Public Health England

NHS

UK Standards for Microbiology Investigations

Investigation of whooping cough

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"NICE has renewed accreditation of the process used by **Public Health England (PHE)** to produce **UK Standards for Microbiology Investigations**. The renewed accreditation is valid until **30 June 2021** and applies to guidance produced using the processes described in **UK standards for microbiology investigations (UKSMIs) Development process, S9365', 2016**. The original accreditation term began in **July 2011.**"

Issued by the Standards Unit, National Infection Service, PHE

Acknowledgments

UK Standards for Microbiology Investigations (UK SMIs) are developed under the auspices of Public Health England (PHE) working in partnership with the National Health Service (NHS), Public Health Wales and with the professional organisations whose logos are displayed below and listed on the website https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. UK SMIs are developed, reviewed and revised by various working groups which are overseen by a steering committee (see https://www.gov.uk/government/groups/standards-for-microbiology-investigations-steering-committee).

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Amendment table

Each UK SMI method has an individual record of amendments. The current amendments are listed on this page. The amendment history is available from standards@phe.gov.uk.

New or revised documents should be controlled within the laboratory in accordance with the local quality management system.

Amendment number/date	11/11.05.18
Issue number discarded	8
Insert issue number	9
Anticipated next review date*	11.05.21
Section(s) involved	**Amendment**
Whole document.	Document presented in a new format. Reorganisation of some text. Edited for clarity. Minor textual changes. All hyperlinked documents updated with the correct address. Added references to PHE guidelines where relevant.
Introduction.	Re-written for more clarity adding detailed section on molecular methods.
Technical information.	Added section for PCR and serology.
4.1 Test selection.	Developed this section to include: 4.1.1 Culture 4.1.2 PCR 4.1.3 Serology
4.5 Culture and investigation.	Added section referring to PCR and serology.
4.6 Identification.	Added section referring to identification with MALDI-TOF.
5 Reporting procedure.	Added section referring to interpreting and reporting PCR and serology results.
Appendix.	Algorithm updated to include PCR and serology as diagnostic methods with emphasis on their relevance in relation to the cough onset.

*Reviews can be extended up to five years subject to resources available.

UK SMI[1]: scope and purpose

Users of UK SMIs

Primarily, UK SMIs are intended as a general resource for practising professionals operating in the field of laboratory medicine and infection specialties in the UK. UK SMIs also provide clinicians with information about the available test repertoire and the standard of laboratory services they should expect for the investigation of infection in their patients, as well as providing information that aids the electronic ordering of appropriate tests. The documents also provide commissioners of healthcare services with the appropriateness and standard of microbiology investigations they should be seeking as part of the clinical and public health care package for their population.

Background to UK SMIs

UK SMIs comprise a collection of recommended algorithms and procedures covering all stages of the investigative process in microbiology from the pre-analytical (clinical syndrome) stage to the analytical (laboratory testing) and post analytical (result interpretation and reporting) stages. Syndromic algorithms are supported by more detailed documents containing advice on the investigation of specific diseases and infections. Quality guidance notes describe laboratory processes which underpin quality, for example assay validation.

Standardisation of the diagnostic process through the application of UK SMIs helps to assure the equivalence of investigation strategies in different laboratories across the UK and is essential for public health surveillance, research and development activities.

Equal partnership working

UK SMIs are developed in equal partnership with PHE, NHS, Royal College of Pathologists and professional societies. The list of participating societies may be found at https://www.gov.uk/uk-standards-for-microbiology-investigations-smi-quality-and-consistency-in-clinical-laboratories. Inclusion of a logo in an UK SMI indicates participation of the society in equal partnership and support for the objectives and process of preparing UK SMIs. Nominees of professional societies are members of the Steering Committee and working groups which develop UK SMIs. The views of nominees cannot be rigorously representative of the members of their nominating organisations nor the corporate views of their organisations. Nominees act as a conduit for two way reporting and dialogue. Representative views are sought through the consultation process. UK SMIs are developed, reviewed and updated through a wide consultation process.

