



Public Health
England

Assessment of risk to close contacts of patients with lower respiratory tract infection due to Panton-Valentine leukocidin-positive *Staphylococcus aureus* in England

Enhanced case and household contact
protocol

Version 1.3

About Public Health England

We are a new national executive agency formed in 2013 from a number of expert organisations in public health. Our status ensures we have operational autonomy and professional and scientific credibility.

We protect and improve the nation's health and wellbeing, and tackle health inequalities so that the poorest and most poorly benefit most.

We provide a nationwide, integrated public health service, supporting people to make healthier choices. We provide expertise, information and intelligence to public health teams based in local authorities and the NHS to secure the biggest improvements in the public's health.

Public Health England
133-155 Waterloo Road
Wellington House
London SE1 8UG
Tel: 020 7654 8000
<http://www.gov.uk/phe>
[@PHE_uk](#)

Prepared by: Dr P Conaglen (April 2013). Updated Dr G Dabrera (10th May 2013)
For queries relating to this document, please contact: Dr G Dabrera
(gavin.dabrera@phe.gov.uk) or Dr I Evlampidou (iro.evlampidou@phe.gov.uk)

© Crown Copyright 2013
Published May 2013
PHE gateway number: 2013063

This document is available in other formats on request. Please call 020 8327 7018
or email publications@phe.gov.uk

Contents

| | |
|--|----|
| About Public Health England | 2 |
| Contents | 3 |
| Introduction | 4 |
| Background | 4 |
| Methods | 6 |
| Study Design | 6 |
| Case definitions | 6 |
| Data Collection for cases and their household contacts | 8 |
| Triggering data collection | 8 |
| Data Collection for cases | 9 |
| Data Collection for household contacts | 10 |
| Assistance with this investigation | 11 |
| Analysis and Interpretation of data | 11 |
| Precision of estimates | 12 |
| Ethical and confidentiality issues | 13 |
| Security of patient identifiable information | 13 |
| Maintenance of confidentiality and anonymity of data | 13 |
| Investigating group in alphabetical order | 13 |
| Acknowledgments | 14 |
| Appendix A: Flow chart of Actions | 15 |
| Appendix B: Fields for household contact line listing | 16 |
| PVL - <i>S. aureus</i> lower respiratory tract infection enhanced surveillance questionnaire | 17 |
| PVL - <i>S. aureus</i> lower respiratory tract infection enhanced surveillance questionnaire | 24 |
| Further assistance with forms | 30 |

Introduction

Background

Panton-Valentine leukocidin (PVL) is a cytotoxin that can destroy white blood cells and cause extensive tissue necrosis and severe infection. It is associated with increased virulence in certain strains of *Staphylococcus aureus*. PVL-positive strains of *S. aureus* typically cause skin and soft tissue infections (SSTI) with the potential for transmission of both carriage and SSTI between household members and close contacts. On very rare occasions, PVL-positive *S. aureus* can lead to more severe invasive infections, such as bacteraemia or necrotising pneumonia. The latter is sometimes associated with an influenza-like prodrome or viral respiratory illness. The factors which predispose any given individual in a household to develop such invasive infections, whilst others do not, are not well understood. The development of secondary cases of PVL-positive severe lower respiratory tract infection (LRTI) in a household is uncommon.

Between 6th December 2012 and 10th May 2013, 54 cases of community-acquired PVL-positive staphylococcal LRTI have been reported for investigation. This compares to a background of approximately 30–40 such cases being confirmed each year in England, usually peaking in the winter months. Amongst these cases, at least 17 have died. There have been at least 3 household clusters of cases identified (compared with 1 such cluster between 2008 and late 2012). Many cases have reported an influenza-like prodrome and 18 have been confirmed as having influenza co-infection, to date.

Whilst PVL testing is not mandatory, based on our experience of referrals and the known association between severe pneumonia and PVL, we believe that a large proportion of isolates of *S. aureus* from LRTIs are sent for PVL testing. Also, we are not aware of any changes to referral patterns or processes which might explain this increase in both confirmed cases and household clusters.

In the light of this, we are undertaking an outbreak investigation that entails gathering information regarding these cases and their contacts, in order to inform measures to prevent and control this serious infection. A better understanding of the risk to household contacts and the effects of prophylactic measures will help direct any public health response to this recent increase in cases and guide the ongoing public health management and investigation of both cases and their contacts (e.g. the use of antiviral agents and vaccinations; optimising treatment algorithms; modifications to surveillance arrangements and guidance documents).

Protocol Objectives

The broad aim of this public health investigation is to define the risks of household transmission and factors that might modify that risk. The investigation will specifically aim to increase our understanding of the epidemiology of known confirmed cases and identify potential risk factors for the development of PVL-positive *S. aureus* LRTI in household contacts of these cases in order to inform public health guidance.

The primary objectives are to identify/provide estimates of:

- Descriptive clinical, epidemiological and microbiological characteristics of known cases.
- Secondary attack rate for household contacts who develop LRTI due to PVL-positive *S. aureus*. The secondary attack rate is defined as the probability that infection occurs among susceptible persons within a reasonable incubation period following known contact with an infectious person or source.
- Relative risk for household contacts of known cases to develop LRTI due to PVL-positive *S. aureus* depending on the following exposures:
 - any influenza-like-illness
 - confirmed respiratory viral infection (e.g. influenza, RSV, parainfluenza etc)
 - other exposures (e.g. smoking, skin or soft tissue infection [SSTI])

This information will be used to inform any further public health recommendations for surveillance, investigation or interventions.

Methods

Study Design

This is a household cohort study in which questionnaires will be used to collect descriptive data for both cases and contacts. The time period for inclusion of cases ranges between 1st December 2012 and 10th May 2013. Data collection will largely be retrospective although some cases may be investigated prospectively. The outcomes for exposed household contacts (for the exposures above) will be compared with non-exposed household contacts.

