



Interim UK guidelines for the public health management of clusters of serious pneumococcal disease in closed settings

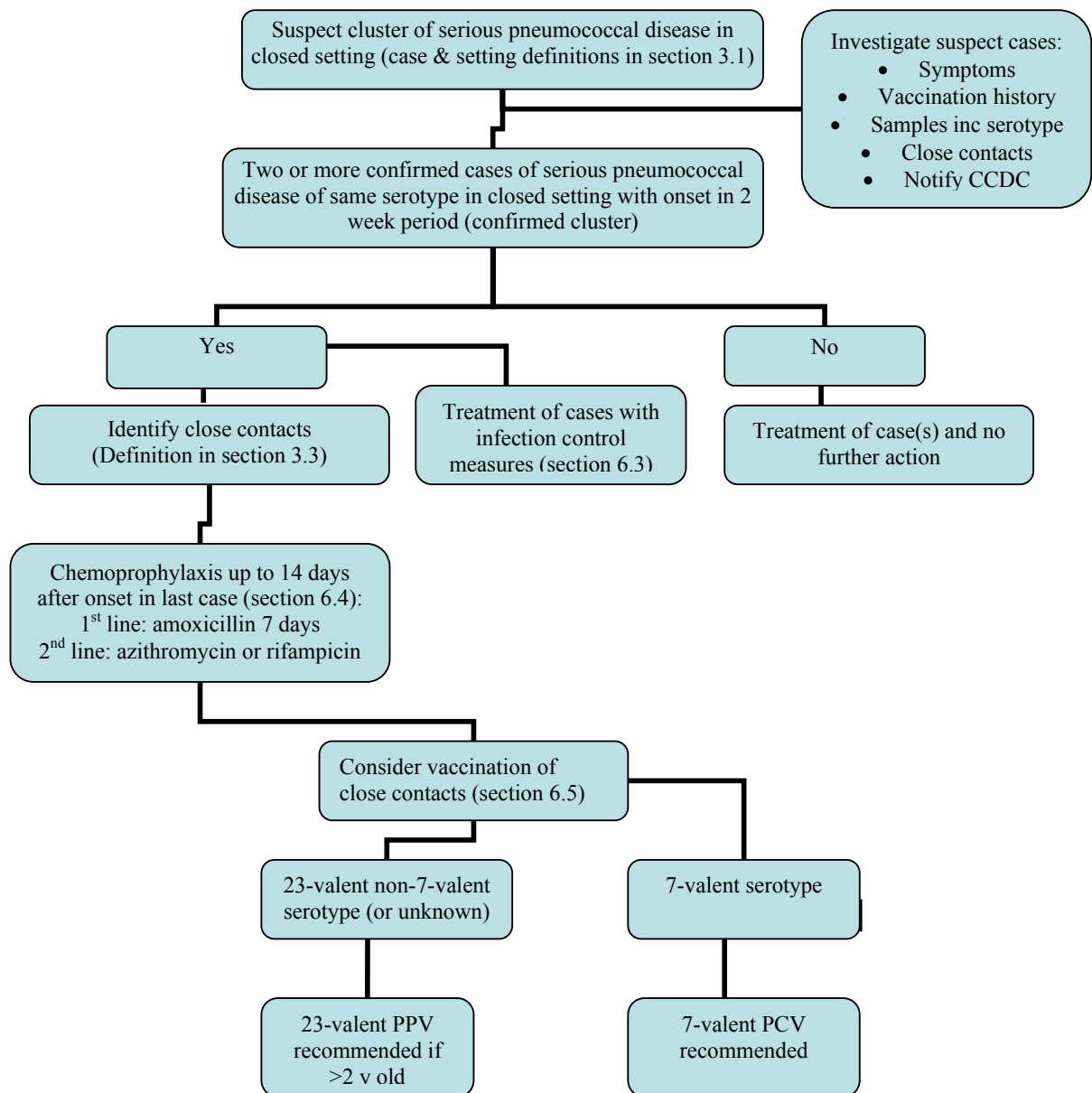
Summary

Streptococcus pneumoniae (pneumococcus) can rarely cause clusters of serious disease including septicaemia, pneumonia and meningitis in closed settings. These closed settings include hospitals, long-term care facilities, prisons, military settings and children's day-care centres.