Quality assurance

NICE has accredited the process used by the UK SMI working groups to produce UK SMIs. The accreditation is applicable to all guidance produced since October 2009. The process for the development of UK SMIs is certified to ISO 9001:2008. UK SMIs represent a good standard of practice to which all clinical and public health microbiology laboratories in the UK are expected to work. UK SMIs are NICE accredited and represent neither minimum standards of practice nor the highest level

[1] Microbiology is used as a generic term to include the two GMC-recognised specialties of Medical Microbiology (which includes Bacteriology, Mycology and Parasitology) and Medical Virology.

of complex laboratory investigation possible. In using UK SMIs, laboratories should take account of local requirements and undertake additional investigations where appropriate. UK SMIs help laboratories to meet accreditation requirements by promoting high quality practices which are auditable. UK SMIs also provide a reference point for method development. The performance of UK SMIs depends on competent staff and appropriate quality reagents and equipment. Laboratories should ensure that all commercial and in-house tests have been validated and shown to be fit for purpose. Laboratories should participate in external quality assessment schemes and undertake relevant internal quality control procedures.

Patient and public involvement

The UK SMI working groups are committed to patient and public involvement in the development of UK SMIs. By involving the public, health professionals, scientists and voluntary organisations the resulting UK SMI will be robust and meet the needs of the user. An opportunity is given to members of the public to contribute to consultations through our open access website.

Information governance and equality

PHE is a Caldicott compliant organisation. It seeks to take every possible precaution to prevent unauthorised disclosure of patient details and to ensure that patient-related records are kept under secure conditions. The development of UK SMIs is subject to PHE Equality objectives https://www.gov.uk/government/organisations/public-health-england/about/equality-and-diversity.

The UK SMI working groups are committed to achieving the equality objectives by effective consultation with members of the public, partners, stakeholders and specialist interest groups.

Legal statement

While every care has been taken in the preparation of UK SMIs, PHE and the partner organisations, shall, to the greatest extent possible under any applicable law, exclude liability for all losses, costs, claims, damages or expenses arising out of or connected with the use of an UK SMI or any information contained therein. If alterations are made by an end user to an UK SMI for local use, it must be made clear where in the document the alterations have been made and by whom such alterations have been made and also acknowledged that PHE and the partner organisations shall bear no liability for such alterations. For the further avoidance of doubt, as UK SMIs have been developed for application within the UK, any application outside the UK shall be at the user's risk.

The evidence base and microbial taxonomy for the UK SMI is as complete as possible at the date of issue. Any omissions and new material will be considered at the next review. These standards can only be superseded by revisions of the standard, legislative action, or by NICE accredited guidance.

Suggested citation for this document

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Scope of document

Type of specimen

Pernasal swab, nasopharyngeal aspirate, nasopharyngeal swab and blood serum.

The UK SMI describes the investigation and confirmation of *Bordetella pertussis* and *Bordetella parapertussis* by culture and PCR in pernasal swabs, nasopharyngeal aspirates and nasopharyngeal swabs and by serology in blood serum.

This UK SMI should be used in conjunction with other UK SMIs.

Introduction

Pertussis, commonly known as whooping cough ("violent cough") has been associated with high morbidity and mortality, particularly in infants[1]. Whooping cough is a highly contagious disease that is caused by the fastidious Gram negative coccobacilli *B. pertussis* and *B. parapertussis* that colonise the respiratory tract[2]. The main symptoms include malaise, fever followed by long bursts of coughing and choking leaving the infected person gasping for breath with a characteristic whoop sound[3].

B. pertussis usually infects and causes severe respiratory disease in young children, with infants under six months of age at most risk of severe complications[3]. The infection can occur in adolescents and adults who exhibit milder symptoms of flu-like illness followed by a prolonged cough[4,5]. The incubation period of pertussis is on average between 7–10 days (range 5–21days)[2].

Despite a sustained period of high vaccine coverage, pertussis continues to display cyclical peaks in activity occurring every three to four years[6]. An increase in pertussis activity in England and Wales was observed from the third quarter of 2011, predominantly in adolescents and adults. This increase continued into 2012 and extended into infants under three months who are at highest risk of severe complications, hospitalisation and death (https://www.gov.uk/government/collections/pertussis-guidance-data-and-analysis).