Case definitions

A] CONFIRMED CASE

- A patient who has PVL-positive *S. aureus* isolated from either a blood culture or respiratory sample (e.g.: broncho-alveolar lavage, tracheal aspirate, sputum, pleural fluid) between 01-Dec-2012 and 10-May-2013, inclusive

AND

- clinical or radiological evidence of a lower respiratory tract infection.

B] PROBABLE CASE (please check footnote variations for children)

- A patient who has presented to hospital with 1 or more of: confusion; urea \geq 7mmol/L; respiratory rate \geq 30 per min¹; blood pressure <90 mmHg systolic or \leq 60 mmHg diastolic²

AND

¹ For infants 6–12 months use RR>50 breaths per min, for children 12 months to 5 years use RR>40 per min.

² For children <5 years please replace blood pressure criteria with capillary refill time >2 secs.

- who at any point during this illness is found to have 2 or more of:
temperature >39°C³; heart rate >140bpm⁴; haemoptysis; leukopaenia;
CRP >200g/L; radiological evidence of lobar or interstitial infiltrates

AND

- who is epidemiologically linked to a confirmed case

AND

- who has **NOT** had a PVL-positive *S. aureus* isolate from either a blood culture or respiratory sample (e.g.: broncho-alveolar lavage, tracheal aspirate, sputum, pleural fluid).

C] HOUSEHOLD CONTACT

- Any person who has had prolonged close contact with a confirmed case in a household-type setting during the five days before onset of this illness in the case. Examples of such contacts would be those living and/or sleeping in the same household (including extended household), pupils in the same dormitory, boy/girlfriends, or university students sharing a kitchen in a hall of residence.

(NB: this is based on the prolonged close contact definition used in the public health management of meningococcal disease. Investigators should therefore employ a similar approach when identifying contacts. If a case resides in an institutional or high occupancy setting (e.g. care home, military barracks etc) then investigators may wish to call Colindale to discuss the most appropriate delineation of 'household contacts'. Telephone details can be found in section 2.3.4 of this protocol).

Other classifications:

1] Primary case: A primary case is defined as an individual who meets the above confirmed case definition and has the earliest date of onset of this illness in a

³ For infants 0–3 months please use temperature >38°C.

⁴ For children < 5 years please do not tick this item at all.

particular household setting. Those cases with onset dates within 24 hours of the onset date of another household case are considered '**co-primary cases**'.

2] Secondary confirmed case: After classifying the primary / co-primary confirmed cases, a secondary confirmed case is defined as any contact who meets the above confirmed case definition and whose illness onset is:

- ≥ 24 hours after the onset of the primary (or first co-primary) case
- AND**
- < 10 days after the last household contact with the primary (or first co-primary) case

3] Secondary probable case: After classifying the primary / co-primary confirmed cases, a secondary probable case is defined as any contact who meets the above probable case definition and whose illness onset is:

- ≥ 24 hours after the onset of the primary (or first co-primary) case
- AND**
- < 10 days after the last household contact with the primary (or first co-primary) case

4] Confirmed household cluster: Two or more confirmed cases in one household.

5] Probable household cluster: Households with one confirmed case and one or more probable cases. A sensitivity analysis will be conducted which will include both probable and confirmed household clusters.

Please note, the only probable cases to be included in this study are secondary probable cases; i.e. an unconfirmed 'primary probable' case would not trigger this enhanced investigation process and management and investigation of such a case would be as per local routine practice.

Data Collection for cases and their household contacts

Triggering data collection

The management of cases of PVL and their contacts should be as per existing PHE guidance.^{5,6} The public health investigation process will be triggered when

⁵ http://www.PHE.org.uk/webc/PHEwebFile/PHEweb_C/1267551719486

microbiology departments inform a Health protection team (HPT) of a confirmed case (this may come from either a local microbiology laboratory or from PHE Colindale). The HPT should then proceed to complete the actions described below (these are also outlined in the flow chart in Appendix A). It is predicted that data collection will be largely retrospective although some cases may be investigated prospectively.

The process below should be conducted for all cases with a positive specimen between 1st December 2012 and 10th May 2013. Information on the case and their household contacts should be sought through a combination of face-to-face or telephone interviews, interviews of health care providers and/or review of medical records where required. Questionnaires can be found in the appendices of this document. Notes on completion of these forms can be found in Appendix E.

When the local microbiology laboratory or PHE Colindale inform a Health Protection Team (HPT) of a new confirmed primary case the process below should be commenced.

Data Collection for cases

i. **Unique case number**

For each case (either primary, secondary confirmed or secondary probable) the HPT should securely e-mail the name, date of birth and case classification to: respiratory.lead@phe.gov.uk to request a unique case number from PHE Colindale. This number should be used on all case and contact forms which relate to that case. In the event of co-primary cases, a different unique case number will be provided for each of the co-primary cases. This will allow investigators to use these unique case numbers to link each of the cases with their respective household contacts on the forms below.⁷

⁶ http://www.PHE.org.uk/webc/PHEwebFile/PHEweb_C/1218699411960

⁷ For example, if co-primary Cases A and B live in the same house, the girlfriend of Case A may live elsewhere and therefore may be a contact of Case A but not a contact of co-primary Case B.

ii. **Contact line list**

For each case, a list of household contacts should be drawn up using the Contact line list (see Appendix B). This list should include the unique case number of the relevant confirmed case. The HPT should then number each household contact with a unique contact number which the HPT will generate themselves (e.g. C001, C002, C003 etc). The contact line list should be securely emailed to PHE Colindale when complete at:

respiratory.lead@phe.gov.uk. Should any subsequent amendments to this line listing be required – please return a revised version to PHE Colindale, noting that this is a revised version.

iii. **Case report – Form 1**

Section A

Each case (or family members, as a proxy, if the case is too ill) should be interviewed as soon as possible after identification using Section A of Case report – Form 1 (see Appendix C). Section A of Form 1 includes: identifiers, basic demographic information, past medical history and presenting illness details.

