelines are split into two sections:

Part 1: Background and rationale

Part 2: Investigation and management of suspected cases of pertussis and their close contacts

Part 1: **Background and rationale**

1.1 Introduction

Pertussis (whooping cough) is an acute bacterial infection caused by *Bordetella pertussis*, an exclusively human pathogen that can affect people of all ages. While adolescents and adults tend to have a prolonged cough illness but without other major symptoms, young unimmunised infants are the most vulnerable group with the highest rates of complications and death. Transmission of the organism occurs as a result of close direct contact with an infected person (2). It is highly contagious, with up to 90% of household contacts developing the disease (3).

The incubation period of pertussis is on average between 7-10 days (range 5-21 days). The usual clinical presentation is an initial catarrhal stage with a cough that becomes paroxysmal. Paroxysms of cough usually increase in frequency and severity as the illness progresses and persist for 2-6 weeks. These paroxysms may end in vomiting, cyanosis and/or a characteristic inspiratory whoop. Patients with pertussis are most infectious in the initial catarrhal stage and during the first 3 weeks after the onset of cough (4). Symptoms slowly improve in the convalescent phase, which generally lasts 2-6 weeks but can persist for months. Adults generally have a non-productive cough illness without fever (5). Serious complications include pneumonia, seizures and encephalitis. Vaccination provides the most effective strategy for preventing pertussis transmission in the population, although protection afforded by vaccination or from past infection is not lifelong.

1.2 History of pertussis control in England and Wales

Whole-cell pertussis vaccination was introduced into the UK routine childhood immunisation schedule in the 1950s. There was a fall in pertussis vaccine coverage in the 1970s linked to high-profile scares about the safety of the vaccine, followed by a period of recovery in the 1980s.

In order to optimise pertussis control, the current accelerated primary schedule consisting of three primary doses at 2, 3 and 4 months of age replaced the previous three, five and ten month schedule in 1990. In October 2001, an acellular pertussis booster was introduced at 3 years 4 months to 5 years of age, subsequently simplified to between 3 years 4 months and 3 years 6 months (6). Since October 2004, combination vaccines containing acellular pertussis have replaced those containing whole-cell pertussis in the routine primary schedule. In addition to being less reactogenic than those containing whole cell pertussis (7–10), these diphtheria/tetanus/acellular pertussis/inactivated polio/*Haemophilus influenzae* type b (DTaP/IPV/Hib) vaccines use an inactivated polio vaccine that removes the risk of vaccine-associated paralytic poliomyelitis associated with live oral polio vaccine (11). In

July 2016, two DTaP/IPV/Hib vaccines were available for the routine primary infant schedule in England, Pediacel® (a 5 component acellular pertussis containing vaccine) and Infanrix-IPV-Hib® (a 3 component acellular pertussis containing vaccine). From autumn 2017, all babies born on or after 1 August 2017 have been eligible for a hexavalent vaccine which additionally includes hepatitis B (HepB) for their primary immunisations. This vaccine, called Infanrix hexa® (DTaP/IPV/Hib/HepB), replaces the pentavalent infant vaccines Infanrix®-IPV-Hib and Pediacel®.

Since 1991, when the accelerated schedule at 2, 3 and 4 months of age was introduced, coverage in England of three primary doses of pertussis-containing vaccine has remained above 90% by second birthday, and since 2009/10, coverage has exceeded 95% (12). High vaccination coverage led to a marked reduction in notifications of pertussis in England and Wales, although the typical 3-4 yearly cyclical pattern continues to occur with 2008 and 2012 reported as the most recent peak years (13).

In England, the burden of disease in children under 1 year has fallen since the introduction of the accelerated schedule and concomitant period of sustained high coverage. However, the highest rates of disease occur in infants less than 3 months of age (laboratory confirmed pertussis: 77 per 100,000 population in 2015 [provisional data]) who account for the highest proportion of all hospitalised cases (14). Since 2006, rates of pertussis in older children and adolescents have also increased with a marked rise among 10 to 14 year olds. Since 2004 for those 15 years and over, initial increases before the rise associated with the 2012 outbreak (see below) were likely to be largely due to improved ascertainment in these older age groups, particularly with the introduction of serology testing in 2001 (14).

Following a national increase in the numbers of laboratory confirmed cases in adolescents and adults starting from the second quarter of 2011, a national outbreak was declared in April 2012. In response to a marked increase in infant disease and deaths, the Department of Health announced the introduction of a temporary immunisation programme for pregnant women, initially ideally between 28-32 weeks of pregnancy (but can be given up to 38 weeks) from 1 October 2012 (15). In April 2016, the recommendation for optimal time of vaccination of pregnant women was revised to around 20 weeks gestation (anytime from week 16 weeks following the detailed ultrasound scan routinely carried out at this stage of pregnancy) (16).

The primary purpose of this maternal programme is to boost the maternal pertussis antibodies that are passively transferred from mother to baby to provide passive protection to the baby from birth. PHE figures report that between January 2017 and December 2017 in England 72.3% (range 69.3% to 75.3%) of mothers had been immunised with a pertussis containing vaccine in pregnancy(17). Evaluation of the pertussis vaccination in pregnancy programme in England has demonstrated no safety concerns (18) and high vaccine effectiveness at >90% (19,20). With the continued raised circulation of pertussis and following a review of evidence of safety and

effectiveness, in June 2014 the Joint Committee on Vaccination and Immunisation (JCVI) advised the continuation of the temporary programme for a further five years (21). Further details on the temporary maternal programme are available on the PHE website (22).

1.3 Surveillance of pertussis

Pertussis remains a notifiable disease under the Health Protection Legislation (England) Guidance 2010. Suspected cases should be notified to the local health protection team (HPT). This should be done by telephone as soon as is practicable and in writing within 3 days.

From October 2010, all diagnostic laboratories have been required to report confirmed cases of *B. pertussis* infection to their local HPT (23). Written notification must be provided within 7 days of the agent being identified, or if the case is considered to be urgent, the HPT should be notified by phone promptly.

HPTs are strongly encouraged to report all pertussis related deaths to the Immunisation Service, National Infection Service (NIS) at PHE Colindale in a timely manner, via Gayatri Amirthalingam and pertussis@phe.gov.uk. In addition, HPTs are requested to notify the Immunisation Service, NIS of any suspected/confirmed cases in healthcare workers and clusters in educational or healthcare settings by submitting the reporting form to pertussis@phe.gov.uk (Appendix 2).

Staff at the Immunisation Service, NIS, PHE Colindale follow-up all cases of confirmed pertussis with the GP to obtain further epidemiological and clinical information as well as vaccination status (Appendix 3). The department is also responsible for reporting epidemiological data on pertussis annually to the European Centre for Disease Prevention and Control (ECDC) and to the World Health Organization (WHO) European region.

1.4 Laboratory confirmation of clinically suspected cases

Laboratory confirmation of clinically suspected cases can be made by culture and isolation of the causative organism, *B. pertussis*, detection of its DNA (from nasopharyngeal swabs (NPS)/pernasal swabs (PNS) or nasopharyngeal aspirates (NPA) or throat swabs) or antibody detection performed on serum or oral fluid, which usually only provide a late or retrospective diagnosis. The strengths and limitations of each of the laboratory methods are discussed below.

1.4.1 Culture

Laboratory confirmation is conventionally performed culture and isolation of *B. pertussis* from NPA or NPS/PNS.

Where local laboratory facilities are available, culture should be attempted as isolation of the causative organism is definitive and characterisation of isolates is important for further surveillance of circulating strains. Pure cultures of any putative isolates of *B. pertussis* should be referred to RVPBRU for confirmation, serotyping and further characterisation.

It is important to note that *B. pertussis* is a delicate organism and therefore, processing delays may affect the likelihood of a positive culture. Sensitivity is also highly dependent on specimen quality and is affected by increasing patient age, vaccination status and length of illness. The likelihood of a positive culture also decreases with time after onset, from approximately 60% within 1 week of symptom onset to culture to 10% or less after 4 weeks (24,25). Cultures are unlikely to be positive in adolescents and adults with more than 3 weeks of coughing (26).

It is also more difficult to recover the organism in vaccinated compared with unvaccinated children (27). Given the limitations of culture methods, it is important to emphasise that a negative culture does not exclude pertussis.

1.4.2 Serology

Detection of anti-pertussis toxin (PT) IgG antibody levels in serum taken at least fourteen days after the onset of cough using an enzyme linked immunosorbent-assay (ELISA) can provide confirmatory evidence of recent infection. Serology may be helpful to confirm the diagnosis of pertussis in patients with a cough duration of 21 days or more, when culture and PCR are unlikely to yield positive results. The anti-PT IgG serology test cannot, however, be used to determine immunity as there are currently no agreed correlates of protection.

This charged-for service is offered by RVPBRU, which defines a serologically confirmed case as an anti-PT IgG concentration >70 International Units per millilitre (IU/ml) in the absence of recent vaccination (within the past year) (28). This serological assay is targeted towards older childen and adults. Interpretation of anti-PT IgG levels among infants and younger children may be confounded by the presence of maternal antibodies or recent primary and booster vaccination, or show an atypical response. Data suggests that the confounding period following vaccination may be up to 10 months after the primary vaccination and up to 3 years or more after the preschool booster (29). Therefore, serological testing should only be undertaken where there is a minimum of 1 year from primary or booster dose of pertussis containing vaccine and results should be interpreted with caution.

1.4.3 Genome detection by real-time PCR

PCR has been shown to have improved sensitivity over culture and is a valuable confirmatory test, particularly in young infants. In the PCR assay two regions of the *B. pertussis* genome are targeted, the pertussis toxin S1 promoter region (*ptxA-pr*), and the insertion element IS*481* which is present in multiple copies in *B. pertussis*, but is also present in some other *Bordetella* species ie *B. holmesii* and some, but not all, *B. bronchiseptica* (30,31). The recommended interpretation is as follows:

IS*481*	*ptxP*	Final reported result
+	+	*B. pertussis* DNA detected by PCR
+	-	*Bordetella* spp. DNA detected by PCR*

A result of IS*481* only is likely to be consistent with a low amount of *B. pertussis* in the specimen, however the cross-reactivity of the IS*481* assay may represent the presence of other *Bordetella* species.

PCR is usually more sensitive than culture as the organism does not need to be viable, however, PCR is less likely to be positive in patients with symptom duration of 21 days or more. A PHE pilot comparing the use of nasopharyngeal swab (NPS) and throat swabs in primary care for pertussis PCR found both swab types to be acceptable. While NPS are preferable for PCR testing, throat swabs may be used if NPS are not available, especially in community settings.

Historically, from 2002, the real-time PCR service offered by RVPBRU was restricted to hospitalised cases less than 6 months of age; extended to less than 12 months of age in 2007 (30). Since 2014, regional PHE laboratories offer a pertussis PCR service for patients in all age groups in both hospital and primary care settings. From January 2015, the B*. pertussis* PCR for routine diagnostic use is no longer offered by RVPBRU Colindale, London.

1.4.4 Oral fluid testing

In England and Wales, an enhanced surveillance test for the follow-up of notified cases of pertussis, which had not already been confirmed by other laboratory methods (PCR, culture or serology) was piloted from 2007 to September 2009. The purpose was to determine the number of notifications which could be confirmed by laboratory testing for pertussis toxin IgG antibodies in oral fluid (OF) samples (32). Based on the evaluation of the pilot which suggested a 32% increase in confirmation of cases through OF testing, particularly in children aged 5-9 years (33), a national OF testing service was rolled out by the Bordetella Reference Laboratory from January 2013. OF testing was previously offered to notified cases aged between 5 to <17 years, where duration of cough was >14 days. In order to improve the ability to ascertain

cases in preschool children and monitor the overall impact of the maternal programme, from May 2018, oral fluid testing for notified cases of pertussis has been extended to all children aged 2 to <17 years who have not received a pertussis-containing vaccine in the preceding year.The OF kits are available from HPTs and should be sent out following notification of a suspected case in the target age group. It should be noted that the OF assay is less sensitive than the serological assay. As with the serological assay, OF testing is also potentially confounded by recent vaccination (as described above) and therefore OF testing should only be undertaken a minimum of 1 year after the most recent dose of pertussis containing vaccine and any results should be interpreted accordingly. As very few pertussis cases arise within a year of the preschool booster being administered, extending the youngest age eligible for OF testing to two years of age should exclude few cases from OF testing. OF testing enables better case ascertainment and confirmation in an age group where serology testing is unlikely to be performed.