In 2012, in response to a significant increase in laboratory confirmed cases of pertussis and the high rates of disease in young infants, the Health Protection Agency (Public Health England since April 2013) declared a Level 3 incident (national outbreak)[7]. On 28th September 2012, the Department of Health announced the introduction of a temporary programme to vaccinate pregnant women against pertussis[8]. This temporary programme, which is an outbreak control measure, aimed to passively protect infants from birth before they reach the age of routine immunisation and during the period of greatest risk of complications and death[9]. From the 1st April 2016, Public Health England suggests that pertussis containing vaccine should be offered to pregnant women from 16 weeks gestation, ideally after their foetal anomaly scan (usually at around 20 weeks)[10].

Diagnosis of pertussis is usually straight forward however, *formes frustes* (abortive or atypical disease; disease stopped before it has run its full course) are known to occur, and may cause diagnostic difficulty. Consideration should be given to appropriate evaluation of patients with pertussis in whom infection with *B. pertussis* or *B. parapertussis* cannot be demonstrated. In addition to sampling for pertussis, it is

recommended that consideration is given to testing the patient for respiratory viruses according to local procedures.

Laboratory confirmation of clinically suspected cases can be made by culture and isolation of the causative organisms *B. pertussis* and *B. parapertussis*, detection of its DNA (typically from nasopharyngeal swabs/pernasal swabs or nasopharyngeal aspirates) or serological tests (which usually only provide a late or retrospective diagnosis)[11] (see Appendix).

Culture is conventionally performed to confirm infection with *B. pertussis* and *B. parapertussis*. The method is highly specific but sensitivity is low 20-40%. Culture is also more likely to be unsuccessful the longer the time since the onset of illness. Diagnostic sensitivity can be maximised by supplementing culture with polymerase chain reaction (PCR) methods and serology. PCR is more sensitive than culture as it does not require organisms to be viable. Serology is particularly useful in diagnosing infection in patients who have been coughing for four weeks, when both culture and PCR would be anticipated to be unhelpful[4,12-22].

Early laboratory diagnosis is important for control and prevention of whooping cough. Isolation and typing of the organism is also important for the continued monitoring of the vaccine programme. 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[9].

Technical information/limitations

Limitations of UK SMIs

The recommendations made in UK SMIs are based on evidence (for example, sensitivity and specificity) where available, expert opinion and pragmatism, with consideration also being given to available resources. Laboratories should take account of local requirements and undertake additional investigations where appropriate. Prior to use, laboratories should ensure that all commercial and in-house tests have been validated and are fit for purpose.

Selective media[23-25]

The nature of selective media requires a balance between the performance characteristics and the costs of the tests. Selective media may not support the growth of all circulating strains of organisms. Refer to manufacturer's instructions and recent evidence for limitations of growth.

The media should support the growth of *B. pertussis* and *B. parapertussis*, suppress nasopharyngeal flora and be stable during storage. There are several different types of medium available that contain blood or charcoal or both, along with selective antibiotic supplements - penicillin, cefalexin or meticillin.

Meticillin is the least inhibitory of these towards *B. pertussis*, but is also the least inhibitory towards nasopharyngeal flora. Cefalexin is the most inhibitory towards nasopharyngeal flora and is superior to penicillin. For these reasons it is the antibiotic of choice for selective media in this UK SMI[25].

Primary isolation plates are incubated at 35-37°C, in an aerobic moist atmosphere maintained for 7 days[24]. A thickly poured plate is necessary to avoid desiccation on prolonged incubation.

Specimen type

Current recommendation for specimen of choice is nasopharyngeal aspirates or nasopharyngeal swabs/pernasal swabs[9]. In addition to sampling for pertussis, it is recommended that consideration is given to testing the patient for respiratory viruses according to local procedures.

Blood serum is the specimen used for pertussis serological test.

Cough plates are not recommended.

Pernasal swabs

Dacron and rayon swabs are the swabs of choice for both PCR and culture. Both types of synthetic material performed well in studies with neither superior to the other[26].

PCR and serology

It should be noted that the implementation of local PCR and serology based diagnosis of whooping cough, should be validated in the routine clinical setting before being used.

Specimen containers[27,28]

UK SMIs use the term “CE marked leak proof container” to describe containers bearing the CE marking used for the collection and transport of clinical specimens. The requirements for specimen containers are given in the EU in vitro Diagnostic Medical Devices Directive (98/79/EC Annex 1 B 2.1) which states: “The design must allow easy handling and, where necessary, reduce as far as possible contamination of, and leakage from, the device during use and, in the case of specimen receptacles, the risk of contamination of the specimen. The manufacturing processes must be appropriate for these purposes”.