Section B

Section B of Form 1 relates to investigation results, treatment and outcomes and should only be completed ≥ 21 days after the onset of this illness in the case. It is anticipated that section B should be able to be completed from medical records and discussion with relevant healthcare staff. It should not require the case to be re-interviewed.

In retrospective investigations, where a contact has become a secondary probable case or secondary confirmed case, please complete all forms relevant to this individual having been both a contact and a case.

Data Collection for household contacts

The key activities for the initial investigation of household contacts are:

i. **Contact report – Form 2**

Once household contacts are identified, they should be interviewed ≥ 10 days

after their last contact with the case in the household setting (i.e. prior to the case being hospitalised). Contact report – Form 2 should be completed for each contact interviewed (see Appendix D). This form contains identifiers, basic demographic information, past medical history, information about exposure to the case and other cases of *S. aureus* infection and details of any illness and interventions in the contact.

A household contact who is subsequently found to meet the criteria of a confirmed or probable case of LRTI due to PVL-positive *S. aureus* would be re-classified as such and the above processes (from ‘Data collection on cases’) should be repeated for this new case. As mentioned above, Form 2 should also be completed in such individuals.

Given the often aggressive nature of these infections, it will be important to attempt to complete each stage of the above processes, even in the unfortunate event of the death of a case.

Assistance with this investigation

Should HPTs require any clarification of this protocol or assistance with investigation they should contact either Gavin Dabrera at PHE Colindale on 0208 327 6166 or Iro Evlampidou at PHE South West on 0117 968 9134. The Field Epidemiology Network may be able to provide support to HPTs for data collection if required; this should be discussed on a unit by unit basis as the need arises.

Analysis and Interpretation of data

Data will be recorded on either hardcopy or electronic data collection forms by health protection teams and e-mailed to PHE Colindale at respiratory.lead@phe.gov.uk to be entered into a database for analysis and interpretation. The descriptive analysis of known cases should provide further insight into the clinical spectrum and course of disease and analysis of data from household contacts may improve our understanding of potential risk factors for severe PVL infection.

Precision of estimates

Table 2 below provides the precision, as measured by 95% confidence intervals (CI), across a range of different assumed household secondary attack rates (SAR), numbers of primary cases and numbers of household contacts.

Table 2: 95% CIs for a range of assumed PVL LRTI secondary attack rates (SAR)

(a) 2 contacts per case

| number of index cases | number of contacts | SAR estimates (95% CI) | | | |
|-----------------------|--------------------|------------------------|---------------|---------------|---------------|
| | | 2.5% | 5.0% | 7.5% | 10.0% |
| 20 | 40 | (0.1%, 13.2%) | (0.6%, 16.9%) | (1.6%, 20.4%) | (2.8%, 23.7%) |
| 25 | 50 | (0.1%, 11.4%) | (0.8%, 15.2%) | (2.0%, 18.6%) | (3.3%, 21.8%) |
| 30 | 60 | (0.2%, 10.3%) | (1.0%, 13.9%) | (2.3%, 17.3%) | (3.8%, 20.5%) |
| 35 | 70 | (0.2%, 9.4%) | (1.2%, 13.0%) | (2.6%, 16.4%) | (4.1%, 19.5%) |

(b) 2.5 contacts per case

| number of index cases | number of contacts | SAR estimates (95% CI) | | | |
|-----------------------|--------------------|------------------------|---------------|---------------|---------------|
| | | 2.5% | 5.0% | 7.5% | 10.0% |
| 20 | 50 | (0.1%, 11.4%) | (0.8%, 15.2%) | (2.0%, 18.6%) | (3.3%, 21.8%) |
| 25 | 63 | (0.2%, 10.0%) | (1.1%, 13.6%) | (2.4%, 17.0%) | (3.9%, 20.2%) |
| 30 | 75 | (0.3%, 9.1%) | (1.3%, 12.6%) | (2.7%, 16.0%) | (4.3%, 19.1%) |
| 35 | 88 | (0.4%, 8.3%) | (1.5%, 11.9%) | (3.0%, 15.1%) | (4.6%, 18.3%) |

(c) 3 contacts per case

| number of index cases | number of contacts | SAR estimates (95% CI) | | | |
|-----------------------|--------------------|------------------------|---------------|---------------|---------------|
| | | 2.5% | 5.0% | 7.5% | 10.0% |
| 20 | 60 | (0.2%, 10.3%) | (1.0%, 13.9%) | (2.3%, 17.3%) | (3.8%, 20.5%) |
| 25 | 75 | (0.3%, 9.1%) | (1.3%, 12.6%) | (2.7%, 16.0%) | (4.3%, 19.1%) |
| 30 | 90 | (0.4%, 8.2%) | (1.5%, 11.7%) | (3.0%, 15.0%) | (4.7%, 18.1%) |
| 35 | 105 | (0.4%, 7.6%) | (1.7%, 11.1%) | (3.3%, 14.3%) | (5.0%, 17.4%) |

(d) 3.5 contacts per case

| number of index cases | number of contacts | SAR estimates (95% CI) | | | |
|-----------------------|--------------------|------------------------|---------------|---------------|---------------|
| | | 2.5% | 5.0% | 7.5% | 10.0% |
| 20 | 70 | (0.2%, 9.4%) | (1.2%, 13.0%) | (2.6%, 16.4%) | (4.1%, 19.5%) |
| 25 | 88 | (0.4%, 8.3%) | (1.5%, 11.9%) | (3.0%, 15.1%) | (4.6%, 18.3%) |
| 30 | 105 | (0.4%, 7.6%) | (1.7%, 11.1%) | (3.3%, 14.3%) | (5.0%, 17.4%) |
| 35 | 123 | (0.5%, 7.1%) | (1.9%, 10.5%) | (3.5%, 13.7%) | (5.3%, 16.7%) |