These guidelines, produced by the Health Protection Agency (HPA), outline the investigation and public health management of such clusters of serious pneumococcal disease.

A suspect cluster is defined as **two or more cases of serious pneumococcal disease occurring in a closed setting within a 14 day period**. Such clusters should be reported to the Health Protection Unit (HPU) for investigation.

Following confirmation of a cluster, recommended interventions to consider include implementation of infection control measures for cases, antimicrobial chemoprophylaxis (first line therapy amoxicillin) and vaccination of close contacts with either pneumococcal conjugate or polysaccharide vaccine (depending upon serotype and age of case).



Closed setting: a place such as a children’s day-care centre, school, residential home, hospital ward, military establishment, prison, homeless shelter, household and other similar settings;

Suspect cluster: Two or more probable cases or one confirmed and one or more probable in a closed setting with onset dates within a two week period;

Confirmed cluster: At least two confirmed cases of serious pneumococcal disease of the same (or not yet determined) serotype in a closed setting with onsets within a two-week period.

Close contact: An individual who has had significant contact with a cluster case in the closed setting. The period of significant contact is from 48 hours before onset of symptoms in the case until completion of 24 hours of systemic antibiotic treatment.

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1 Introduction

1.1 Microbiology and clinical presentation

Streptococcus pneumoniae, commonly called pneumococcus, is a Gram positive diplococcus of which there are more than 90 serotypes. It is a normal inhabitant of the nasopharynx, being transmitted by droplets from person-to-person. Pneumococci primarily causes otitis media, sinusitis and pneumonia, but it may invade other sites.

Invasive pneumococcal disease (IPD) is defined as pneumococcal infection of any usually sterile site. Clinical presentation includes meningitis, bacteraemia, empyema, arthritis and peritonitis.

1.2 Epidemiology of pneumococcal carriage and disease

Carriage of pneumococci is relatively common: estimated to be in excess of 40% in pre-school children, falling to <10% in young adults in the UK ¹. Increased rates of carriage are associated with several risk factors including children's day-care attendance, number of siblings and smoking ². The mean duration of carriage is estimated to be approximately 50 days in children and 20 days in adults ⁷. Rarely acquisition may progress to IPD.

Risk factors for IPD include age (being very young or elderly), splenic dysfunction, solid organ (e.g. lung, heart, liver and kidney) dysfunction and immunosuppression ¹⁸.

In the UK, the crude annual incidence of IPD is approximately 12/100 000 at present. Age-specific attack rates are highest in young children and the elderly, exceeding 40/100 000 in children < 2 years and in adults more than 75 years of age ^{20;21}. The highest incidence is observed in the winter.

1.3 Background to the guidelines

There have been numerous reports in the literature of clusters of serious pneumococcal disease (IPD and pneumococcal pneumonia) in a range of closed settings both in the UK and elsewhere. These settings have included hospitals, long-term care facilities, children's day-care centres, schools and military barracks (see literature review below for detailed referencing). A variety of public health interventions have been implemented in an attempt to control these outbreaks. However, no evidence-based guidance for the management of these clusters has been published to date.

In 2006, the Health Protection Agency (HPA) Pneumococcus and *Haemophilus influenzae* type b (Hib) forum established a working group to develop evidence-based guidance for the investigation and management of clusters of cases of IPD or pneumococcal pneumonia occurring in closed settings (henceforth referred to as serious pneumococcal disease). The working group comprised representatives from the HPA Pneumococcus and Hib forum, HPA Centre for Infections, HPA Local and Regional Services, Health Protection Scotland (HPS), the Association of Medical Microbiologists, the Public Health Medicine Environmental Group (PHMEG) and the Community Infection Control Nurses Network. The guidelines have been signed off by the HPA Pneumococcus forum and also by the HPA Vaccine Programme Board.

The review is based on available published evidence, with the levels of evidence graded according to established guidelines (Scottish Intercollegiate Guidelines Network, SIGN). Where insufficient evidence was available on which to base guidance, agreement was reached through consensus expert opinion.