Public health management

Refer to the following guidance:

England and Wales:

https://www.gov.uk/government/collections/pertussis-guidance-data-and-analysis

Scotland:

http://www.hps.scot.nhs.uk/immvax/pertussis-whoopingcough.aspx

Northern Ireland:

http://www.publichealth.hscni.net/whooping-cough

1 Safety considerations[27-42]

1.1 Specimen collection, transport and storage[27-32,43]

Use aseptic technique.

Collect specimens in appropriate transport medium in CE marked leak proof containers and transport in sealed plastic bags.

Compliance with postal, transport and storage regulations is essential.

1.2 Specimen processing[27-42]

Containment Level 2.

Laboratory procedures that give rise to infectious aerosols must be conducted in a microbiological safety cabinet[35].

As a minimum, it is recommended that the processing of any culture that may result in generation of aerosols should be processed in a microbiological safety cabinet in accordance with the relevant risk assessment, ACDP and HSE guidelines. Processing of diagnostic sample cultures that are assessed to be at higher risk of containing hazard group 3 organisms must be undertaken under appropriate containment conditions as determined by risk assessment, and as required by Biological agents: managing the risks in laboratories and healthcare premises[35]. This will normally be under full CL3 conditions. Such organisms include *Mycobacterium* species, *Brucella* species, *Bacillus anthracis*, *Blastomyces dermatitidis*, *Histoplasma capsulatum*, *Coccidiodes immitis,* etc.

Refer to current guidance on the safe handling of all organisms documented in this UK SMI.

The above guidance should be supplemented with local COSHH and risk assessments.

2 Specimen collection

2.1 Type of specimens

Pernasal swab, nasopharyngeal aspirate, nasopharyngeal swab and/or blood, as appropriate for the test performed.

2.2 Optimal time and method of collection[44]

For safety considerations refer to Section 1.1.

Collect specimens before antimicrobial therapy where possible[44].

Swabs should be collected and transported in medium designed to support the growth of organisms.

Pernasal swabs

A pernasal swab (Dacron or rayon with flexible ultrafine wire shaft) is inserted through a nostril and advanced along the floor of the nose until it reaches the nasopharynx. It has been suggested that the swab is held against the posterior nasopharynx for up to

30s or until the patient coughs. In practice, it is more likely that a patient will only be able to tolerate this for a few seconds.

Nasopharyngeal specimens

Sampling of nasopharyngeal secretions in patients with whooping cough may precipitate a paroxysm of coughing and cause obstruction of the airways. Resuscitation equipment must be available if whooping cough is suspected. The specimen collector should avoid exposure to direct coughs from the patient.

Nasopharyngeal exudate may be obtained using a suction catheter (No.8 French) inserted through the nose. The exudate is collected in a sterile plastic trap in which the specimen is transported to the laboratory, or in a sterile clear plastic universal container (30mL or 60mL, to BS 5213).

Note: Cough plates are not recommended[45].

Collect specimens other than swabs into appropriate CE marked leak proof containers and place in sealed plastic bags.

Unless otherwise stated, swabs for bacterial and fungal culture should then be placed in appropriate transport medium[46-50].

Note that culture can be affected by a number of factors, as the organism is delicate including delays in processing and specimen quality[51].

2.3 Adequate quantity and appropriate number of specimens[44]

Numbers and frequency of specimen collection are dependent on clinical condition of patient.

3 Specimen transport, storage and retention[27,28]

3.1 Optimal transport and storage conditions

For safety considerations refer to Section 1.1.

Specimens should be transported and processed as soon as possible[44].

Samples should be retained in accordance with The Royal College of Pathologists guidelines ‘The retention and storage of pathological records and specimens’[52].

4 Specimen processing/procedure[27,28]

4.1 Test selection

4.1.1 Culture

Laboratory confirmation is conventionally performed by culture and isolation of *B. pertussis* / *B. parapertussis* from nasopharyngeal aspirate or nasopharyngeal swab/ pernasal swab. Culture has an excellent specificity and is useful for confirming pertussis diagnosis when an outbreak is suspected.

It is best to obtain a culture from nasopharyngeal specimens collected during the first 2 weeks of cough. This is when viable bacteria are still present in the nasopharynx. After the first 2 weeks, sensitivity decreases and the risk of false-negatives increases.