The OF test offers practical and clinical advantages to confirm suspected cases in pertussis outbreaks but HPTs are required to discuss this with RVPBRU before use in outbreak situations.

1.4.5 PHE Laboratory services for *B. pertussis* diagnosis

Tests are available as follows from PHE laboratories:

1. ***PCR***: For all age groups presenting <21 days after symptom onset, PCR for pertussis is available free of charge from PHE specialist microbiology services (SMS) laboratories in Birmingham, Bristol, Cambridge, Leeds, Manchester, Newcastle and London. PHE SMS laboratories should be contacted directly for details of services provided. *B. pertussis* PCR positive specimens and/or DNA extracts from the PHE SMS laboratories should be forwarded to RVPBRU for further characterisation. PCR positive specimens are also requested from other NHS or commercial providers.
2. ***Serology***: Suitable for older children and adults with more than 14 days history of cough and at least one year after the most recent dose of pertussis vaccine (including any dose administered in pregnancy). The serological service provided by RVPBRU is a charged for test.
3. ***Oral fluid testing***: This service is for notified cases aged 2 to <17 years, with a history of more than 14 days of cough and at least one year after the most recent dose of pertussis vaccine. The test kit is available from PHE HPTs upon notification of suspected cases. Testing is performed by RVPBRU.

A summary of these options is detailed in Table 1.

For the Bordetella reference services provided by the RVPBRU (pertussis serology; submission of *B.pertussis* isolates; submission of PCR positive respiratory specimens), the appropriate request form (currently PHE R3 Vaccine Preventable Bacteria Section)

must be used. The request forms for the OF test (Appendix 4) are supplied with the testing kit. For the investigation of suspected clusters, outbreaks, or incidents of pertussis infection, RVPBRU can be contacted for advice on the most appropriate testing methods.

Table 1: Summary of characteristics of microbiological tests for pertussis

Test method	Patient criteria	Sample	Access	RVPBRU
Culture	Suspected cases in all age groups with cough <21 days duration	NPS/NPA/PNS	NHS laboratories	Confirmed isolates to be sent to RVPBRU
PCR	Suspected cases in all age groups with cough <21 days cough duration	NPS/PNS preferred; throat swab acceptable for community patients	Regional PHE laboratories	Positive samples to be referred to RVPBRU
OF	Suspected cases aged 2 to <17 years with cough >14 days* duration	OF kit	OF kit sent to patient upon notification to PHE HPT	Samples tested and reported by RVPBRU
Serology	Suspected cases in older children/ adults with cough >14 days* duration	Serum	Charged for service at RVPBRU	Samples tested and reported by RVPBRU

* Antibody levels confounded by recent vaccination. Recommended for those who have not received a dose of pertussis vaccine in the preceding year

1.5 Rationale for public health action

Outbreaks of pertussis can occur in households and in institutional settings. If outbreaks are detected at an early stage, prompt action including chemoprophylaxis and vaccination of close contacts can limit the spread (34,35) and may also be of benefit in reducing transmission to those who are most at risk of severe or complicated infection such as infants and young children. Therefore this is recommended in settings where there is a vulnerable person or an individual who may facilitate ongoing transmission to vulnerable groups. As such, a list of priority groups for public health action has been defined. This has been updated from earlier guidance and is based upon identifying groups who are either:

Group 1. At increased risk of severe or complicated pertussis (‘vulnerable’)
Group 2. At increased risk of transmitting infection to individuals in group 1 (see below)

Appendix 1 details the flow of appropriate public health actions.

Cases of parapertussis do not require public health action.

Group 1:

Groups at increased risk of severe or complicated pertussis (‘vulnerable’)

Young, unimmunised infants (particularly those prematurely born, under three months of age, or born to unimmunised mothers) (36) are at greatest risk of severe complications, hospitalisation and death following *B. pertussis* infection. Partially immunised infants are not fully protected, although disease severity may be reduced. In a study of 201 hospitalised infants (<6 months of age), the median duration of hospitalisation was significantly shorter (4 versus 11 days; p=0.03) for those who had received at least 1 dose of vaccine previously, when compared with those who were unimmunised (37).

Serious complications such as pneumonia, syncope and rib fracture can occur in older individuals but there is little evidence to suggest that any specific clinical groups are at increased risk of pertussis or its complications (38–40). Pregnant women are not considered at increased risk of severe disease compared with non-pregnant women. The relative immunosuppression of pregnant women to viral disease in the third trimester does not appear to be replicated with bacterial infections such as *B. pertussis* (41), although symptoms in late pregnancy may be more intense due to constraints on pulmonary function.

Current evidence suggests that immunocompromised individuals are not at higher risk of complications from pertussis (42). Those with underlying immunosuppression may be less likely to mount a sufficient immune response to vaccination (43) but there is little evidence of increased severity of illness (single case reports only) (44–46). A number of case studies have also described prolonged illness in patients with HIV infection (47–49) but pertussis infection among HIV infected individuals is again not thought to be particularly common (50). It might be expected that some underlying long-term conditions, such as asthma, congestive heart failure or chronic obstructive pulmonary disease, would exacerbate illness following pertussis infection, but there is little evidence to support this (51–53).

Given the lack of evidence to support an increased risk of severe pertussis infection among individuals with long-term disease or those who are immunosuppressed, the list of ‘vulnerable’ individuals at increased risk of severe or complicated disease has been updated.

In light of the high effectiveness of the maternal pertussis vaccine programme in preventing disease for those infants less than 2 months of age, the definition for those vulnerable infants has been amended as follows:

- unimmunised infants (born ≤32 weeks) less than 2 months of age regardless of maternal vaccine status OR
- unimmunised infants (born >32 weeks) less than 2 months of age whose mothers did not receive maternal pertussis vaccine after 16 weeks and at least 2 weeks before delivery OR
- infants aged 2 months or over who are unimmunised or partially immunised (less than three doses of DTaP/IPV/Hib/HepB up to 1 year of age) regardless of maternal vaccine status

Group 2:

Groups at increased risk of transmitting pertussis to those at risk of severe or complicated infection

a. Pregnant women

Parents and particularly mothers are found to be a frequent and important source of pertussis infection amongst young infants (54–58). In a US study of infants with reported pertussis, over 70% had been infected by their mother or another family member, the majority of whom were aged 20 years or more (59). A further study of infants admitted to a UK paediatric intensive care unit with respiratory complications, demonstrated that 20% had laboratory evidence of pertussis and half of these were infected from an adult family member (60). More recent data from the current national outbreak in England identified mothers as the source of infection in 38% of confirmed infant cases during 2012, where a source was known (unpublished data). Women in the later stages of pregnancy may be at particular risk of transmitting pertussis to newborn infants. Although pertussis in pregnant women is not thought to be more severe than in other adults, and no obstetric or foetal adverse outcomes have been described (50), mother to infant transmission at the time of, or shortly after, birth has been described (61,62) and is often associated with severe neonatal illness (63–65). In a Dutch study of 201 infants hospitalised with pertussis 46 (23%) of the index cases were mothers, of whom 14 (22%) had onset of symptoms during pregnancy (37).

Given the increased risk of ongoing transmission to newborn infants, women in the later stages of pregnancy are considered to be a priority group for public health action and post-exposure prophylaxis. Previous guidance recommended post exposure prophylaxis to any woman exposed in the last month of pregnancy. However, to allow for preterm delivery, the delay between exposure and outcome, and the protection conferred to the infant from maternal vaccination, this has been revised to be any

pregnant woman exposed >32 weeks gestation who has not received a maternal pertussis vaccine at least one week prior to exposure (66).

b. Healthcare workers

In addition to parents, other adults in close contact with vulnerable young infants including healthcare workers may be responsible for transmission (67). Serological studies suggest that infection in healthcare workers can be frequent, but often unrecognised (68). Outbreaks in healthcare settings may be prolonged due to waning immunity in adults, with multiple opportunities for secondary and tertiary transmission. As such, specific guidance for the public health management of pertussis incidents in healthcare settings is also available (69). Likely transmission from healthcare worker to patient and vice versa has frequently been described (70–73) although the greatest risk of nosocomial transmission is likely to be from a healthcare worker to a patient or other member of staff. A five year analysis of clusters of pertussis infection in France revealed that the most frequent reports of healthcare associated clusters were from paediatric, maternity and neonatal units (74).

Due to the risk of ongoing transmission to individuals vulnerable to severe or complicated pertussis, healthcare staff and any other individuals working with infants or pregnant women are therefore considered a priority group for public health action in these guidelines.

1.6 Use of antibiotics in the treatment and prevention of pertussis

UK guidelines published in 2002 recommend chemoprophylaxis with erythromycin in households with vulnerable contacts within 21 days from the onset of disease (34). Prior to the widespread use of newer macrolides, erythromycin was recommended as the drug of choice for the prophylaxis and treatment of pertussis, except for infants below one month. Erythromycin has a limited effect in improving the clinical course of the illness especially if administered beyond 2-3 weeks after the onset of symptoms. Treatment is therefore primarily aimed at eradicating *B. pertussis* from cases and preventing secondary transmission. However, studies investigating the use of antibiotics for preventing onward transmission have only demonstrated efficacy if treatment is given within 7-14 days of onset of illness (75–77). Erythromycin is poorly tolerated, causing gastrointestinal side-effects in up to 30% of patients (78,79) which may lead to non-compliance with therapy (34). A 1998 UK review of the use of erythromycin in the management of persons exposed to pertussis reported little effect in preventing secondary transmission, which was limited to close prolonged household type contact. Effects of erythromycin were modest, short term and associated with gastrointestinal side-effect (34).

As a result, the use of chemoprophylaxis in the UK has been limited to households with vulnerable contacts where the risk of severe complications and/or ongoing transmission is high (2). This compares with the US approach of recommending more widespread use of chemoprophylaxis to all household contacts and other close contacts regardless of age and immunisation status (80).

1.6.1 Treatment of suspected cases

In a 2007 Cochrane systematic review of antibiotics for pertussis, the authors concluded that although antibiotic therapy for cases was effective in eliminating *B. pertussis*, it did not alter the subsequent clinical course of the illness (87). Short-term antibiotics (azithromycin for 3-5 days; clarithromycin or erythromycin for 7 days) were as effective as long term (erythromycin for 10-14 days) in eradicating *B. pertussis* from the nasopharynx (RR 1.02, 95% CI 0.98, 1.05) but had fewer side-effects (RR 0.66, 95% CI 0.52, 0.83). Since publication of the Cochrane review, more recent studies have demonstrated that early treatment of cases (within 7-14 days of onset) can prevent onward transmission (75–77).

Newer macrolides such as azithromycin and clarithromycin are now the preferred choice for the treatment and prophylaxis of pertussis, with clarithromycin being the preferred antibiotic for use in neonates. Both antibiotics offer the advantages of improved absorption, a longer half-life, good in vitro activity against *B. pertussis* and a better side-effect profile (66). In addition, these agents involve less frequent dosing and shorter duration of therapy. A number of studies have established the safety and efficacy of newer macrolides for eradicating *B. pertussis* (81,82). The improved side-effect profile has also been shown to improve compliance with treatment (83). Prior to 1994, erythromycin resistance in *B. pertussis* was not observed, however since then resistance has been reported in the US and Taiwan and recently in France (84). From 2001 to 2009, UK *B. pertussis* isolates were tested against three agents, erythromycin, clarithromycin and azithromycin and all isolates (n=583) were found to be fully susceptible to all three agents tested (85).

For those patients where a macrolide is contra-indicated or is not tolerated, co-trimoxazole is effective in eradicating *B. pertussis* from the nasopharynx and can serve as an alternative agent, although it is unlicensed for chemoprophylaxis (86–88).

1.6.2 Prophylaxis for close contacts

The Cochrane review concluded that there was insufficient evidence to determine the benefit of prophylactic treatment of pertussis contacts (87). In the two trials included in the review, which investigated the effectiveness of chemoprophylaxis with erythromycin, clinical symptoms in the treatment group were slightly less severe (not statistically significant) than the placebo group (79,89). The number of contacts that became culture-positive were less in the erythromycin group (3/142, 2.1%) compared to

placebo (8/158, 5.1%) but this difference was not statistically significant (RR 0.42; 95% CI 0.11, 1.54) (79). Although there have been no specific studies of prevention of secondary transmission using these newer macrolides, their biological effect is considered to be similar to erythromycin.