(e) 4 contacts per case

| number of index cases | number of contacts | SAR estimates (95% CI) | | | |
|-----------------------|--------------------|------------------------|---------------|---------------|---------------|
| | | 2.5% | 5.0% | 7.5% | 10.0% |
| 20 | 80 | (0.3%, 8.7%) | (1.4%, 12.3%) | (2.8%, 15.6%) | (4.4%, 18.8%) |
| 25 | 100 | (0.4%, 7.8%) | (1.6%, 11.3%) | (3.2%, 14.5%) | (4.9%, 17.6%) |
| 30 | 120 | (0.5%, 7.1%) | (1.9%, 10.6%) | (3.5%, 13.8%) | (5.3%, 16.8%) |
| 35 | 140 | (0.6%, 6.5%) | (2.0%, 10.0%) | (3.7%, 13.2%) | (5.6%, 16.2%) |

Ethical and confidentiality issues

Security of patient identifiable information

Collection of patient data for this public health outbreak investigation initiative falls within the PHE's National Information Governance Board (NIGB) approval to process patient identifiable information for the purposes of "monitoring and managing outbreaks of communicable disease", as defined in the Health Service (Control of Patient Information) Regulations 2002 (SI 1438), and in accordance with Section 251 of the NHS Act 2006. This allows NHS organisations to disclose identifiable patient information to the PHE without the explicit consent of the patient concerned while remaining within the confines of the Data Protection Act. Accordingly the PHE Research and Development Office have approved this investigation and confirmed that formal ethical approval is not required.

Maintenance of confidentiality and anonymity of data

The PHE has in place a number of security measures to prevent unauthorised or unlawful access to personal data held on site. All Health Protection Teams and PHE-Colindale staff handling surveillance data will do so according to established information security procedures as a means of ensuring integrity and confidentiality of data gathered and generated by the this surveillance initiative. These procedures apply both to physical and electronic data formats.

Patient identifiable information will be removed as soon as practicable and in accordance to Caldicott data retention policy. All electronic data will be held in restricted access password protected files and all paper documents locked in filing cabinets.

Investigating group in alphabetical order

Ms Rachel Campbell; Dr Philip Conaglen; Dr Gavin Dabrera; Dr Joanna Ellis; Dr Iro Evlampidou; Dr Maya Gobin; Dr Robert Hill; Professor Alan Johnson; Professor Angela Kearns; Dr Theresa Lamagni; Dr Angie Lackenby; Ms Janet McCulloch; Dr Isabel Oliver; Professor Richard Pebody; Dr Bruno Pichon; Dr Nandini Shetty; Dr Mary Slack; Dr Anna Vickers.

Acknowledgments

With sincere thanks to all Health protection teams throughout England for their support in conducting this investigation. Thanks also go to Dr Vanessa Saliba and Ms Oluwakemi Legbe from the North East and North Central London Health protection team for their help in piloting this survey; the staff of the Field Epidemiology Network; and to Dr George Kafatos at PHE Colindale for statistical support.

Appendix B: Fields for household contact line listing

For each case, please copy the fields below into one row of a new Excel spreadsheet and complete details in a new row for each household contact. The first four items relate to the associated case and will be repeated against each contact. If a household has co-primary cases please generate a new household contact line listing for each primary case and make a note that these are co-primary cases.

The first four columns relate to the

The remaining columns relate to each contact of the case

Examples only

| Unique case number | Case DOB (DD/MM/YYYY) | Form 1 completed (Y/N) (for case) | Unique contact number (e.g.C001)* | First name(s) | Surname | Sex (M/F) | Age (years) | Relationship to case | Status (primary case, co-primary case, secondary confirmed case, secondary probable case, contact)† | Form 2 completed (for contact) | Notes (any relevant remarks) |
|--------------------|-----------------------|-----------------------------------|-----------------------------------|---------------|---------|-----------|-------------|----------------------|---|--------------------------------|------------------------------|
| e.g. 999 | 12/05/1985 | Y | C001 | John | Smith | M | 22 | Brother | Secondary confirmed | Y | |
| e.g. 999 | 12/05/1985 | Y | C002 | Elizabeth | Smith | F | 67 | Grandmother | Secondary probable | N | |

* Note: please number the contacts sequentially e.g. C001, C002, C003 etc. If an HPT has more than one case, this contact numbering can start again from C001 on each line listing. † Please choose the first status description from this list which applies.

Appendix C: Case report Form-1, SECTION A

PVL - *S. aureus* lower respiratory tract infection enhanced surveillance questionnaire

Case report Form-1

Suggested key elements to discuss with informants

You (or your family member/other) recently had a respiratory infection with a particular type of bacteria called: PVL-positive *Staphylococcus aureus*. These bacteria are occasionally found on the skin of healthy individuals and sometimes cause infections, such as boils and abscesses. In very rare instances they can cause severe respiratory infections such as the one you (your family member/other) had.

Public Health England is currently investigating an apparent increase in the number of cases of respiratory infections around England caused by these bacteria. To investigate why some people become severely ill with these bacteria and others do not, we are conducting interviews with people who have had this disease and with their household contacts. We hope this will improve our understanding of this condition and help guide the future prevention and treatment of this disease.

For this reason we would be grateful if you would answer a series of questions relating to this condition. Any information you give us will be treated in strict confidence. It will be stored securely and used only by the researchers and doctors involved in this investigation. Any published findings will be anonymised such that you (your family member/other) cannot be identified.

The questionnaire contains questions about your (your family member's/other) medical history, possible risk factors for PVL infection and details about the illness. Your participation is entirely voluntary. If you choose to participate you are free to withdraw from the interview at any point.

If you have any questions about this investigation, please do not hesitate to contact us, either by email or phone [*please provide local HPT contact details*].

Form completion

If completing this form electronically:

- for multiple choice questions please delete as appropriate to leave the correct response.
- for checkboxes, please place an X in the appropriate box.

If completing this form by hand please tick checkboxes or circle the correct response as appropriate.

Appendix D (notes on form completion) further clarifies the intent of a number of questions.