It is important to note that *B. pertussis* and *B. parapertussis* are delicate organisms 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.

Cultures are unlikely to be positive in adolescents and adults with more than 3 weeks of coughing[15].

It is also more difficult to recover the organism in vaccinated compared with unvaccinated children[53]. Given the limitations of culture methods, it is important to emphasise that a negative culture does not exclude pertussis.

4.1.2 PCR

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 more than 4 weeks. While nasopharyngeal swabs are preferable for PCR testing, throat swabs may be used if nasopharyngeal swabs are not available, especially in community settings.

Developments in PCR have enabled the detection of co-infections and the differentiation of *B. pertussis* and *B. parapertussis* from other species of *Bordetella* [54-59].

4.1.3 Serology

Detection of anti-pertussis toxin (PT) IgG and anti-filamentous hemagglutinin (FHA) IgG antibodies 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 with *Bordetella* species.

Serology may be helpful to confirm the diagnosis of whooping cough in patients with cough duration of more than 2 to 3 weeks, 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 serological assay is targeted towards older children 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[60]. 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.

4.2 Appearance

N/A

4.3 Sample preparation

For safety considerations refer to Section 1.2.

4.4 Microscopy

N/A

4.5 Laboratory investigation

4.5.1 Culture media, conditions and organisms

Pernasal and nasopharyngeal swabs

Inoculate each agar plate with the swab (refer to Q 5 - Inoculation of culture media for bacteriology).

For the isolation of individual colonies, spread inoculum with a sterile loop.

Nasopharyngeal aspirate

With a sterile loop select a representative portion of specimen and inoculate a loopful to each agar plate (refer to Q 5 - Inoculation of culture media for bacteriology).

For the isolation of individual colonies, spread inoculum with a sterile loop.

Clinical details/ conditions	Specimen	Standard media	Incubation			Cultures read	Target organism(s)
			Temp °C	Atmos	Time		
Pertussis or whooping cough	Pernasal swab, nasopharyngeal aspirate, nasopharyngeal swab	Charcoal blood agar with cefalexin	35-37	air, moist chamber	7d	4d and 7d	*B. pertussis* *B. parapertussis*

4.5.2 PCR and serology

Follow your local validated and approved PCR, qPCR and serology tests (ELISA or others).

The following table describes a comprehensive approach to some of the PCR targets used for detecting co-infections and for species identification and differentiation, at the time of writing [61].

Species	IS*481* [a]	*ptxS1* [b]	hIS*1001* [c]	pIS*1001* [d]
B. pertussis	+	+	-	-
B. parapertussis [e]	-	+	-	+
B. holmesii	+	-	+	-
B. pertussis and *B. paraperussis*	+	+	-	+
B. pertussis and *B. holmesii*	+	+	+	-

(a) Insertion element commonly found in *B. pertussis* and *B. holmesii*
(b) Pertussis toxin subunit S1 found in *B. pertussis* and *B. parapertussis*
(c,d) Targets present in *B. holmesii* and *B. parapertussis*, used in multiplex PCR with IS481 to detect and differentiate *B. pertussis*, *B. parapertussis* and *B. holmesii*.
(e) A specimen positive for pIS1001 may be considered to most probably contain *B. parapertussis*, but the possibility that it is positive for *B. bronchiseptica* cannot be totally excluded.

4.6 Identification

Refer to individual UK SMIs for organism identification.

Matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS) has been shown to be a rapid and powerful identification tool for cultured

isolates because of its reproducibility, speed and sensitivity of analysis. The advantage of MALDI-TOF as compared with other identification methods is that the results of the analysis are available within a few hours rather than several days[62]. Increasingly MALDI-TOF is being used to identify bacteria (including *Bordetella* species) in hospital microbiology laboratories [63]. However, there is currently very little scientific information published on use of MALDI-TOF MS for detection of *Bordetella* species[64]. Refer to UK SMI TP 40 - MALDI TOF MS test procedure.

4.6.1 Minimum level of identification in the laboratory

Bordetella species	"species" level

4.7 Antimicrobial susceptibility testing

N/A

4.8 Referral for outbreak investigations

N/A

4.9 Referral to reference laboratories

For information on the tests offered, turnaround times, transport procedure and the other requirements of the reference laboratory click here for user manuals and request forms.