1.4 Purpose of the guidelines

This guidance is intended for those in the Health Protection Agency (HPA) and the National Health Service (NHS) (including microbiology laboratories) and equivalent organisations in Scotland, Wales and Northern Ireland who will be involved in the clinical, microbiological and public health management of the incident. Proposed lines of communication are outlined in section 8.

The responsible person for leading the management of a cluster will vary depending upon the setting and location. For a cluster in a hospital, it is likely that the hospital infection control team will take the lead; for a community cluster, it is likely to be the local Health Protection Unit (HPU) team; for a PCT community hospital, the Director of Infection Prevention and Control. Reference should be made to the local outbreak control plans.

For expert advice please contact the HPA Centre for Infections (CfI) pneumococcal team (within the Respiratory and Systemic Infection Laboratory and CfI Immunisation department) and in Scotland, Health Protection Scotland. As these events are infrequent and this guidance is preliminary, an early teleconference including the local HPU, local microbiologists and epidemiologists and national experts from both public health and microbiology should take place to ensure optimal cluster management and good communication. The HPA regional Communication Manager should also be informed.

1.5 Guideline objectives

These guidelines outline interventions needed to effectively manage the public health consequences of a cluster of serious pneumococcal disease and reduce the risk of secondary cases occurring amongst close contacts.

Primary intervention strategies are providing information, offering antimicrobial prophylaxis and vaccination (with conjugate or polysaccharide vaccines) to defined close contacts.

The guidelines do not cover the management of clusters of less serious clinical manifestations of pneumococcal infection such as conjunctivitis or otitis media.

These guidelines do not cover the management of individual cases of IPD occurring in closed settings. Chemoprophylaxis/vaccination is not recommended for close contacts of individual cases of IPD.

2. Literature review: epidemiology and management of clusters of serious pneumococcal disease

A critical systematic review of the literature was undertaken using Pub-Med for the period 1966 to 2007 using initially the MeSH terms “*Streptococcus pneumoniae*”, “Pneumonia, Pneumococcal”, and “Meningitis, Pneumococcal”. Evidence was evaluated according to the Scottish Intercollegiate Guidelines Network (SIGN).

We found 42 reports of clusters of serious pneumococcal disease described in 39 papers. The majority have been reported from hospitals^{8;10;12;14;38-46} and long term care facilities^{9;13;15-17;47-51}. A handful of reports are of outbreaks in households⁵²⁻⁵⁴ military barracks^{11;23;25} day care centres^{22;24;37}, homeless shelters^{55;56} and jails⁵⁷.

Sixteen articles report interventions to prevent secondary cases and give details of their impact^{8-17;19;22-25;37;57}. Of these uncontrolled observational studies, thirteen report an intervention including use of antibiotic chemoprophylaxis^{8-11;13;14;16;17;22-25}, in seven the intervention included pneumococcal polysaccharide vaccination^{9;11;13;15-17}, and one infection control only¹². No interventions with pneumococcal conjugate vaccine were reported. Further information on the literature review is presented in the body of the guidelines (boxes 2-5).

3. Case definitions for cases, contacts and settings in a cluster

3.1 Cases

A hierarchy of case definitions for serious pneumococcal disease is recommended from confirmed to probable to possible.

Confirmed case

Clinical diagnosis of IPD or pneumococcal pneumonia

AND at least one of:

- Pneumococcus isolated from normally sterile site (blood, CSF, joint, peritoneum, pleural fluid or other, but not sites such as eye)
- Pneumococcal DNA or antigen detected in fluid from a normally sterile site (except for blood in children under 2 years of age in whom pneumococcal carriage alone may result in blood PCR positivity, positive blood PCR results in children under 2 years of age must therefore be interpreted with caution and always in the light of clinical observations¹).
- Pneumococcal antigen detected in urine (except in children under 2 years of age in whom pneumococcal carriage alone may result in urine antigen positivity⁵⁹; positive results in children under 2 must therefore be interpreted with caution and always in the light of clinical observations²).