In summary, post-exposure chemoprophylaxis for contacts over 6 months of age did not significantly improve clinical symptoms or the number of cases developing culture positive *B. pertussis*, although timing of prophylaxis was thought to be a critical factor. Whilst early administration may improve the efficacy of chemoprophylaxis in preventing secondary transmission, this requires a clinical diagnosis, which is likely to be a challenge given that adolescents and adults who are often the source of infection, generally do not seek timely health advice.

1.6.3 Use of antibiotics in pregnant women

The primary purpose for treating cases with antibiotics is to eradicate *B. pertussis* from the nasopharynx and prevent secondary transmission. Antibiotics are unlikely to have any clinical benefit unless administered in the early stages of the illness. Although there is no evidence of harm, avoidance of all drugs in the first trimester of pregnancy is generally advised (90). Erythromycin may be offered to treat women early in pregnancy but this is only likely to be of any clinical benefit if it can be administered in the early stages of the illness. For women diagnosed with pertussis in the last month of pregnancy, erythromycin is recommended to prevent transmission to her infant. Potential concerns regarding an association between maternal erythromycin therapy (in late pregnancy) and infant hypertrophic pyloric stenosis have largely been refuted (91–93). Therefore, while these guidelines recommend the use of erythromycin to treat cases in the last month of pregnancy, its use in earlier stages of pregnancy should be a clinical decision based on the likely clinical benefit for the woman and the presence of any vulnerable close contacts.

Antibiotics are also recommended for women exposed during pregnancy. In these circumstances, chemoprophylaxis is only recommended for women exposed after 32 weeks of pregnancy, who have not received a pertussis containing vaccine more than one week and less than five years prior (see section 1.7.1). Since the introduction of the temporary maternal vaccination programme in England, coverage has been consistently above 50%, peaking at over 60% in December 2014. Therefore many pregnant women exposed after 32 weeks are likely to have received the vaccine and therefore will not require chemoprophylaxis. Given that it takes at least one week to develop an antibody response from a pertussis booster dose in adults, pregnant contacts (32+ weeks gestation) who have received a pertussis containing vaccine within the past one week will still require chemoprophylaxis.

1.7 Post-exposure vaccination

1.7.1 History of pertussis vaccination

In the UK, use of pertussis-containing vaccines at the time of exposure has been recommended for unvaccinated or partially immunised contacts up to 10 years of age to provide long term protection (16). More recently, a number of studies have demonstrated the safety and immunogenicity of a combined tetanus/low dose diphtheria vaccine/low dose acellular pertussis (Tdap) vaccine in adolescents and adults (94–96). Two licensed low dose acellular pertussis containing vaccines (Repevax® and Boostrix®-IPV) are suitable for boosting in adolescents and adults in the UK. However, due to current supply shortages of Repevax® and Boostrix®-IPV vaccines, post exposure vaccination may not be feasible where large numbers of contacts are involved and it would be important to check that stocks are available before considering vaccination in these circumstances.

Although duration of immunity following initial acellular pertussis vaccination has not been clearly established, a recent review based on limited studies suggested duration of protection for 5-6 years (97). Persistence of immunity for 6-9 years after a booster administered in the second year of life was reported for children receiving a 3-component acellular pertussis vaccine (98).

In October 2001, a booster dose of an acellular pertussis-containing vaccine was introduced into the UK routine schedule for children aged between 3 years 4 months and 5 years. Children born before November 1996 would have been eligible for only 3 primary doses of (whole cell) pertussis-containing vaccine during infancy. In these individuals in particular, protection is likely to have waned (99). Therefore, in the event of exposure, contacts over 10 years (many of whom would only have been eligible to receive a 3-dose primary course), whether they be unvaccinated, partially or fully immunised, are likely to benefit from a dose of pertussis-containing vaccine, especially given their role in transmission.

To determine the potential value of vaccination as part of an outbreak control strategy in adults, the immediate immune response to vaccination in adult healthcare workers at the time of exposure has been investigated (35). Of the 106 healthcare staff immunised during a 2006 US outbreak, Tdap antibody responses were noticeable at one week following vaccination with more than 50% of subjects showing a response to filamentous haemagglutinin, pertactin and fimbriae and 46% showing a booster response to pertussis toxoid (35). By two weeks between 88% and 94% showed a booster response, depending on the specific pertussis antigen. Vaccine effectiveness could not be determined in this study because there was no unvaccinated control population (100). However, the data suggest early Tdap vaccination may be valuable in

preventing illness and transmission among adults in outbreak settings, reducing susceptibility of the population within 1-2 weeks.

One concern regarding the use of pertussis-containing vaccines in children over ten years is increased rates of severe local reactions, including Arthus-type reactions, if Tdap (Tetanus, diphtheria and pertussis) containing vaccine is administered too soon after a previous Td-IPV vaccine in older children and adults, either as part of the adolescent booster (which is offered to all 14 year olds in the UK), as a booster prior to travel or as part of the post exposure management for diphtheria or tetanus (101,102). In pre-licensure clinical trials of Tdap in adolescents, those who had received doses of a diphtheria or tetanus toxoid-containing vaccine during the preceding 5 or 10 years were excluded (103). However, a Canadian study, which investigated the safety of administering a dose of Tdap at intervals less than five years after paediatric DTaP or Td concluded that Tdap can be safely administered at intervals of more than 18 months since a previous Td vaccine (104). Two smaller Canadian post-licensure safety studies in adolescents have also shown acceptable safety when Tdap is administered at intervals less than five years (105,106). Based on these findings, Canada's National Advisory Committee on Immunization (NACI) concluded that there is no evidence of increased risk of severe adverse events for Canadian adolescents after receiving diphtheria and tetanus toxoid-containing vaccines at intervals of less than five years (106). In 2006, the US Advisory Committee on Immunization Practices (ACIP) recommended that adolescents who had received Td booster vaccine should receive Tdap for added protection, preferably with a five year interval to reduce the risk of local and systemic reactions, although an interval of less than 5 years may be used (104).

More recently, the authors of a randomised, double-blind study in France, which assessed the safety of Tdap-IPV administered one month after vaccination with Td-IPV in 500 healthy adults, concluded that Tdap-IPV may be administered to adults as little as one month after Td-IPV without significantly increasing the frequency or severity of side-effects relative to considerably longer vaccination intervals (107).

1.7.2 Current pertussis vaccination recommendations

Based on the currently available evidence, these PHE guidelines recommend extending the offer of post-exposure vaccination with pertussis containing vaccine beyond unimmunised or partially immunised contacts below 10 years of age. In households where there is a clinically suspected or confirmed case of pertussis and a close contact in a priority group (as defined in section 2.6) pertussis containing vaccine should also be offered to all household contacts over 10 years of age, who have not received a dose of pertussis containing vaccine in the last five years and no Td-IPV vaccine in the preceding month (see section 2.6.3).

The duration of immunity following immunisation with pertussis-containing vaccines is not fully established (97,98) but the relatively high incidence of laboratory-confirmed

pertussis in the 10-14 year age group during re-emergence of the disease in 2012 suggests that protection from the booster lasts less than 10 years (108). As such, the period for which previous doses of pertussis containing vaccine should be considered has been revised from 10 years to 5 years. No upper limit of age for adult vaccination is specified in the summary of product characteristics (SPC) for Repevax® or Boostrix®-IPV (94) and the limit of 64 years for booster vaccination referred to in the previous pertussis guidance (1) has also been removed.

1.7.3 Use of vaccination in pregnant women

Post-exposure vaccination in pregnancy is important and specifically recommended in the following individuals who have not received a pertussis containing vaccine in the previous 5 years.:

- for women exposed to pertussis after 32 weeks, ***OR***
- for women exposed to pertussis at any stage of pregnancy if they are at risk of transmitting to 'vulnerable' individuals in 'Group 1' eg a healthcare worker

It is important that all pregnant women from 16 weeks gestation onwards have been vaccinated or scheduled for vaccination in line with the maternal programme.

Although many pregnant women in the UK may not have been eligible for the pre-school booster, some may have received adult or adolescent booster doses overseas. In addition, the recent introduction of a temporary programme to offer pertussis containing vaccine to all pregnant women in the UK (109) means that women who have been vaccinated routinely after 16 weeks gestation in their current pregnancy will not require post-exposure vaccination if exposed later in that pregnancy. Post-exposure chemoprophylaxis in pregnant women is not recommended when pertussis vaccination has been administered at least one week earlier in that pregnancy.

In addition to the temporary programme to vaccinate pregnant women in the UK (15), updated recommendations by the ACIP in the US in 2012 (110) recommend that pregnant women receive a Tdap vaccine regardless of their previous vaccine history, in every pregnancy, ideally between 27 and 36 weeks. Ireland, Argentina, Israel and some parts of New Zealand and Australia also recommend the use of pertussis-containing vaccine during pregnancy (111–115).

Although pregnant women themselves are not thought to be at any greater risk of severe or complicated infection (80), the rationale for vaccination during pregnancy is to provide direct passive protection to vulnerable newborn infants through transplacental transfer of antibody. Studies of antibody response suggest that a maximum response to pertussis containing vaccines is not achieved until 14 days after vaccination, and as such, post-partum vaccination may not provide timely protection for newborn infants during the most vulnerable period (116).

All subclasses of IgG are transferred from mother to infant across the placenta, primarily during the third trimester of pregnancy (117). Data from the pre-vaccine era suggest that maternal antibodies may provide at least short-term protection, for newborn infants, the proportion of deaths being lower in children less than one month of age when compared with those aged 1-3 months (118). Transplacental transfer of pertussis IgG antibody has been demonstrated with concentrations in the newborn (119,120) or cord serum samples (121–123) reflecting those in the mother. Indeed, higher concentrations of pertussis antibodies have been demonstrated in cord blood for newborn infants of vaccinated when compared with unvaccinated mothers (41,123). These are said to have a half-life of approximately six weeks and so if boosted to sufficiently high levels are likely to provide time-limited, passive protection for newborn infants prior to administration of the first childhood pertussis-containing immunisation at age eight weeks (119,124). Evaluation of the maternal vaccination programme in England has demonstrated a more than 90% reduction in the risk of disease in infants up to 3 months of age when the mothers were vaccinated more than one week prior to delivery compared to infants of unvaccinated mothers, though the reduction between 2 to 3 months attributable to vaccination was unclear (19,20).

The main rationale for offering post exposure vaccination to pregnant women is different to the main rationale for offering vaccination routinely to all pregnant women. In the post-exposure situation the vaccine is given to reduce the risk of the infant (prior to their own routine pertussis immunisation) getting exposed to maternal pertussis infection, hence vaccination being given to those exposed late enough in pregnancy (>32 weeks). The current temporary programme to vaccinate all pregnant women (from week 16 of pregnancy) will be continued until at least 2019 when the programme will be reviewed by the JCVI.

If a woman has had confirmed or suspected whooping cough during pregnancy, she should still be offered the pertussis vaccine as not all women may make sufficiently high levels of antibodies following natural infection to ensure high levels can be passed across the placenta to the infant. As high levels of antibodies are made following vaccination, offering vaccine from 16 weeks of pregnancy should ensure that optimal antibody levels can be passed to her baby.

Appendix 5 details the strength of evidence for the various chemoprophylaxis and vaccination strategies, which are highlighted in Appendix 1.