For the investigation of suspected clusters or outbreaks of pertussis, please contact the Respiratory and Vaccine Preventable Bacteria Reference Unit (RVPBRU), Colindale for the most appropriate test.

Information regarding specialist and reference laboratories is available via the following website: PHE - specialist and reference microbiology tests and services.

Refer to the PHE guidelines for public health management of pertussis.

Organisms with unusual or unexpected resistance, and whenever there is a laboratory or clinical problem, or anomaly that requires elucidation should be sent to the appropriate reference laboratory.

Contact appropriate devolved national reference laboratory for information on the tests available, turnaround times, transport procedure and any other requirements for sample submission:

England and Wales

https://www.gov.uk/specialist-and-reference-microbiology-laboratory-tests-and-services

Scotland

http://www.hps.scot.nhs.uk/reflab/index.aspx

Northern Ireland

http://www.publichealth.hscni.net/directorate-public-health/health-protection

5 Reporting procedure/interpretation

5.1 Culture

Negatives

"*Bordetella pertussis* NOT isolated" or

"*Bordetella parapertussis* NOT isolated"

Positives

"*Bordetella pertussis* isolated" or

"*Bordetella parapertussis* isolated".

5.2 PCR

Suggested reporting for the mentioned targets used in PCR detection of whooping cough.

IS*481*	*ptxS1*	hIS*1001*	pIS*1001*	Reporting
+	+	-	-	*B. pertussis* DNA detected
-	+	-	+	*B. parapertussis* DNA detected
+	-	+	-	*B. holmesii* DNA detected
+	+	-	+	*B. pertussis and B. parapertussis* DNA detected
+	+	+	-	*B. pertussis* and *B. holmesii* DNA detected

5.3 Serology

A case of pertussis is serologically confirmed when anti-PT IgG concentration is >70 International Units per millilitre (IU/mL) in the absence of recent vaccination (within the past year)[65].

A case of parapertussis is serologically confirmed when there is significant anti-FHA IgG increase without an increase in anti-PT IgG, IgM, and IgA antibodies. If both anti-PT IgG and anti-FHA IgG are significantly increase, the results are indicative of infection with *Bordetella* species[66].

6 Notification to PHE[67,68], or equivalent in the devolved administrations[69-72]

The Health Protection (Notification) regulations 2010 require diagnostic laboratories to notify Public Health England (PHE) when they identify the causative agents that are listed in Schedule 2 of the Regulations. Notifications must be provided in writing, on paper or electronically, within seven days. Urgent cases should be notified orally and as soon as possible, recommended within 24 hours. These should be followed up by written notification within seven days.

For the purposes of the Notification Regulations, the recipient of laboratory notifications is the local PHE Health Protection Team. If a case has already been notified by a registered medical practitioner, the diagnostic laboratory is still required to notify the case if they identify any evidence of an infection caused by a notifiable causative agent.