-

Please complete Section A as soon as possible after the identification of a case

Most Section A responses will come from case interview

Appendix C: Case report Form-1, SECTION A

Unique case number (please request from PHE Colindale†)

| | | |
|--|--|--|
| | | |
|--|--|--|

Initial case classification

a) Was PVL positive *S. aureus* isolated from a blood culture **or** respiratory samples?

Yes / No

b) Is there clinical or radiological evidence of a lower respiratory tract infection

Yes / No

- If a = Yes and b = Yes, then this is a **confirmed case**.
- If not and you believe this is a secondary probable case, then you should have already completed Contact report Form 2 for this person; the last page of which will tell you if they are a probable case.

Please mark:

Confirmed case

Probable case

Case sequence

Please mark:

Primary

Co-primary

Secondary

Link to Form-2

Was this case also the household contact of another case?

Yes / No

If yes, please provide the two codes from the top of Form 2 for this case:

Unique contact number

C

Unique case number (of associated household case)

Reporter details (staff member completing this form)

Name of reporter

Position

E-mail

Date of interview

Organisation

Telephone

Informant details (case or family member responding to questions about the case)

Informant (please circle)

Case / Other

If other:

Relationship with case

Contact details including telephone

Patient information

NHS number

Forename(s)

Sex

Occupation

Ethnic background

Residential setting

Date of birth

Surname

Address including postcode

Carer

Smoking history at the time of illness onset

Please mark:

Smoker

Ex-smoker

Never smoked

Unknown

If ex-smoker or never smoked, do others smoke inside shared-areas of the house?

Yes / No / Unknown

Appendix C: Case report Form-1, SECTION A

| Patient medical history in the six months prior to this illness | | |
|---|--------------------|---------|
| Condition or behaviour | Yes / No / Unknown | Details |
| Chronic lung problems | Yes / No / Unknown | |
| Diabetes | Yes / No / Unknown | |
| Dialysis | Yes / No / Unknown | |
| Immunosuppression | Yes / No / Unknown | |
| Tattoo, piercing or other body modification | Yes / No / Unknown | |
| Injecting drug use | Yes / No / Unknown | |
| Other recreational drug use | Yes / No / Unknown | |
| Eczema | Yes / No / Unknown | |
| Atopic dermatitis | Yes / No / Unknown | |
| Psoriasis | Yes / No / Unknown | |
| Skin and soft tissue infections (e.g. boils or abscesses) | Yes / No / Unknown | |
| Other skin lesions | Yes / No / Unknown | |

If yes to either skin and soft tissue infections or other skin lesions, please describe the type of infection and date of onset

Travel outside the UK in the **3 months** prior to this illness?

Yes / No / Unknown

If yes, where to (country) and when (month, year)

Previous confirmed S. aureus infection (any body site) or colonisation in the 12 months prior to this illness

Yes / No / Unknown

If yes, provide the following for this previous infection

Methicillin resistance

MRSA / MSSA / Unknown

PVL-status

Positive / Negative / Unknown

Please check all which apply for the case:

Health or social care worker Takes part in contact sports Care home resident

Visits a gymnasium Military personnel Attends any other institutional setting (e.g. prison, nursery – please specify)

Was the case eligible for seasonal influenza vaccination this flu season?

Yes / No / Unknown

If yes, what was the indication?:

Age >65 years

Health/social care worker

Long-stay facility resident

Chronic disease (please circle any which apply)

Respiratory / Renal / Liver / Neurological / Diabetes / Immunosuppression / Pregnant

Carer

Other (please state)

Did the case receive seasonal influenza vaccination during the current flu season?

Yes / No / Unknown

If yes, date of vaccination, if known:

/ /

Appendix C: Case report Form-1, SECTION A

| Contact with other cases | | | |
|---|--|---|----------------------|
| Has the patient had contact with another confirmed or suspected case of PVL <i>S. aureus</i> infection (of any kind, not only pneumonia) in the 6 months prior to this illness? | Yes / No / Unknown | If yes: Date of onset of PVL infection <u>in the other case</u> , if known: | / / |
| | | Unique case number of the other case (if known) | |
| If yes, please provide the following information of this other confirmed or suspected case (if available): | | | |
| Type of contact | Household / Social / Work / Healthcare setting / Other (please state): | | |
| Clinical status | Infected / Colonised / Suspected / Unknown / Other (please state): | | |
| Forename | | Surname | |
| Sex | Male / Female / Unknown | Date of birth | / / |
| Date of onset of infection | / / | Estimated dates of contact | From: / / To: / / |
| | | Estimated duration of contact | |

| Illness in the case | |
|--|-----|
| Date of first onset of symptoms of this illness DD/MM/YYYY | / / |
| Date of hospital admission | / / |

| Signs and symptoms in the time between onset of this illness and hospital admission | | |
|---|--------------------|---------------|
| Sign/symptom | Yes / No / Unknown | Date of onset |
| Altered mental status | Yes / No / Unknown | / / |
| Shortness of breath | Yes / No / Unknown | / / |
| Cough | Yes / No / Unknown | / / |
| Haemoptysis | Yes / No / Unknown | / / |
| Fever | Yes / No / Unknown | / / |
| Chills | Yes / No / Unknown | / / |
| Rash | Yes / No / Unknown | / / |
| Nausea | Yes / No / Unknown | / / |
| Vomiting | Yes / No / Unknown | / / |
| Sore throat | Yes / No / Unknown | / / |
| Chest pain | Yes / No / Unknown | / / |
| Muscle aches | Yes / No / Unknown | / / |
| Headache | Yes / No / Unknown | / / |

«« STOP »»

Please do not complete section B of Form 1 (overleaf) until ≥ 21 days after the onset of this illness in this case

Appendix C: Case report Form-1, SECTION B

«« STOP »»

Please do not complete the remainder of Form 1 until ≥ 21 days after the onset of this illness symptoms in this case
Most Section B responses will come from clinical records