Part 2: **Case definitions, management and investigation of suspected cases of pertussis and their close contacts**

2.1 Case definition

Suspected case of pertussis:

- any person in whom a clinician suspects pertussis infection **or**
- any person with an acute cough lasting for 14 days or more, without an apparent cause plus one or more of the following:
  - paroxysms of coughing
  - post-tussive vomiting
  - inspiratory whoop

AND

- absence of laboratory confirmation
- no epidemiological link to a laboratory confirmed case

Confirmed case of pertussis:

- Any person with signs and symptoms consistent with pertussis with:-
  - *B. pertussis* isolated from a respiratory sample (typically an NPA or NPS/PNS (or throat swab) **or**
  - anti-pertussis toxin IgG titre >70 IU/ml from a serum or >70 aU from an OF specimen (19) (in the absence of vaccination within the past year[a]) **or**
  - *B. pertussis* PCR positive in a respiratory clinical specimen

Epidemiologically linked case of pertussis:

- a suspected case with signs and symptoms consistent with pertussis, but no laboratory confirmation, who was in contact with a laboratory confirmed case of pertussis in the 21 days before the onset of symptoms

[a] This is currently under review and will be modified as more data is available

2.2 Recommended details to be recorded when a case is reported

Caller details:

- name, address, designation and contact number

Demographic details:

- name, date of birth, sex, ethnicity, NHS number
- address including postcode
- contact details including phone number
- occupation (if applicable)
- place of work/education (if applicable)
- GP name and contact details (including address and phone number)

Clinical/epidemiological details:

- clinical information – onset dates, cough (including duration), presence of inspiratory whoop/apnoea/post-tussive vomiting, complications, treatment
- need for admission to hospital (including dates where relevant)
- pertussis immunisation history* (including dates)
- pregnancy status
- contact with confirmed or suspected case
- any close contacts within a priority group including:
  - healthcare workers in high-risk settings
  - unimmunised infants born after 32 weeks but less than 2 months of age whose mother did not receive pertussis vaccine after 16 weeks and at least 2 weeks prior to delivery
  - unimmunised infants born ≤32 weeks and less than 2 months of age regardless of maternal vaccine status
  - unimmunised or partially immunised aged 2 months and over regardless of maternal vaccine status
  - pregnant women >32 weeks and have not received pertussis vaccine at least a week prior to exposure
- context: household, school, healthcare setting (including name)

* including pertussis vaccines administered to mother during pregnancy for cases born after 30 September 2012

2.3 Risk assessment for the index case

The positive predictive value (PPV) of a clinical diagnosis of pertussis is not very high, particularly among adolescents and adults who may present with atypical features. However, the PPV will increase during periods of heightened pertussis activity and will vary with age. Risk assessment should be based on a combination of clinical and epidemiological factors such as clinical presentation, vaccination history and epidemiological links. Management of the index case and any vulnerable contacts should proceed based on this risk assessment without waiting for the results of laboratory testing and prompt public health actions to prevent onward transmission should be considered.

2.4 Laboratory confirmation and public health action

Appropriate public health action should not wait for laboratory results as negative results cannot be used to exclude pertussis infection. In the event of an outbreak, the local HPT and the testing laboratory should be informed in order that testing can be appropriately prioritised.

Please contact RVPBRU on 0208 327 7327 and discuss with senior staff prior to sending serological specimens for priority testing. Please note, these services are not available outside of regular working hours at PHE Colindale, see *user manual* for details.

2.4.1 Recommendations for testing

Infants and children under the age of two years:

- **PCR** testing is recommended for infants and children with suspected pertussis in the early stages of the illness and <21 days post cough onset
- if local laboratory facilities permit, **culture** should also be performed. Please ask local laboratory for any putative *B. pertussis* isolates (pure cultures) to be sent to RVPBRU for confirmation
- in those who present late, **serology** can be undertaken (>14 days post cough onset) but is not usually recommended for infants under 12 months as the antibody response of infants may not be typical of that seen in older children and adults. Serology is not recommended in children who have received a pertussis containing vaccine in the previous year as the results may be confounded by recent vaccination and therefore is unlikely to be useful in children under the age of two years. Liaise with local NHS or regional PHE microbiologist, HPT staff, or RVPBRU for further advice.

Children aged from two years of age and adults:

- **PCR** is recommended in the early stages of illness (<21 days post cough onset) and within 48 hours of antibiotic therapy
- if local laboratory facilities permit, **culture** should also be performed. Please ask local laboratory for any putative *B. pertussis* isolates (pure cultures) to be sent to RVPBRU for confirmation
- **for children aged 2 to <17 years**, **OF** or **serology** is recommended for notified cases where the onset of cough is greater than 14 days **AND** who have not been immunised against pertussis in the previous year
- **for children aged 17 or older and adults**, **serology** is recommended where the onset of cough is greater than 14 days **AND** who have not been immunised against pertussis in the previous year.

2.4.2 Swab types and sampling for culture and PCR

The posterior nasopharynx should be sampled using a NPS/PNS [typically flexible ultrafine twisted wire shaft with nylon/Rayon swab]. The Copan style swab is also acceptable; or an NPA.

For hospitalised cases NPS/PNS/NPA are the recommended specimens.
For primary care cases if NPS/PNS are not available, throat swabs may be used (please check with regional laboratory for exact requirements for acceptable swab types). A template for informing primary care about testing (See Appendix 6)

2.5 Case management

2.5.1 Exclusion

Children with suspected, epidemiologically linked or confirmed pertussis should be excluded from schools or nurseries for 48 hours following commencement of recommended antibiotic therapy or for 21 days from onset of symptoms (in those who are not treated with appropriate antibiotics) (125). Cases (suspected, epidemiologically linked or confirmed) amongst staff working in nursery and school setting should also be excluded for 48 hours following commencement of recommended antibiotic therapy (or for 21 days from onset of symptoms if not treated) if they report active uncontrollable coughing. For other cases, consideration should be given to reallocate their work for 48 hours from commencement of appropriate antibiotic therapy to reduce the risk of ongoing transmission if they report active coughing where potential exposure cannot be minimised by adherence to good respiratory hygiene.

If the case is a healthcare worker, or patient in a healthcare setting, see PHE Guidelines for management of pertussis incidents in healthcare settings (69) for further details. For cases working in other settings, contact with ‘vulnerable’ individuals (as defined in section 1.6) should be avoided for 48 hours from commencing appropriate/recommended antibiotic therapy or for 21 days from onset of symptoms (in those who are not treated).

2.5.2 Antibiotic therapy

The decision to offer antibiotics and the choice of treatment is a clinical decision. Ideally antibiotics should be administered as soon as possible after onset of illness in order to eradicate the organism and limit ongoing transmission. The effect of treatment on reducing symptoms, however, is limited or lacking especially when given late during the disease. For suspected, epidemiologically linked or confirmed cases, recommended antibiotic regimens are summarised in Table 2. Antibiotics are not recommended or thought to be beneficial after three weeks of symptoms.

Clarithromycin is the preferred agent for use in infants below 1 month of age. Azithromycin may be used although there are limited data in this age group. Azithromycin and clarithromycin are the preferred antibiotics in children over 1 year and adults given the adverse effects associated with erythromycin. For individuals in whom macrolides are contra-indicated or not tolerated, co-trimoxazole may be used although this is not licensed in infants below 6 weeks of age.

Erythromycin is the preferred antibiotic for treating women in the last month of pregnancy to prevent ongoing transmission to their infant. While erythromycin can be administered for treatment earlier in pregnancy, this needs to be a clinical decision based on the likely clinical benefit for the woman. Use of erythromycin before the last

month of pregnancy would only be of value for treatment if administered early in the course of the illness. Although any potential concern regarding the use of erythromycin in pregnancy has been largely refuted, avoidance of all drugs in the first trimester is generally advised.

2.5.2 Immunisation

It is important that unvaccinated and partially immunised cases up to 10 years of age complete their course of primary immunisation and booster vaccine once they have recovered from their acute illness, following the PHE guidance document 'Vaccination of individuals with uncertain or incomplete immunisation status'.

Pregnant women who have been diagnosed with pertussis (at any stage of pregnancy) and have not been vaccinated after 16 weeks of pregnancy, should be offered a dose of pertussis containing vaccine in line with national recommendations. Pregnant women diagnosed with pertussis before 16 weeks gestation should wait until they reach 16 weeks of pregnancy (and ideally following the detailed ultrasound scan) to have the vaccine.

Table 2: Recommended antibiotic treatment and post exposure prophylaxis by age group[b]

Age group	Clarithromycin*	Azithromycin*	Erythromycin	Co-trimoxazole*[c]
Neonates (<1 month)	Preferred in neonates 7.5mg/kg twice a day for 7 days	10mg/kg once a day for 3 days	Not recommended due to association with hypertrophic pyloric stenosis	Not licensed for infants below 6 weeks
Infants (1 month – 12 months) **&** **Children (>12 months)**	**1 month to 11 years**: **Under 8kgs** 7.5mg/kg twice a day for 7 days **8-11kg** 62.5mg twice a day for 7 days **12-19kg** 125mg twice a day for 7 days **20-29kg** 187.5mg twice a day for 7 days **30-40kg** 250mg twice a day for 7 days **12 to 17 years**: 500mg twice a day for 7 days	**1 to 6 months**: 10mg/kg once a day for 3 days **> 6 months**: 10mg/kg (max 500mg) once a day for 3 days	**1 to 23 months**: 125mg every 6 hours for 7 days≠ **2 to 7 years**: 250mg every 6 hours for 7 days≠ **8 to 17 years**: 500mg every 6 hours for 7 days≠	**6 weeks to 5 months**: 120mg twice a day for 7 days **6 months to 5 years:** 240mg twice a day for 7 days **6 to 11 years**: 480mg twice a day for 7 days **12 to 17 years**: 960mg twice a day for 7 days
Adults	500mg twice a day for 7 days	500mg once a day for 3 days	500mg every 6 hours for 7 days≠	960mg twice a day for 7 days
Pregnant women[d]	Not recommended	Not recommended	Preferred antibiotic - not known to be harmful	**Contraindicated in pregnancy**

≠ Doses can be doubled in severe infections

*** Please note that the doses for treatment and prophylaxis are the same**

[b] The above information has been taken from BNF 75 (March 2018) and BNF for Children 2017-18. The recommendation to use azithromycin for infants less than six months of age is based on advice from experts on the Pertussis Guidelines Group and CDC Guidelines. Azithromycin and co-trimoxazole doses are extrapolated from treatment of respiratory tract infections.

[c] Consider if macrolides contra-indicated or not tolerated.

[d] For pregnant contacts, a risk assessment would need to be done to looks at the risk and benefits of antibiotic therapy/prophylaxis. The aim of treating/prophylaxing women in pregnancy is to prevent transmission to the newborn infant, and should be considered in those who have not received a pertussis containing vaccine more than one week and less than five years prior. Where possible, pregnant women should begin treatment at least three days prior to delivery.

2.6 Contact management

Management of contacts should proceed for all clinically suspected, epidemiologically linked and laboratory confirmed cases.

Definition of close contacts
Family members or people living in the same household are considered close 'household contacts'. Contacts in institutional settings with an overnight stay in the same room, eg boarding school dormitories, during the infectious period should also be considered close contacts. Other types of contact, eg contact at work or school, would generally not be considered close contact although each situation would need to be assessed on an individual basis where vulnerable contacts are involved. For the definition of a significant exposure in a healthcare setting, please refer to PHE Guidelines for the Public Health Management of Pertussis Incidents in Healthcare Settings (69).

Definition of contacts considered as priority groups for public health action
These include individuals who are themselves at increased risk of complications following pertussis (Group 1) as well as those at risk of transmitting the infection to others at risk of severe disease (Group 2).

Group 1

Individuals at increased risk of severe complications ('vulnerable'):

- unimmunised infants (born after 32 weeks) less than 2 months of age whose mothers did not receive pertussis vaccine after 16 weeks of pregnancy and at least 2 weeks prior to delivery
- unimmunised infants (born $\leq$ 32 weeks) less than 2 months of age regardless of maternal vaccine status
- unimmunised and partially immunised infants (less than 3 doses of vaccine) aged 2 months and above regardless of maternal vaccine status

Contacts of parapertussis do not require public health action.

Group 2

Individuals at increased risk of transmitting to 'vulnerable' individuals in 'group 1' who have not received a pertussis containing vaccine more than 1 week and less than 5 years ago:

a) pregnant women (>32 weeks gestation)
b) healthcare workers working with infants and pregnant women
c) people whose work involves regular, close or prolonged contact with infants too young to be fully vaccinated
d) people who share a household with an infant too young to be fully vaccinated

2.6.1 Exclusion of contacts

Exclusion for asymptomatic contacts is **NOT** required.