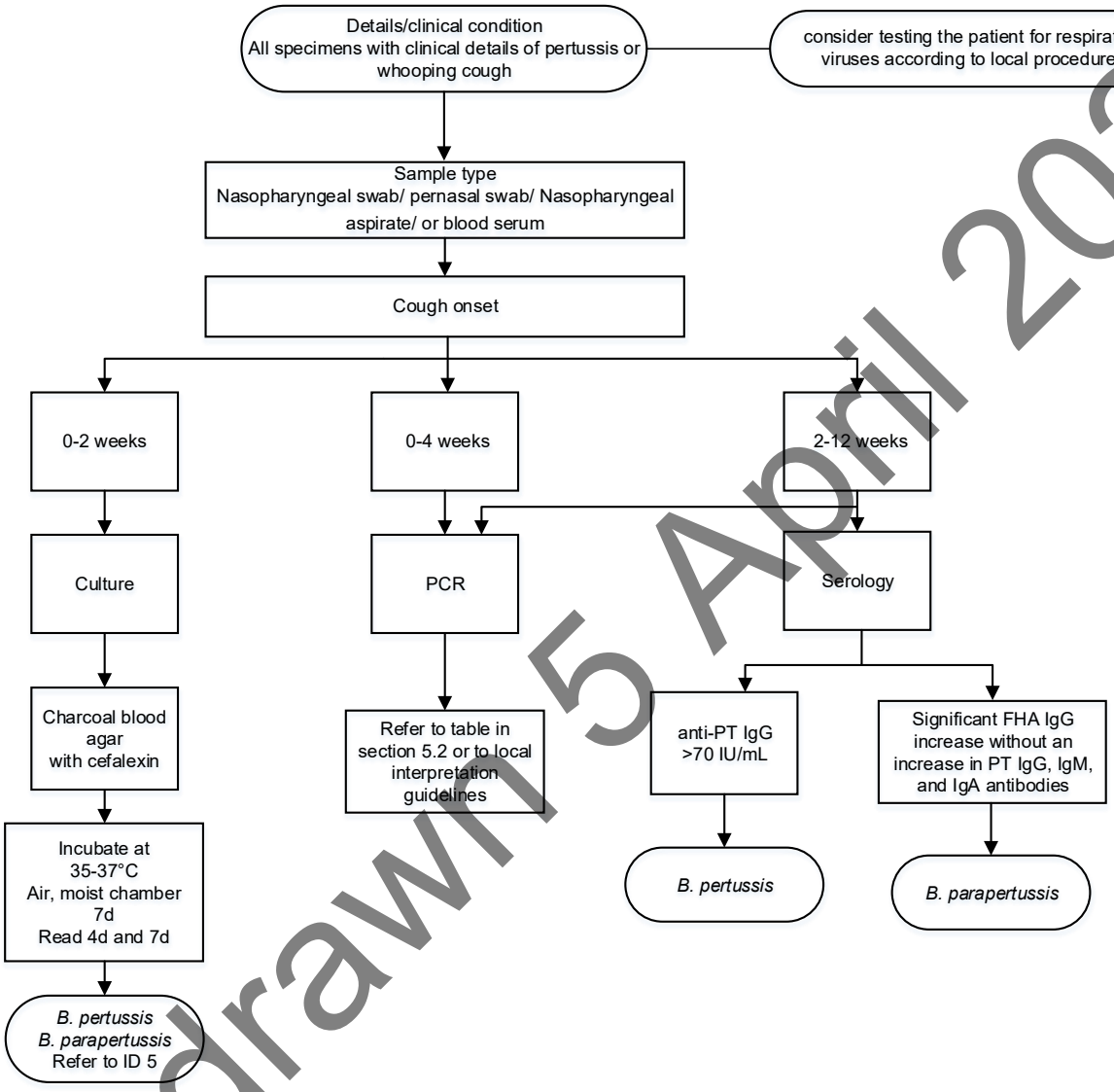
Notification under the Health Protection (Notification) Regulations 2010 does not replace voluntary reporting to PHE. The vast majority of NHS laboratories voluntarily report a wide range of laboratory diagnoses of causative agents to PHE and many PHE Health protection Teams have agreements with local laboratories for urgent reporting of some infections. This should continue.

Note: The Health Protection Legislation Guidance (2010) includes reporting of Human Immunodeficiency Virus (HIV) & Sexually Transmitted Infections (STIs), Healthcare Associated Infections (HCAIs) and Creutzfeldt–Jakob disease (CJD) under 'Notification Duties of Registered Medical Practitioners': it is not noted under 'Notification Duties of Diagnostic Laboratories'.

https://www.gov.uk/government/organisations/public-health-england/about/our-governance#health-protection-regulations-2010

Other arrangements exist in Scotland[69,70], Wales[71] and Northern Ireland[72].

Appendix: Investigation of whooping cough



References

Modified GRADE table used by UK SMIs when assessing references

Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) is a systematic approach to assessing references. A modified GRADE method is used in UK SMIs for appraising references for inclusion. Each reference is assessed and allocated a grade for strength of recommendation (A-D) and quality of the underlying evidence (I-VI). A summary table which defines the grade is listed below and should be used in conjunction with the reference list.

Strength of recommendation	**Quality of evidence**
A Strongly recommended	I Evidence from randomised controlled trials, meta-analysis and systematic reviews
B Recommended but other alternatives may be acceptable	II Evidence from non-randomised studies
C Weakly recommended: seek alternatives	III Non-analytical studies, for example, case reports, reviews, case series
D Never recommended	IV Expert opinion and wide acceptance as good practice but with no study evidence
	V Required by legislation, code of practice or national standard
	VI Letter or other

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7. Public Health England. Pertussis: laboratory confirmed cases reported in England 2017. 2017. **A, V**

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