Unique case number (repeated from the top of Section A)

| | | |
|--|--|--|
| | | |
|--|--|--|

Date of completion of the remainder of this form

| | | | | |
|--|---|--|---|--|
| | / | | / | |
|--|---|--|---|--|

Reporter details (staff member completing this section)

Name

Organisation

Final case classification

Please mark:

Confirmed

Probable

At the time of initial hospital assessment did the patient have any of the following

| | |
|-------------------------------------|--------------------|
| Confusion | Yes / No / Unknown |
| Erythroderma | Yes / No / Unknown |
| Adult respiratory distress syndrome | Yes / No / Unknown |
| Cardiac arrhythmia | Yes / No / Unknown |

NB: for the remaining items, if 'Yes' please give the most extreme value in the final column

| | | |
|--|--------------------|--|
| Urea ≥ 7 mmol/L | Yes / No / Unknown | |
| Respiratory rate ≥ 30 per min | Yes / No / Unknown | |
| Blood pressure < 90 mmHg systolic or ≤ 60 mmHg diastolic | Yes / No / Unknown | |
| Temperature $> 39^\circ\text{C}$ | Yes / No / Unknown | |
| Heart rate > 140 bpm | Yes / No / Unknown | |

Clinical and laboratory findings (most abnormal value, on day of PVL positive *S. aureus* culture ± 1 day)

WBC count

| | |
|--|---------------|
| | mm^3 |
| | |

Neutrophil count

| | |
|--|---------------|
| | mm^3 |
| | |

Platelets

CRP

g/L

Was PVL positive *S. aureus* isolated from any non-respiratory site (please circle)?

Blood culture / CSF / Abscess / Joint fluid / Other (please state):

Was any other organism(s) isolated from respiratory samples?

Yes / No / Unknown

If yes, please name the organism(s) and give sample date of first positive culture(s):

Was the patient tested for influenza or other respiratory viruses?

Yes / No / Unknown

If yes, please enter results here:

Type of sample

Date of sample

Positive results

| |
|-----|
| |
| / / |
| |

Radiology findings

If chest X-ray was performed, was it abnormal?

Yes / No / Unknown

Appendix C: Case report Form-1, SECTION B

If yes, please mark all which apply:

| | | | | | |
|-------------------------|--------------------------|----------------------------|--------------------------|--------------------------|--------------------------|
| Single lobar infiltrate | <input type="checkbox"/> | Multiple lobar infiltrates | <input type="checkbox"/> | Interstitial infiltrates | <input type="checkbox"/> |
| Empyema | <input type="checkbox"/> | Cavitation | <input type="checkbox"/> | Pleural effusions | <input type="checkbox"/> |
| Other, please state | <input type="text"/> | | | | |

Please describe any additional findings on CT or MRI, if done:

Treatment

Which antibiotics were used initially?

| Drug | Dose | Frequency | Date started | Date stopped |
|------|------|-----------|--------------|--------------|
| | | | | |

Were the antibiotics changed empirically on clinical grounds?

Yes / No / Unknown

Were the antibiotics changed as a result of microbiological confirmation?

Yes / No / Unknown

If yes, please describe rationale for changes here and add details of the revised regimen below

| Drug | Dose | Frequency | Date started | Date stopped |
|------|------|-----------|--------------|--------------|
| | | | | |

Appendix C: Case report Form-1, SECTION B

Was intravenous immunoglobulin (IVIG) used?

Yes / No / Unknown

If yes, date given:

/ /

Which antivirals were given (if any)?

| Drug | Dose | Frequency | Date started | Date stopped |
|------|------|-----------|--------------|--------------|
| | | | | |

If antivirals given, were they for:

Treatment

Prophylaxis

Unknown

Augmented or critical care

| | | | | | |
|----------------------------|----------------|------------------------------|--|----------------------------|----------------|
| ICU admission | Yes/No/Unknown | Ventilation required | Non-invasive / Mechanical / None / Unknown | Was ECMO <u>required</u> ? | Yes/No/Unknown |
| Date of ICU admission | / / | Date of ventilation | / / | Was ECMO <u>provided</u> ? | Yes/No/Unknown |
| Date of discharge from ICU | / / | Length of ventilation (days) | / / | Date of ECMO (days) | / / |
| Developed septicaemia | Yes/No/Unknown | Multi-organ failure | Yes/No/Unknown | Length of ECMO (days) | |

Patient status at ≥21 days after the onset of this illness

Location of patient:

Inpatient

At home

Other (please state)

Vital status:

Alive

Deceased

If the patient is deceased, please complete the following:

Date of death

/ /

Please select the single most appropriate option from the following:

Death attributed to PVL LRTI
 PVL LRTI contributed to death
 PVL LRTI was incidental to death
 Unknown

Please return all completed forms to: respiratory.lead@phe.gov.uk

Appendix D: Contact report Form-2

PVL - *S. aureus* lower respiratory tract infection enhanced surveillance questionnaire

Contact report Form-2

Suggested key elements to discuss with informants

You (or your family member/other) have been identified as someone who has had close contact with a patient who had a respiratory infection with a particular type of bacteria called: PVL-positive *Staphylococcus aureus*. These bacteria are occasionally found on the skin of healthy individuals and sometimes cause infections, such as boils and abscesses. In very rare instances they can cause severe respiratory infections such as the one you (your family member/other) had.

Public Health England is currently investigating an apparent increase in the number of cases of respiratory infections around England which are caused by these bacteria. To investigate the reasons why some people become severely ill with these bacteria and others do not, we are conducting interviews like this, with people who have had this disease and with their close contacts. We hope this will improve our understanding of this condition and help guide the future prevention and treatment of this disease.

For this reason we would be grateful if you would answer a series of questions relating to this condition. Any information you give us will be treated in strict confidence. It will be stored securely and used only by the researchers and doctors involved in this investigation. Any results or findings will be anonymised so that you (your family member/other) cannot be identified.