2.6.2 Chemoprophylaxis of contacts

Given the limited benefit of chemoprophylaxis, antibiotic prophylaxis should only be offered to close contacts when both of the following conditions apply:

- onset of disease in the index case is within the preceding 21 days **AND**
- there is a close contact in one of the priority groups as defined above

Where both these conditions are met, **ALL** close contacts of a confirmed case (regardless of age and previous immunisation history) should be offered chemoprophylaxis. The dose of antibiotics for use as chemoprophylaxis is the same as for the treatment of cases (see Table 1). Chemoprophylaxis is **NOT** required where there are no close contacts in the priority groups defined in section 2.6, or for healthy contacts. Pregnant women exposed after 32 weeks pregnancy (group 2a) should be offered erythromycin, if they have not received a pertussis containing vaccine within the past five years. For pregnant contacts who have received a pertussis containing vaccine within the past one week, chemoprophylaxis would still be indicated given the delay in antibody response. For individuals who fall into groups 2b, 2c or 2d who happen to be pregnant as well, chemoprophylaxis and vaccine is recommended at any stage of pregnancy. A further dose of pertussis containing vaccine will be required after 16 weeks of pregnancy. For pregnant women with suspected or confirmed pertussis, who are still infectious at delivery (ie within 21 days of onset), the newborn infant should be

offered chemoprophylaxis with clarithromycin or azithromycin regardless of the mother's vaccination status.

2.6.3 Immunisation of contacts

Immunisation should be considered for those who have been offered chemoprophylaxis:

- unimmunised and partially immunised contacts up to the age of 10 years should complete the schedule with the appropriate vaccine
- a booster dose of pertussis containing vaccine is recommended for individuals aged 10 years or older (for pregnant women see Section 1.7.3), who have not received a dose of pertussis-containing vaccine in the last five years and no Td-IPV vaccine in the preceding month.

2.7 Special situations

2.7.1 Outbreaks

Where disease transmission is widespread, the benefit of wider chemoprophylaxis is likely to be of limited value. In the event of a hospital or community outbreak, an outbreak control team should be convened at the earliest opportunity and the local HPT informed. The priority in these circumstances is active case finding and therefore a less specific case definition should be used to ensure no cases are missed. Once laboratory confirmation of pertussis infection has been demonstrated in a cluster (eg school), it is not usually necessary to perform extensive additional testing.

An appropriate hospital incident control team is likely to include:

- director of infection prevention and control
- hospital microbiologist (if different)
- infection control nurse
- consultant/s from relevant clinical specialties
- occupational health physician/nurse
- Screening and Immunisation team representative
- HPT representative
- communications leads (from PHE and acute trust as necessary)

For community outbreaks, include the relevant individuals listed above plus:

- director of public health or their nominated representative
- GPs or GP representative
- NHS England or clinical commissioning group representative
- school nursing service representative for a school outbreak

Where appropriate, relevant lead public health microbiologist, field epidemiologist, RVPBRU and PHE Colindale Immunisation Department representatives should also be included.

Expert advice on outbreak investigation and management is available from Immunisation Services, NIS Colindale, PHE (020 8200 6868/4400) and on laboratory investigation from the Respiratory and Vaccine Preventable Bacteria Reference Unit (0208 327 7327).

2.7.2 Healthcare settings

Healthcare workers can be an important source of pertussis transmission to high-risk patients, particularly infants and pregnant women in the later stages of pregnancy (>32 weeks gestation).

Specific guidance for the public health management of pertussis incidents in healthcare settings (69) is available on the PHE website.

2.7.3 Nursery and school settings

Confirmed and suspected cases should be excluded from nursery or school for 48 hours from commencing appropriate/recommended antibiotic therapy or for 21 days from onset of symptoms (in those who are not treated). Asymptomatic contacts do NOT need to be excluded.

In certain circumstances, wider chemoprophylaxis and vaccination for a school/nursery outbreak may be considered by the outbreak control team and may be informed by a number of factors including:

- duration of the outbreak and thus the likely benefit of chemoprophylaxis and/or vaccination
- presence of a clearly defined group who can be identified for chemoprophylaxis and/or vaccination
- practicality and feasibility of widespread chemoprophylaxis and/or vaccination
- acceptability and compliance with antibiotics
- residential setting eg boarding school, children's respite care homes. Once a single case of pertussis has arisen in a boarding school setting it is highly likely that further cases will arise because of the enhanced opportunities for transmission

Where there has been more than one case reported from an educational institution, other parents should be informed in order to raise awareness including emphasising the groups at risk of severe infection and to encourage timely reporting of further cases to

enhance case finding. Regardless of these control measures, this should be used as an opportunity to remind parents about routine immunisations and ensure children are up to date.

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Pertussis Guidelines Group

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Abbreviations

ACIP	Advisory Committee on Immunization Practices
aU	Arbitrary Units
CDC	Centres for Disease Control & Prevention
DTaP/IPV	Diphtheria/tetanus/acellular pertussis/inactivated polio vaccine
GP	General Practitioner
HPA	Health Protection Agency
HPT	Health Protection Team
ICT	Incident Control Team
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IU	International Units
JCVI	Joint Committee on Vaccination and Immunisation
NHS	National Health Service
NIS	National Infection Service
NPA	Nasopharyngeal aspirate
NPS	Nasopharyngeal swab
OF	Oral fluid
PCR	Polymerase chain reaction
PHE	Public Health England
PNS	Pernasal swab
PT	Pertussis toxin
RVPBRU	Respiratory and Vaccine Preventable Vaccine Bacteria Reference Unit
SMS	Specialist Microbiology Services
SPC	Summary of product characteristics
Td/IPV	Tetanus/low dose diphtheria/inactivated polio vaccine
Tdap	Tetanus, diphtheria and pertussis
UK	United Kingdom
WHO	World Health Organization

References

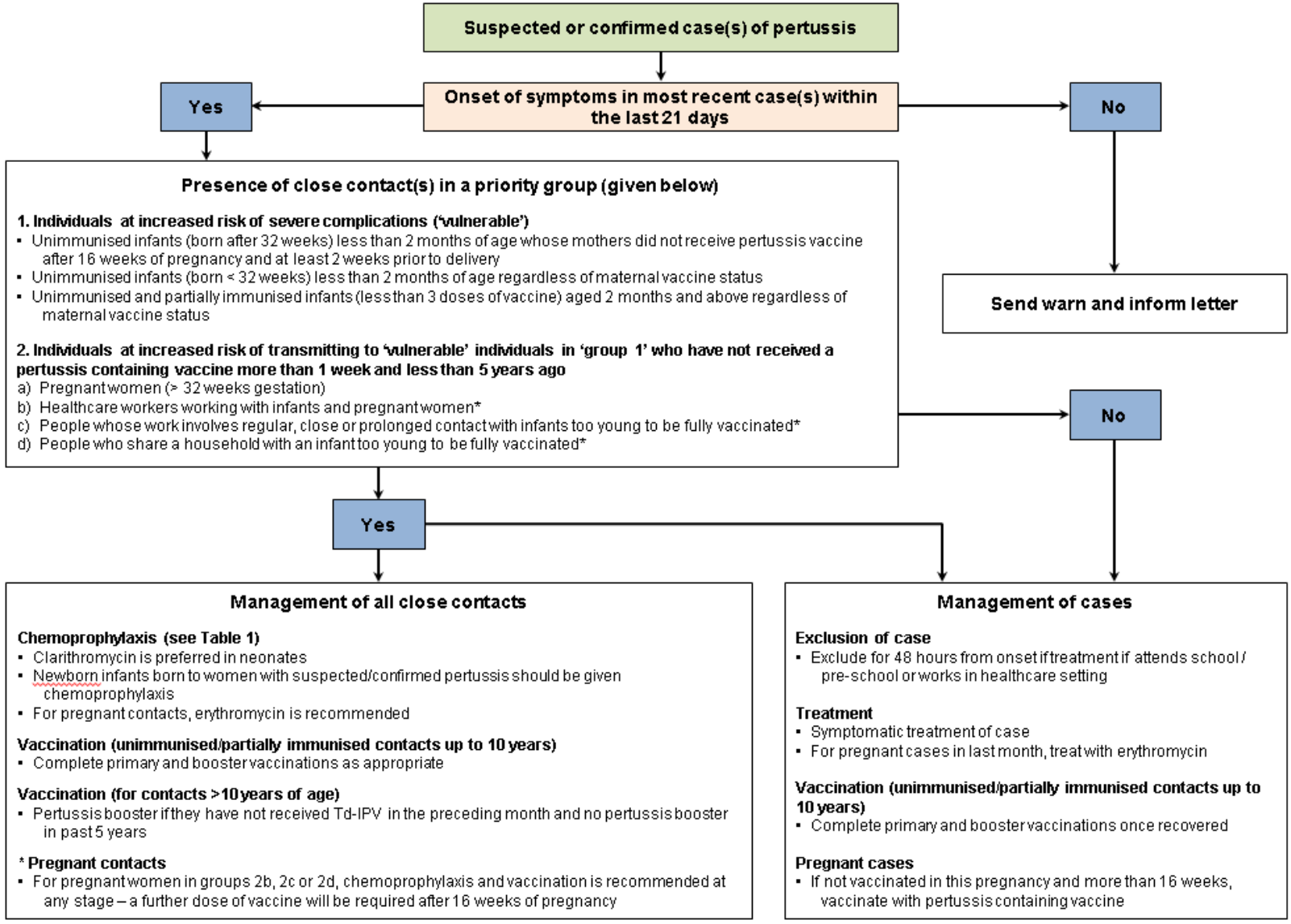
1. Amirthalingam G & The Pertussis Guidelines Group. Guidelines for the Public Health Management of Pertussis. London: HPA, 2011.
2. Dodhia H, Crowcroft NS, Bramley JC, Miller E. UK guidelines for use of erythromycin chemoprophylaxis in persons exposed to pertussis. *J Public Health Med* 2002;24(3):200–6.
3. Hodder SL, Mortimer EA. Epidemiology of pertussis and reactions to pertussis vaccine. *Epidemiol Rev* 1992;14:243–67.
4. Tiwari T, Murphy T V, Moran J. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. *MMWR Recomm Rep* 2005;54(RR-14):1–16.
5. Cherry JD, Tan T, Wirsing von König C-H, Forsyth KD, Thisyakorn U, Greenberg D, et al. Clinical definitions of pertussis: Summary of a Global Pertussis Initiative roundtable meeting, February 2011. Clin Infect Dis 2012 Jun;54(12):1756–64.
6. Donaldson L, Beasley C, Ridge K (Department of Health). Haemophilus Influenzae Type B (HIB) Vaccine for Young Children - Catch-up Programme. London: DH, 2007.
7. Kitchin N, Southern J, Morris R, Hemme F, Cartwright K, Watson M, et al. A randomised controlled study of the reactogenicity of an acellular pertussis-containing pentavalent infant vaccine compared to a quadrivalent whole cell pertussis-containing vaccine and oral poliomyelitis vaccine, when given concurrently with meningococc. *Vaccine* 2006;24(18):3964–70.
8. Olin P, Rasmussen F, Gustafsson L, Hallander HO, Heijbel H. Randomised controlled trial of two-component, three-component, and five-component acellular pertussis vaccines compared with whole-cell pertussis vaccine. Ad Hoc Group for the Study of Pertussis Vaccines. *Lancet* 1997;350(9091):1569–77.
9. Pichichero ME. Acellular pertussis vaccines. Towards an improved safety profile. *Drug Saf* 1996;15(5):311–24.
10. Van Der Meeren O, Kuriyakose S, Kolhe D, Hardt K. Immunogenicity of Infanrix™ hexa administered at 3, 5 and 11 months of age. *Vaccine* 2012;30(17):2710–4.
11. Vaccine-derived polioviruses--update. *Wkly Epidemiol Rec* 2006;81(42):398–404.
12. Screening and Immunisations Team, Health and Social Care Information Centre. NHS Immunisation Statistics England, 2014-15. London: HSCIC, 2015.
13. Amirthalingam G, Gupta S, Campbell H. Pertussis immunisation and control in England and Wales, 1957 to 2012: a historical review. *Euro Surveill* 2013;18(38).
14. Campbell H, Amirthalingam G, Andrews N, Fry NK, George RC, Harrison TG, et al. Accelerating control of pertussis in England and Wales. *Emerg Infect Dis* 2012;18(1):38–47.
15. Department of Health. Whooping Cough Vaccination Programme for Pregnant Women London: DH, 2012.
16. Public Health England. Immunisation against infectious disease, Chapter 24 - “Pertussis”. London: PHE, 2016.
17. Public Health England. Vaccine uptake guidance and the latest coverage data [Internet]. Health Protection Report 12(15), 27 April 2018: https://www.gov.uk/government/publications/pertussis-immunisation-in-pregnancy-vaccine-coverage-estimates-in-england-october-2013-to-march-2014 [cited 27/04/2018].
18. Donegan K, King B, Bryan P. Safety of pertussis vaccination in pregnant women in UK: observational study. *BMJ* 2014;349:g4219.
19. Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, Donegan K, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. *Lancet* 2014;384(9953):1521–8.
20. Dabrera G, Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, et al. A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn infants in England and Wales, 2012-2013. *Clin Infect Dis* 2015;60(3):333–7.
21. Department of Health & Public Health England. Continuation of whooping cough vaccination programme in pregnancy advised [Internet]. London: PHE, 2014. Available from: https://www.gov.uk/government/news/continuation-of-whooping-cough-vaccination-programme-in-pregnancy-advised [cited Juy 12th 2016].
22. Public Health England. Vaccination against pertussis (whooping cough) for pregnant women [Internet]. London: PHE, 2014. Available from: https://www.gov.uk/government/publications/vaccination-against-pertussis-whooping-cough-for-pregnant-women [cited Juy 12th 2016].
23. Department of Health. Health protection legislation guidance 2010. London: PHE, 2010.

24. Sotir MJ, Cappozzo DL, Warshauer DM, Schmidt CE, Monson TA, Berg JL, et al. Evaluation of polymerase chain reaction and culture for diagnosis of pertussis in the control of a county-wide outbreak focused among adolescents and adults. *Clin Infect Dis* 2007;44(9):1216–9.
25. Paisley RD, Blaylock J, Hartzell JD. Whooping cough in adults: an update on a reemerging infection. *Am J Med* 2012;125(2):141–3.
26. Wirsing von König C-H. Pertussis diagnostics: overview and impact of immunization. *Expert Rev Vaccines* 2014;13(10):1167–74.
27. Bamberger ES, Srugo I. What is new in pertussis? *Eur J Pediatr* 2008;167(2):133–9.
28. Xing D, Wirsing von König CH, Newland P, Riffelmann M, Meade BD, Corbel M, et al. Characterization of reference materials for human antiserum to pertussis antigens by an international collaborative study. *Clin Vaccine Immunol* 2009;16(3):303–11.
29. Fry NK, Litt DJ, Duncan J, Vaghji L, Warrener L, Samuel D, et al. Modelling anti-pertussis toxin IgG antibody decay following primary and preschool vaccination with an acellular pertussis vaccine in UK subjects using a modified oral fluid assay. *J Med Microbiol* 2013;62(Pt 9):1281–9.
30. Fry NK, Duncan J, Wagner K, Tzivra O, Doshi N, Litt DJ, et al. 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* 2009;58(Pt 8):1023–9.
31. Loeffelholz M. Towards improved accuracy of Bordetella pertussis nucleic acid amplification tests. *J Clin Microbiol* 2012;50(7):2186–90.
32. Litt DJ, Samuel D, Duncan J, Harnden A, George RC, Harrison TG. Detection of anti-pertussis toxin IgG in oral fluids for use in diagnosis and surveillance of Bordetella pertussis infection in children and young adults. *J Med Microbiol* 2006;55(Pt 9):1223–8.
33. Campbell H, Amirthalingam G, Fry NK, Litt D, Harrison TG, Wagner K, et al. Oral fluid testing for pertussis, England and wales, June 2007-August 2009. *Emerg Infect Dis* 2014;20(6):968–75.
34. Dodhia H, Miller E. Review of the evidence for the use of erythromycin in the management of persons exposed to pertussis. *Epidemiol Infect* 1998;120(2):143–9.
35. Kirkland KB, Talbot EA, Decker MD, Edwards KM. Kinetics of pertussis immune responses to tetanus-diphtheria-acellular pertussis vaccine in health care personnel: implications for outbreak control. *Clin Infect Dis* 2009;49(4):584–7.
36. Jenkinson D. Natural course of 500 consecutive cases of whooping cough: a general practice population study. *BMJ* 1995;310(6975):299–302.
37. De Greeff SC, Mooi FR, Westerhof A, Verbakel JMM, Peeters MF, Heuvelman CJ, et al. Pertussis disease burden in the household: how to protect young infants. *Clin Infect Dis* 2010;50(10):1339–45.
38. Cortese MM, Baughman AL, Brown K, Srivastava P. A "new age" in pertussis prevention new opportunities through adult vaccination. *Am J Prev Med* 2007;32(3):177–85.
39. Gidengil CA, Sandora TJ, Lee GM. Tetanus-diphtheria-acellular pertussis vaccination of adults in the USA. *Expert Rev Vaccines* 2008;7(5):621–34.
40. Milord F. Resurgence of pertussis in Montérégie, Quebec--1990-1994. *Canada Commun Dis Rep* 1995;21(5):40–4.
41. Gall SA, Myers J, Pichichero M. Maternal immunization with tetanus-diphtheria-pertussis vaccine: effect on maternal and neonatal serum antibody levels. *Am J Obstet Gynecol* 2011;204(4):334.e1–5.
42. Schellekens J, von König C-HW, Gardner P. Pertussis sources of infection and routes of transmission in the vaccination era. *Pediatr Infect Dis J* 2005;24(5 Suppl):S19–24.
43. De Martino M, Podda A, Galli L, Sinangil F, Mannelli F, Rossi ME, et al. Acellular pertussis vaccine in children with perinatal human immunodeficiency virus-type 1 infection. *Vaccine* 1997;15(11):1235–8.
44. Janda WM, Santos E, Stevens J, Celig D, Terrile L, Schreckenberger PC. Unexpected isolation of Bordetella pertussis from a blood culture. *J Clin Microbiol* 1994;32(11):2851–3.
45. Trøseid M, Jonassen TØ, Steinbakk M. Isolation of Bordetella pertussis in blood culture from a patient with multiple myeloma. *J Infect* 2006;52(1):e11–3.
46. Fatal case of unsuspected pertussis diagnosed from a blood culture--Minnesota, 2003. *MMWR Morb Mortal Wkly Rep* 2004;53(6):131–2.
47. Doebbeling BN, Feilmeier ML, Herwaldt LA. Pertussis in an adult man infected with the human immunodeficiency virus. *J Infect Dis* 1990;161(6):1296–8.
48. Colebunders R, Vael C, Blot K, Van Meerbeeck J, Van den Ende J, Ieven M. Bordetella pertussis as a cause of chronic respiratory infection in an AIDS patient. *Eur J Clin Microbiol Infect Dis* 1994;13(4):313–5.
49. Adamson PC, Wu TC, Meade BD, Rubin M, Manclark CR, Pizzo PA. Pertussis in a previously immunized child with human immunodeficiency virus infection. *J Pediatr* 1989;115(4):589–92.

50. Centers for Disease Control and Prevention. Guidelines for the Control of Pertussis Outbreaks. Atlanta: CDC, 2000.
51. De Serres G, Shadmani R, Duval B, Boulianne N, Déry P, Douville Fradet M, et al. Morbidity of pertussis in adolescents and adults. *J Infect Dis* 2000;182(1):174–9.
52. Harju TH, Leinonen M, Nokso-Koivisto J, Korhonen T, Räty R, He Q, et al. Pathogenic bacteria and viruses in induced sputum or pharyngeal secretions of adults with stable asthma. *Thorax* 2006;61(7):579–84.
53. Bonhoeffer J, Bär G, Riffelmann M, Solèr M, Heininger U. The role of Bordetella infections in patients with acute exacerbation of chronic bronchitis. *Infection* 2005;33(1):13–7.
54. Wendelboe AM, Njamkepo E, Bourillon A, Floret DD, Gaudelus J, Gerber M, et al. Transmission of Bordetella pertussis to young infants. *Pediatr Infect Dis J* 2007;26(4):293–9.
55. Baron S, Njamkepo E, Grimprel E, Begue P, Desenclos JC, Drucker J, et al. Epidemiology of pertussis in French hospitals in 1993 and 1994: thirty years after a routine use of vaccination. *Pediatr Infect Dis J* 1998;17(5):412–8.
56. Izurieta HS, Kenyon TA, Strebel PM, Baughman AL, Shulman ST, Wharton M. Risk factors for pertussis in young infants during an outbreak in Chicago in 1993. *Clin Infect Dis* 1996;22(3):503–7.
57. Valenti WM, Pincus PH, Messner MK. Nosocomial pertussis: possible spread by a hospital visitor. *Am J Dis Child* 1980;134(5):520–1.
58. Spearing NM, Horvath RL, McCormack JG. Pertussis: adults as a source in healthcare settings. *Med J Aust* 2002;177(10):568–9.
59. Bisgard KM, Pascual FB, Ehresmann KR, Miller CA, Cianfrini C, Jennings CE, et al. Infant pertussis: who was the source? *Pediatr Infect Dis J* 2004;23(11):985–9.
60. Crowcroft NS, Booy R, Harrison T, Spicer L, Britto J, Mok Q, et al. Severe and unrecognised: pertussis in UK infants. *Arch Dis Child* 2003;88(9):802–6.
61. McGregor J, Ogle JW, Curry-Kane G. Perinatal pertussis. *Obstet Gynecol* 1986;68(4):582–6.
62. Brouwer AF, van Gils JF, Brand PL, de Graaf JH. Perinatal pertussis: from mother to child, *Ned Tijdschr Geneeskd* 2001;145(47):2257–9.
63. Christie CD, Baltimore RS. Pertussis in neonates. *Am J Dis Child* 1989;143(10):1199–202.
64. Beiter A, Lewis K, Pineda EF, Cherry JD. Unrecognized maternal peripartum pertussis with subsequent fatal neonatal pertussis. *Obstet Gynecol* 1993 Oct;82(4 Pt 2 Suppl):691–3.
65. Armangil D, Tekinalp G, Yurdakök M, Yalçin E. Maternal pertussis is hazardous for a newborn: a case report. *Turk J Pediatr* 2010;52(2):206–10.
66. Public Health England. Vaccination against pertussis (Whooping cough) for pregnant women - 2014. London: PHE, 2014.
67. Elliott E, McIntyre P, Ridley G, Morris A, Massie J, McEniery J, et al. National study of infants hospitalized with pertussis in the acellular vaccine era. *Pediatr Infect Dis J* 2004;23(3):246–52.
68. Deville JG, Cherry JD, Christenson PD, Pineda E, Leach CT, Kuhls TL, et al. Frequency of unrecognized Bordetella pertussis infections in adults. *Clin Infect Dis* 1995;21(3):639–42.
69. Amirthalingam G & The Pertussis Guidelines Working Group. Public Health Management of Pertussis - HPA Guidelines for the Public Health Management of Pertussis Incidents in Healthcare Settings. London: HPA, 2012.
70. Linnemann CC, Ramundo N, Perlstein PH, Minton SD, Englender GS. Use of pertussis vaccine in an epidemic involving hospital staff. *Lancet* 1975;2(7934):540–3.
71. Kurt TL, Yeager AS, Guenette S, Dunlop S. Spread of pertussis by hospital staff. *JAMA* 1972;221(3):264–7.
72. Hospital-acquired pertussis among newborns--Texas, 2004. *MMWR Morb Mortal Wkly Rep* 2008;57(22):600–3.
73. Goh A, Chong CY, Tee N, Loo LH, Yeo JG, Chan YH. Pertussis--an under-diagnosed disease with high morbidity in Singapore children. *Vaccine* 2011;29(13):2503–7.
74. Bonmarin I, Poujol I, Levy-Bruhl D. Nosocomial infections and community clusters of pertussis in France, 2000-2005. *Euro Surveill* 2007;12(11):E11–2.
75. Khetsuriani N, Bisgard K, Prevots D, Brennan M, Wharton M, Pandya S, et al. Pertussis outbreak in an elementary school with high vaccination coverage. *Pediatr Infect Dis J* 2001;20(12):1108–12.
76. Terry J, Flatley C, van den Berg D, Morgan G, Trent M, Turahui J, et al. A field study of household attack rates and the effectiveness of macrolide antibiotics in reducing household transmission of pertussis. *Commun Dis Intell Q Rep* 2015;39(1):E27–33.
77. Wirsing von König C, Postels-Multani S, Bogaerts H, Bock H, Laukamp S, Kiederle S, et al. Factors influencing the spread of pertussis in households. *Commun Dis Intell Q Rep* 2015;39(1):E27–33.