The questionnaire contains questions about your (your family member's/other) contact with the patient, your medical history, risk factors for PVL infection and the development of flu-like symptoms. Your participation is voluntary. If you choose to participate you are free to withdraw from the interview at any point.

If you have any questions about this investigation, please do not hesitate to contact us, either by email or phone [*insert local contact details here*].

Form completion

If completing this form electronically:

- for multiple choice questions please delete as appropriate to leave the correct response.
- for checkboxes, please place an X in the appropriate box.

If completing this form by hand please tick checkboxes or circle the correct response as appropriate.

Appendix D (notes on form completion) further clarifies the intent of a number of questions.

-

Appendix D: Contact report Form-2

Please complete this form ≥ 10 days after last contact with the case in a household setting
Most of Form-2 will come from contact interview

Unique contact number*

| | | | |
|----------|--|--|--|
| C | | | |
|----------|--|--|--|

Unique case number (of associated household case)†

| | | |
|--|--|--|
| | | |
|--|--|--|

Reporter details (staff member completing this form)

| | | | |
|------------------|--|------------------|-----|
| Name of reporter | | Date interviewed | / / |
| Position | | Organisation | |
| E-mail | | Telephone | |

Informant details (contact or family member responding to questions about the contact)

| | | | | |
|---------------------------|-----------------|-----------|---------------------------|--|
| Informant (please circle) | Contact / Other | If other: | Relationship with contact | |
| | | | Telephone | |

Contact information

| | | | |
|--|---|---|--------------------|
| Forename(s) | | Surname | |
| Sex | Male / Female / Unknown | Address including postcode | |
| Date of birth | / / | Relationship to the case | |
| Occupation | | Carer | Yes / No / Unknown |
| Date of last household contact with the case | / / | How many days of household contact occurred since the onset of this illness in the case | |
| Ethnic background | White / Chinese / Asian / African / Caribbean / Mixed / Other (please state): | | |
| Setting where contact occurred | Own home / other (please state, e.g. care home, army barracks) | | |

Contact smoking history at the time of illness onset in the case

Please mark: Smoker Ex-smoker Never smoked Unknown

If ex-smoker or never smoked, do others smoke inside shared-areas of the house?

Contact medical history in the six months prior to illness onset in the case

| Condition or behaviour | Yes / No / Unknown | Details |
|---|--------------------|---------|
| Chronic lung problems | Yes / No / Unknown | |
| Diabetes | Yes / No / Unknown | |
| Dialysis | Yes / No / Unknown | |
| Immunosuppression | Yes / No / Unknown | |
| Tattoo, piercing or other body modification | Yes / No / Unknown | |
| Injecting drug use | Yes / No / Unknown | |
| Other recreational drug use | Yes / No / Unknown | |
| Eczema | Yes / No / Unknown | |

* The HPT should generate a unique contact number for each household contact of a case.

† A unique case number will be provided by PHE Colindale for each case (see Form 1).

Appendix D: Contact report Form-2

| | | |
|--|--------------------|--|
| Atopic dermatitis | Yes / No / Unknown | |
| Psoriasis | Yes / No / Unknown | |
| Skin and soft tissue infections (e.g. boils or abscesses) | Yes / No / Unknown | |
| Other skin lesions | Yes / No / Unknown | |

If yes to either skin and soft tissue infections **or** other skin lesions, please describe the type of infection and date of onset

If yes to skin or soft tissue infections please provide the following detail:

Did this infection start before or after the onset of this illness in the primary case

Before / After / Same time / Unknown

How long before or after the case became unwell did this infection start (in days/weeks/months)

Travel outside the UK in the **3 months** prior to illness in the case?

Yes / No / Unknown

If yes, where to (country) and when (month, year):

Please check all which apply for the contact:

| | | | | | |
|------------------------------|--------------------------|------------------------------|--------------------------|---|--------------------------|
| Health or social care worker | <input type="checkbox"/> | Takes part in contact sports | <input type="checkbox"/> | Care home resident | <input type="checkbox"/> |
| Visits a gymnasium | <input type="checkbox"/> | Military personnel | <input type="checkbox"/> | Attends any other institutional setting (e.g. prison, nursery – please specify) | <input type="text"/> |

Was the case eligible for seasonal influenza vaccination this flu season?

Yes / No / Unknown

If yes, what was the indication?:

Age >65 years

Health/social care worker

Long-stay facility resident

Chronic disease (please circle any which apply)

Respiratory / Renal / Liver / Neurological / Diabetes / Immunosuppression / Pregnant

Carer

Other (please state)

Did the contact receive seasonal influenza vaccination during the current flu season?

Yes / No / Unknown

If yes, date of vaccination, if known:

/ /

Previous confirmed *S. aureus* infection (any body site) or colonisation in the contact during the 12 months prior to illness in the case

Yes / No / Unknown

If yes, provide the following for this previous infection

Methicillin resistance

MRSA / MSSA / Unknown

PVL-status

Positive / Negative / Unknown

Contact with other cases

Other than the associated case (from Form 1), has this contact had contact with any other confirmed or suspected case of PVL positive *S. aureus* infection (of any kind, not only respiratory infections) in the 6 months prior to the associated case becoming unwell?

Yes / No / Unknown

Appendix D: Contact report Form-2

If yes, please provide the following information of this other confirmed or suspected case (if available):

| | | | | | |
|----------------------------|--|--|----------------------------|-----------|-------------------------------|
| Type of contact | Household / Social / Work / Healthcare setting / Other (please state): | | | | |
| Clinical status | Infected / Colonised / Suspected / Unknown / Other (please state): | | | | |
| Forename | | | Surname | | |
| Sex | Male / Female / Unknown | | Date of birth | / / | |
| Date of onset of infection | / / | | Estimated dates of contact | From: / / | Estimated duration of contact |
| | | | To: / / | | |

Interventions in the contact

During the above time period has the contact been tested for influenza or other respiratory viruses (e.g. influenza, RSV, parainfluenza etc)?