78. Halperin SA, Bortolussi R, Langley JM, Miller B, Eastwood BJ. Seven days of erythromycin estolate is as effective as fourteen days for the treatment of Bordetella pertussis infections. *Pediatrics* 1997;100(1):65–71.
79. Halperin SA, Bortolussi R, Langley JM, Eastwood BJ, De Serres G. A randomized, placebo-controlled trial of erythromycin estolate chemoprophylaxis for household contacts of children with culture-positive bordetella pertussis infection. *Pediatrics* 1999;104(4):e42.
80. American Academy of Pediatrics Committee on Infectious Disease. Pertussis. In: Kimberlin D, Brady M, Jackson M, Long S, editors. Red Book®: 2015 Report of the Committee on Infectious Diseases, 30th Edition. AAP: Elk Grove Village, IL, 2015.
81. Lebel MH, Mehra S. Efficacy and safety of clarithromycin versus erythromycin for the treatment of pertussis: a prospective, randomized, single blind trial. *Pediatr Infect Dis J* 2001;20(12):1149–54.
82. Langley JM, Halperin SA, Boucher FD, Smith B. Azithromycin is as effective as and better tolerated than erythromycin estolate for the treatment of pertussis. *Pediatrics* 2004;114(1):e96–101.
83. Giugliani C, Vidal-Trecan G, Traore S, Blanchard H, Spiridon G, Rollot F, et al. Feasibility of azithromycin prophylaxis during a pertussis outbreak among healthcare workers in a university hospital in Paris. *Infect Control Hosp Epidemiol* 2006;27(6):626–9.
84. Guillot S, Descours G, Gillet Y, Etienne J, Floret D, Guiso N. Macrolide-resistant Bordetella pertussis infection in newborn girl, France. *Emerg Infect Dis* 2012;18(6):966–8.
85. Fry NK, Duncan J, Vaghji L, George RC, Harrison TG. Antimicrobial susceptibility testing of historical and recent clinical isolates of Bordetella pertussis in the United Kingdom using the Etest method. *Eur J Clin Microbiol Infect Dis* 2010;29(9):1183–5.
86. Hoppe JE, Halm U, Hagedorn HJ, Kraminer-Hagedorn A. Comparison of erythromycin ethylsuccinate and co-trimoxazole for treatment of pertussis. *Infection* 1989;17(4):227–31.
87. Altunaiji S, Kukuruzovic R, Curtis N, Massie J. Antibiotics for whooping cough (pertussis). *Cochrane database Syst Rev* 2007;(3):CD004404.
88. Henry RL, Dorman DC, Skinner JA, Mellis CM. Antimicrobial therapy in whooping cough. *Med J Aust* 1981;2(1):27–8.
89. Ribeiro CD. Prophylactic erythromycin for whooping-cough contacts. *Lancet* 1981;1(8226):951.
90. Joint Formulary Committee. British National Formulary 70th Edition. London: BMJ Group and Pharmaceutical Press; 2015.
91. Louik C, Werler MM, Mitchell AA. Erythromycin use during pregnancy in relation to pyloric stenosis. *Am J Obstet Gynecol* 2002;186(2):288–90.
92. Cooper WO, Ray WA, Griffin MR. Prenatal prescription of macrolide antibiotics and infantile hypertrophic pyloric stenosis. *Obstet Gynecol* 2002;100(1):101–6.
93. Mahon BE, Rosenman MB, Kleiman MB. Maternal and infant use of erythromycin and other macrolide antibiotics as risk factors for infantile hypertrophic pyloric stenosis. *J Pediatr* 2001;139(3):380–4.
94. Van der Wielen M, Van Damme P, Joossens E, François G, Meurice F, Ramalho A. A randomised controlled trial with a diphtheria-tetanus-acellular pertussis (dTpa) vaccine in adults. *Vaccine* 2000;18(20):2075–82.
95. Halperin SA, Smith B, Russell M, Scheifele D, Mills E, Hasselback P, et al. Adult formulation of a five component acellular pertussis vaccine combined with diphtheria and tetanus toxoids and inactivated poliovirus vaccine is safe and immunogenic in adolescents and adults. *Pediatr Infect Dis J* 2000;19(4):276–83.
96. Southern J, Andrews N, Burrage M, Miller E. Immunogenicity and reactogenicity of combined acellular pertussis/tetanus/low dose diphtheria vaccines given as a booster to UK teenagers. *Vaccine* 2005;23(29):3829–35.
97. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. *Pediatr Infect Dis J* 2005;24(5 Suppl):S58–61.
98. Guiso N, Njamkepo E, Vié le Sage F, Zepp F, Meyer CU, Abitbol V, et al. Long-term humoral and cell-mediated immunity after acellular pertussis vaccination compares favourably with whole-cell vaccines 6 years after booster vaccination in the second year of life. *Vaccine* 2007;25(8):1390–7.
99. Van Buynder PG, Owen D, Vurdien JE, Andrews NJ, Matthews RC, Miller E. Bordetella pertussis surveillance in England and Wales: 1995-7. *Epidemiol Infect* 1999;123(3):403–11.
100. Birkebaek NH. Bordetella pertussis booster vaccination for health care personnel immediately following a pertussis outbreak in a hospital? *Clin Infect Dis* 2009;49(4):588–90.
101. Galazka AM, Robertson SE. Immunization against diphtheria with special emphasis on immunization of adults. *Vaccine* 1996;14(9):845–57.

102. Ramsay M, Joce R, Whalley J. Adverse events after school leavers received combined tetanus and low dose diphtheria vaccine. *Commun Dis Rep CDR Rev* 1997;7(5):R65–7.
103. Broder KR, Cortese MM, Iskander JK, Kretsinger K, Slade BA, Brown KH, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;55(RR-3):1–34.
104. Halperin SA, Sweet L, Baxendale D, Neatby A, Rykers P, Smith B, et al. How soon after a prior tetanus-diphtheria vaccination can one give adult formulation tetanus-diphtheria-acellular pertussis vaccine? *Pediatr Infect Dis J* 2006;25(3):195–200.
105. David ST, Hemsley C, Pasquali PE, Larke B, Buxton JA, Lior LY. Enhanced surveillance for vaccine-associated adverse events: dTap catch-up of high school students in Yukon. *Canada Commun Dis Rep* 2005;31(11):117–26.
106. National Advisory Committee on Immunisation. An Advisory Committee Statement, National Advisory Committee on Immunisation (NACI): interval between administration of vaccines against diphtheria, tetanus and pertussis. *Canada Commun Dis Rep* 2015;31(9):17–24.
107. Beytout J, Launay O, Guiso N, Fiquet A, Baudin M, Richard P, et al. Safety of Tdap-IPV given one month after Td-IPV booster in healthy young adults: a placebo-controlled trial. *Hum Vaccin* 2009;5(5):315–21.
108. Health Protection Agency. Laboratory confirmed cases of pertussis reported to the Enhanced pertussis surveillance programme in 2011. London: HPA, 2012.
109. eMC. Summary of Product Characteristics. Repevax [Internet] Available from: http://www.medicines.org.uk/EMC/medicine/15256/SPC/REPEVAX/#INDICATIONS . 2012. 20-8-2012 [cited July 12th 2016].
110. Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) in pregnant women--Advisory Committee on Immunization Practices (ACIP), 2012. *MMWR Morb Mortal Wkly Rep* 2013;62(7):131–5.
111. Health Service Executive. Immunisation Guidelines for Ireland [Internet]. Available from: http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/ [cited July 12th 2016].
112. Vizzotti C, Neyro S, Katz N, Juárez M V, Perez Carrega ME, Aquino A, et al. Maternal immunization in Argentina: A storyline from the prospective of a middle income country. *Vaccine* 2015;33(47):6413–9.
113. State of Israel: Ministry of Health. Whooping Cough Vaccination in Pregnant Women [Internet]. Available from: http://www.health.gov.il/English/Topics/Pregnancy/during/Pages/Vaccination-Whooping_cough.aspx [cited July 12th 2016].
114. Ministry of Health of New Zealand. Immunisation for pregnant women [Internet]. Available from: http://www.health.govt.nz/your-health/healthy-living/immunisation/immunisation-pregnant-women [cited July 12th 2016].
115. Australia Government Department of Health. Whooping Cough (pertussis) - The Australia Immunisation Handbook. Canberra: DH, 2016.
116. Halperin BA, Morris A, Mackinnon-Cameron D, Mutch J, Langley JM, McNeil SA, et al. Kinetics of the antibody response to tetanus-diphtheria-acellular pertussis vaccine in women of childbearing age and postpartum women. *Clin Infect Dis* 2011;53(9):885–92.
117. Van Rie A, Wendelboe AM, Englund JA. Role of maternal pertussis antibodies in infants. *Pediatr Infect Dis J* 2005;24(5 Suppl):S62–5.
118. Sako W. Early immunization against pertussis with alum precipitated vaccine. *JAMA* 1945;127(7):379–84.
119. Van Savage J, Decker MD, Edwards KM, Sell SH, Karzon DT. Natural history of pertussis antibody in the infant and effect on vaccine response. *J Infect Dis* 1990;161(3):487–92.
120. Healy CM, Munoz FM, Rench MA, Halasa NB, Edwards KM, Baker CJ. Prevalence of pertussis antibodies in maternal delivery, cord, and infant serum. *J Infect Dis* 2004;190(2):335–40.
121. Healy CM, Rench MA, Edwards KM, Baker CJ. Pertussis serostatus among neonates born to Hispanic women. *Clin Infect Dis* 2006;42(10):1439–42.
122. Gonik B, Puder KS, Gonik N, Kruger M. Seroprevalence of Bordetella pertussis antibodies in mothers and their newborn infants. *Infect Dis Obstet Gynecol* 2005;13(2):59–61.
123. Leuridan E, Hens N, Peeters N, de Witte L, Van der Meeren O, Van Damme P. Effect of a prepregnancy pertussis booster dose on maternal antibody titers in young infants. *Pediatr Infect Dis J* 2011;30(7):608–10.
124. Healy CM, Baker CJ. Prospects for prevention of childhood infections by maternal immunization. *Curr Opin Infect Dis* 2006;19(3):271–6.
125. Richardson M, Elliman D, Maguire H, Simpson J, Nicoll A. Evidence base of incubation periods, periods of infectiousness and exclusion policies for the control of communicable diseases in schools and preschools. *Pediatr Infect Dis J* 2001;20(4):380–91.



Appendix 1: PHE Guidelines for the management of cases and close contacts of pertussis

Appendix 2: Reporting form for pertussis cases in healthcare workers and clusters in educational settings

Public Health England

Version 1: January 2015

Notification of a pertussis case/s in healthcare workers and of pertussis clusters in healthcare, pre-school, school or other educational settings

Details for the first cluster case or a single HCW case

Notification date	____/____/____
HPT	
HPZone case reference number	
First name	
Surname	
Sex	
DOB	
Setting type (eg. maternity ward, ICU, general practice, pre-school, university)	
Was a sample sent for testing*	Yes / no
Was contact tracing undertaken*	Yes / no
If yes – number of contacts	
Number of contacts offered prophylaxis	
Number of contacts offered vaccine	
Were any symptomatic contacts identified*	Yes / no
If yes - number of symptomatic contacts	

Please complete this form for:

any <u>single case in a health care worker</u> (HCW) who has <u>direct patient contact</u> and;
<u>All clusters</u> ie two or more cases in a 21 day period <u>in a healthcare, pre-school or educational setting</u>

*** Please delete as appropriate**

Name of setting (eg hospital name, practice name, school name)			
Date	____/____/____	**Sample type***	Serum/ NP swab /throat swab / oral fluid

Please complete this form as fully as possible and email to: pertussis@phe.gov.uk

Any queries please contact Sonia Ribeiro on 0208 327 6058 or sonia.ribeiro@phe.gov.uk

Details for HCW case only

Type of HCW (eg practice nurse, midwife, surgeon)	
Does this HCW have direct patient contact with infants and/or pregnant women?	Yes / no

Details of all subsequent clinically diagnosed cases with sample submitted for testing

	Cluster case 2	**Cluster case 3**	**Cluster case 4**	**Cluster case 5**	**Cluster case 6**
Contact/cluster case first name					
Contact/cluster case surname					
Contact/cluster case DOB					
Sample date	____/____/____	____/____/____	____/____/____	____/____/____	____/____/____
Sample type*	Serum / NP swab / throat swab/ oral fluid	Serum / NP swab / throat swab/ oral fluid	Serum / NP swab / throat swab/ oral fluid	Serum / NP swab / throat swab/ oral fluid	Serum / NP swab / throat swab/ oral fluid
HPZone contact reference number					
Nature of relationship (eg patient, pupil, household)					

Appendix 3: Enhanced surveillance form

Form version 11/16

Public Health England

Public Health England Enhanced Pertussis Surveillance
Confidential follow-up of laboratory confirmed *B. pertussis*

NHS Number:	**Specimen date:**

Study No:

Please complete as far as possible, ticking appropriate boxes where applicable.