Yes / No / Unknown

If yes, please enter results here:

Type of sample

Date of sample

/ /

Name of virus(es) with positive results

Was the contact offered *S. aureus* decolonisation?

Yes / No / Unknown

If yes, what action was taken?

Decolonisation declined

Decolonisation accepted (please give dates)

Started: / /

Completed: / /

Was the contact offered antiviral prophylaxis?

Yes / No / Unknown

If yes, what action was taken?

Antivirals declined

Antivirals accepted (please give details)

Drug given:

Dose:

Started: / /

Completed: / /

Illness in the contact

In the time between the five days prior to onset of the illness in the case and 10 days after the last household contact with the case, has the contact become unwell?
Please circle one option and follow instructions to the right.

Yes

Please complete the remainder of this questionnaire

No

Stop here, this questionnaire is complete

Unknown

Stop here, this questionnaire is complete

Has the contact has any of the following signs or symptoms in the time between the five days prior to onset of the illness in the case and 10 days after the last household contact with the case

| Sign/symptom | Yes / No / Unknown | Date of onset |
|-----------------------|--------------------|---------------|
| Altered mental status | Yes / No / Unknown | / / |
| Shortness of breath | Yes / No / Unknown | / / |
| Cough | Yes / No / Unknown | / / |
| Haemoptysis | Yes / No / Unknown | / / |
| Fever | Yes / No / Unknown | / / |
| Chills | Yes / No / Unknown | / / |
| Rash | Yes / No / Unknown | / / |

Appendix D: Contact report Form-2

| | | |
|--------------|--------------------|-----|
| Nausea | Yes / No / Unknown | / / |
| Vomiting | Yes / No / Unknown | / / |
| Sore throat | Yes / No / Unknown | / / |
| Chest pain | Yes / No / Unknown | / / |
| Muscle aches | Yes / No / Unknown | / / |
| Headache | Yes / No / Unknown | / / |

Finally, please complete all of the following questions (if known). Please check footnotes for any contact under 5 years

Question A
 Has the contact had PVL-positive *S. aureus* isolated from either a blood culture or respiratory sample (e.g.: broncho-alveolar lavage, tracheal aspirate, sputum, pleural fluid)? (please tick)

Yes
 No

Question B
 Does the contact have clinical or radiological evidence of a lower respiratory tract infection? (please tick)

Yes
 No

Question C
 Since the first onset of this illness in the case, has the contact had any of the following (please tick all that apply)

Temperature >39°C *
 Heart rate >140bpm **
 Haemoptysis
 Leucopenia
 CRP >200g/L
 Radiological evidence of lobar or interstitial infiltrates

Question D
 Since the first onset of this illness in the case, has the contact been assessed and found to have any of the following (please tick all that apply)

Confusion
 Urea ≥ 7mmol/L
 Respiratory rate ≥30 per min ***
 Blood pressure <90 mmHg systolic or ≤60 mmHg diastolic ****

This contact is also a confirmed case IF:

- ❖ The response was 'Yes' to Question A **AND**
- ❖ The response was 'Yes' to Question B

This contact is also a probable case IF:

- ❖ The response was 'NO' to Question A **AND**
- ❖ There are two or more ticks against Question C **AND**
- ❖ There are one or more ticks against Question D

If this individual is either a confirmed or probable case (see above), please ensure you have completed **all** of the questions on this page and then follow the algorithm in Appendix A to identify the further actions.

IMPORTANT: For confirmed or probable cases please add their unique case number here once you have obtained it from PHE Colindale (as per Form 1):

Unique case number

Footnotes for children

- * Temperature: for infants 0–3 months use >38°C;
- ** Heart rate: for children <5 years please do not tick this item at all;
- *** Respiratory rate: for ages 6–12 months use RR>50 breaths per min, for 12 months to 5 years use RR>40 per min;
- **** Blood pressure: for children <5 years please ignore blood pressure and tick this box if capillary refill time is

General notes

Please complete all sections of these forms wherever possible.

If completing forms electronically: for multiple choice questions please delete as appropriate to leave the correct response; for checkboxes, please place an X in the appropriate box.

If completing forms by hand: for multiple choice questions please circle the correct response; for checkboxes, please place an X in the appropriate box.

Notes for Case report Form–1

Unique case number: Please request a unique case number for each case by securely e-mailing respiratory.lead@phe.gov.uk including the name and DOB of each case in your e-mail.

Case classification: See section 2.2 of protocol for case definitions.

Previous confirmed *S. aureus* infection (any body site) or colonisation in the 12 months prior to this illness: In the 12 months prior to the current illness, has the patient previously had a *S. aureus* infection of any kind (i.e. not just a lower respiratory tract infection)?

Notes for Contact report Form–2

Unique contact number: The HPT should generate a new sequential contact number for each household contact of a case (e.g. C001, C002, C003 etc). If an HPT has more than one case, this contact numbering will start again from C001 on each line listing.

Unique case number: Please include the case number from the associated household case. If there are co-primary cases in the household, please note the case numbers of each of the co-primary cases which are associated with this contact.

Relationship with case: Please describe the relationship between this contact and the associated case (e.g. boyfriend, sister, housemate)

How many days of household contact occurred since the onset of this illness in the case. Please provide the number of days during which any household contact occurred between the date of onset of this illness in the case and the date of last household contact with the case.

Previous confirmed *S. aureus* infection (any body site) or colonisation in the contact during the 12 months prior to illness in the case In the 12 months prior to the current illness, has the patient previously had a *S. aureus* infection of any kind (i.e. not just a lower respiratory tract infection)?

Appendix D: Contact report Form-2

Further assistance with forms

Should you have any questions relating to these forms, please contact Dr Gavin Dabrera at PHE Colindale at: gavin.dabrera@phe.gov.uk or telephone 0208 327 6166; or Dr Iro Evlampidou at: iro.evlampidou@phe.gov.uk or telephone on: 0117 968 9134.

Please return all completed forms to: respiratory.lead@phe.gov.uk