Patient details

Patient name:	Sex:	Date of birth __/___/___

Ethnicity: White\White British ☐Mixed ☐Asian/Asian British ☐ Black/Black British ☐ Other ☐ _____

Clinical History of Patient

Date of onset of first symptom: ___/___/____ **Did they have the following complications?**

Apnoeic attacks: Yes ☐ No ☐ NK ☐	Pneumonia: Yes ☐ No ☐ NK ☐
Convulsions: Yes ☐ No ☐ NK ☐	Conjunctival haemorrhage: Yes ☐ No ☐ NK ☐

Death: Yes ☐ No ☐ NK ☐ If yes, date of death: _____/_____/_____

Please indicate if this patient is:

☐Diagnosed with chronic respiratory disease (incl. asthma) ☐Diagnosed with chronic heart disease

☐Diabetic ☐ Immunocompromised ☐Pregnant

☐ Diagnosed with another condition. Please specify_____

Was the patient admitted to hospital? Yes ☐ No ☐ NK ☐ If yes, which hospital_____

Date admitted: ___/___/_____ Date discharged: ___/___/_____

If this patient was admitted please include a copy of the hospital discharge summary with this form.

VACCINATION HISTORY OF CASE. Please complete the table as fully as possible.

How many doses of pertussis vaccine did they receive before onset? 1 ☐ 2 ☐ 3 ☐ 4 ☐ NK ☐

	Vaccination date	Trade name	Manufacturer	Batch Number
1st dose				
2nd dose				
3rd dose				
4th dose				

MATERNAL INFORMATION (PLEASE COMPLETE FOR INFANTS BORN ON OR AFTER 01/10/2012)

Mother's Ethnicity: White ☐Mixed ☐Asian/Asian British ☐ Black/Black British ☐ Other ☐ please specify:_____

Mother's first language: English ☐ other ☐ **Mother's date of birth:**____/___/_____

Mother's Parity (at time of & including this child's birth) _____ **Weeks' gestation at delivery of this child** _____

Was the mother vaccinated against pertussis whilst pregnant with this child? Yes ☐ No ☐ NK ☐

If yes: Number of weeks gestation at vaccination:_____ **Date of vaccination:** ____/____/_____

Trade name / manufacturer_____ **Batch No:**_____

PLEASE LIST ALL PREGNANCIES BETWEEN 2012 AND THE CHILD ABOVE

	Outcome (please circle)	Vaccinated with DTaP-IPV in pregnancy	Date of vaccination	Date of birth	Trade name / manufacturer	Batch number
Pregnancy 1	Live birth / no live birth	Y / N				
Pregnancy 2	Live birth / no live birth	Y / N				

Pregnancy 3	Live birth / no live birth	Y / N				

Did the patient have contact with a suspected or known case of pertussis in the month before onset?

Any known contact with pertussis	Yes □ No □ NK □
If yes, where was this contact	home □ playgroup □ school □ work □ hospital □ other □
How old was/were the contact/s	<1 □ 1-4 □ 5-9 □ 10-14 □ 15-44 □ 45+ □
If in the home, who was the contact	mother □ father □ sibling □ other □

Does this patient work as a front line health care worker? Yes ☐ No ☐ NK ☐

Completed by (please print):_____ Telephone No::_____
Date: _____ Position:_____

Appendix 4: Oral fluid submission form

PHE Microbiology Services request form

Public Health England

***B.pertussis* (Whooping Cough) antibodies in Oral Fluid**
for notified cases aged 2 to <17 years of age

Respiratory and Vaccine Preventable Bacteria Reference Unit
61 Colindale Avenue
London NW9 5HT

+44 (0)20 8327 7331 (Lab)
+44 (0)20 8327 6906 (Head of Unit)
https://www.gov.uk/rvpbru-reference-and-diagnostic-services

★ R A P P 7 ★

SENDERS INFORMATION

GP name, address including postcode & telephone (IN BLOCK CAPITALS).

Name of PHE Centre:

Name of CCDC:

PATIENT / SOURCE INFORMATION

HPZone number _____

NHS number _____

Surname _____

Forename _____

Sex Male ☐ Female ☐

Date of birth _____ Age _____

Patient's postcode _____

SAMPLE INFORMATION

Date Sample taken: _____

CLINICAL INFORMATION

Date of onset of coughing: _____

What was the date of the above patient's last whooping cough vaccine*? _____

*also known as the 5-in-1, 6-in-1, DTP, DTaP, pertussis, Pediacel, Infanrix or Repevax

Instructions for taking and posting the swab:

N.B. Do not take sample until patient has been coughing for more than 14 days

1. In this package you should have the following items:
   - A pink/blue swab (A) inside a clear tube (B) (both in a sealed paper packet)
   - A self-adhesive clear plastic bag (C)
   - A cardboard box (D)
   - A request form (E) and
   - A pre-paid grey plastic envelope (F)

2. Open the paper packet, remove the cap from the clear tube (B) and pull out the pink/blue swab (A) using the handle. Rub the pink/blue sponge swab (A) all along the gumline, a bit like using a toothbrush, for one to two minutes.
3. Place the wet pink/blue swab (A) back inside the clear tube (B), and replace the cap. Please write the patient's name, date of birth and today's date on the label area on the clear tube.
4. Please now wash your hands.
5. Place the labelled tube (B) containing the pink/blue swab (A) inside the self-adhesive clear plastic bag (C). Push air out of clear plastic bag (C). Remove red strip from top fold down corner and stick down
6. Please complete the date the sample was taken and the clinical information in the request form (E) as shown on picture 5 of the instruction sheet *How To Take An Oral Fluid Swab*. Please, ensure that the patient's name and the GP name and address are correct.
7. Place both the completed request form (E) and the clear plastic bag (with the swab) (C) back into the cardboard box (D), and then into the pre-paid grey plastic envelope (F).
8. Seal the pre-paid grey plastic envelope (F). Post as soon as you can in a Royal Mail post box – a stamp is not required.
9. The results should be available from your doctor within a few weeks.

Thank you

If you are unclear about these instructions you can phone 020 8327 7412 within office hours. IF THE PAPER PACKET HAS BEEN OPENED, DO NOT USE THE SWAB, BUT STOP AND RING THE NUMBER ABOVE.

Appendix 5: Table of quality of evidence for recommendations

Strongly recommended on the basis of more than two consistent, well-conceived, well executed studies with control groups or longitudinal measurements.

Recommended on the basis of more than one well-conceived, well executed, controlled, or time series study; or more than three studies with more limited execution.

Indicated on the basis of previous scientific observations and theoretic rationale, but case controlled or prospective studies do not exist.

Recommendation	**Level of evidence**
Children with suspected/epidemiologically linked/confirmed pertussis should be excluded from school/nursery for 48 hours from commencing antibiotic therapy.	Indicated
Suspected/epidemiologically linked/confirmed cases should be treated with antibiotics if within 21 days of onset of symptoms.	Strongly recommended
Unvaccinated and partially immunised cases and contacts up to 10 years of age should complete their course of primary immunisation and booster vaccine according to the recommended UK schedule.	Indicated
Chemoprophylaxis should be offered to all close contacts when onset of illness in index case is within the preceding 21 days AND there is a close contact in a priority group present.	Recommended
For those who are offered chemoprophylaxis, a booster dose of Pertussis containing vaccine is recommended for contacts aged 10 years or above.	Indicated
Post-exposure vaccination in pregnancy is important and specifically recommended in the following individuals who have not already received a pertussis containing vaccine more than one week and less than five years ago: • for women exposed to pertussis after 32 weeks, OR • for women exposed to pertussis at any stage of pregnancy if they are at risk of transmitting to ‘vulnerable’ individuals in ‘Group 1’, eg a healthcare worker It is important that all pregnant women from 16 weeks gestation onwards have been vaccinated or scheduled for vaccination in line with the maternal programme.	Indicated

Appendix 6:Testing for Pertussis in Primary Care

Suspect pertussis in patients with a **cough illness lasting 14 days or more** without an apparent cause **plus one** of the following: (a) paroxysms of coughing; (b) inspiratory 'whoop'; (c) post-tussive vomiting.

ALL CASES should be notified to your local HPT (*insert phone number/email address*)
When notifying, it is helpful to let the HPT know if the case has had contact with pregnant individuals or children aged under 1 year, including through occupational exposure (e.g. healthcare or nursery settings).

Recommended tests for pertussis testing vary according to the length of time since symptom onset.

- Less than 2 weeks from symptom onset: PCR and culture
- Between 2 and 3 weeks from symptom onset: PCR **and** culture **and either** oral fluid kit (if aged 2 to < 17 yrs) **or** serology
- More than 3 weeks from symptom onset: **Either** oral fluid kit (if aged 2 - <17 yrs) **or** serology

Sending a pertussis PCR test – FREE SERVICE

Insert local info:

Please submit samples to your local laboratory as per normal protocol. Samples will then be referred for Pertussis PCR detection your local Public Health Laboratory (PHL). Pertussis PCR testing is not chargeable, when performed at a PHL. Please label clearly 'for **Bordetella pertussis PCR testing'**

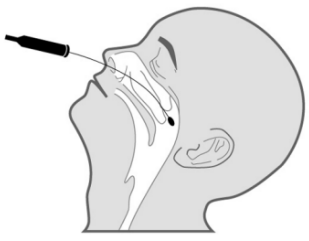
PCR testing can be performed on the following specimens:

- Throat swabs

Collected using a virology swab or dry swab in a sterile container

- Pernasal swabs

Use a dry swab with a flexible wire shaft and a rayon / Dacron / nylon bud. A rigid shaft is not suitable. Push the swab along the floor of the nasal cavity, as far towards the posterior wall of the nasopharynx as possible.



- Nasopharyngeal swabs

Use a dry or Copan style nasopharyngeal swab. See the following link for further guidance:
CDC video how to take a nasopharyngeal swab.

- Nasopharyngeal aspirate

Provide not less than 400microlitres in a sterile container. See the following link for further guidance:
CDC video how to take a nasopharyngeal aspirate.

Sending a pertussis culture

A nasopharyngeal swab or pernasal swab may be taken for culture. The swab should be placed in a culture medium (ideally charcoal) and submitted to your local microbiology lab. **Please clearly label as 'for pertussis culture'.**

Requesting an oral fluid kit – FREE SERVICE

For cases aged 2 years to less than 17 years, notify the case to your local HPT and they will post an oral fluid kit (OFK) directly to the case.

Note that oral fluid testing is not recommended if the case has been immunised against pertussis in the previous year as a positive result cannot be interpreted.

Sending a pertussis serology test

For cases not aged 2 years to less than 17 years, a charged-for serology test using serum can be arranged via your local laboratory and then sent on to the Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU). Form B3 can be used.

Note that serology is not recommended if the case has been immunised against pertussis in the previous year as the result cannot be interpreted.

Managing cases

If three weeks or less from symptom onset, treat with appropriate antibiotics once PCR and culture tests have been taken. Exclude the case from school/work until they have completed two days of the antibiotic course. Work with the local HPT to identify and manage vulnerable close contacts. There is no need to prescribe a second course of antibiotics *even if* symptoms are not resolving.

If more than three weeks from symptom onset, antibiotics are not required to manage pertussis *even if* the case still has symptoms. No exclusion of the case is necessary.

Further information on the testing for and management of pertussis is available at:
https://www.gov.uk/government/publications/pertussis-guidelines-for-public-health-management
Or please call your local HPT for further advice (*insert relevant contact details*)