¹ Advice should be sought from the laboratory providing the pneumococcal PCR testing, and, if appropriate, from a reference laboratory

² Advice should be sought from the laboratory providing the test result and if appropriate from a reference laboratory

Probable case

Clinical diagnosis of IPD or pneumococcal pneumonia where the responsible clinician or microbiologist in consultation with the public health physician considers that serious pneumococcal disease based on available clinical, microbiological and epidemiological evidence is the most likely diagnosis. A probable case would be supported by certain clinical signs e.g. lobar pneumonia or empyema.

An epidemiological link to a confirmed case further supports a probable case.

Possible case

Clinical diagnosis of IPD or pneumococcal pneumonia where the responsible clinician or microbiologist in consultation with the public health physician considers that diagnoses other than serious pneumococcal disease are at least as likely.

Probable and possible cases should have appropriate microbiological investigations to rapidly confirm or exclude the diagnosis (see section 5).

3.2 Closed setting

A closed setting is defined as a place such as a children's day-care centre, school, residential home, hospital ward or unit ³, military establishment, prison, homeless shelter, household and other similar settings.

3.3 Close contact

Close contacts of clusters in closed settings as defined in section 3.2 are those that require public health action.

A close contact is defined as an individual who has had significant contact with a cluster case in one of the closed settings defined in section 3.2. The period of significant contact is from 48 hours before onset of symptoms in the case until completion of 24 hours of systemic antibiotic treatment.

Significant contact may be either prolonged or transient.

Prolonged contact is defined as either overnight and/or daytime stay in the same closed setting.

Transient close contact is defined as when the mouth or nose is directly exposed to large particle droplets/secretions from the respiratory tract of a cluster case during acute illness. General medical or nursing care of cases is not included.

Within the closed setting where the cluster occurred, an attempt should be made to identify a clear sub-group at elevated risk of carriage (and hence disease) with the outbreak strain e.g. a school class.

³ Only when nosocomial transmission is suspected, defined as two or more cases occurring in a health care setting with the date of onset of the second case more than 48 hours after admission.

4. Identification and confirmation of cluster

4.1 Initial recognition of cluster

The local responsible person/s should make a careful and rapid assessment, when:

Two or more cases of serious pneumococcal infection (confirmed or probable) are reported from a closed setting within a two-week period (see Box 1 for evidence-base)⁴,

Cfl is willing to discuss clusters of pneumococcal infection not covered by these guidelines e.g. eye, otitis media.

Depending upon local arrangements and the setting, the local HPU and/or the Hospital Infection Control Team should be notified by the responsible clinician/microbiologist, and agreement reached as to who will lead the outbreak control response.

The following information should be gathered on the cases and the setting (see proforma section 1).

Cases

- Basic demographics – age, sex, address, occupation/school/nursery
- Risk factors for pneumococcal disease – e.g. splenic dysfunction, immunosuppression, solid organ (heart, lung, liver, kidney) dysfunction.
- Clinical features, particularly
 - Dates of onset of illness
 - Signs and symptoms of bacteraemia, acute pneumonia or meningitis
 - Outcome – hospitalised, dead
 - Supportive diagnostic information
 - E.g. Radiological information (for example lobar pneumonia - highly predictive of pneumococcal infection)
- Microbiological data, particularly
 - Culture and/or detection of DNA antigen from blood, CSF, urine, sputum, pleural fluid, joint aspirates, etc
 - Antimicrobial susceptibility⁵
 - Serotype information^{6 7}
- Date of initial referral to HPU/hospital infection control team
- Vaccination status
 - Type of vaccine (23-valent polysaccharide, 7-valent conjugate)
 - Number of doses and when administered

⁴ Longer periods may be considered depending upon the setting and the nature of the cluster

⁵ This should be available from the local laboratory

⁶ Invasive pneumococcal isolates should be sent for serotyping to the HPA Respiratory and Systemic Infection Laboratory.

Setting and population at risk

- Type of setting
- Number of persons in the setting with basic epidemiological description (age, sex, employment, vaccination status, duration in setting)
- Identification of any highly exposed sub-group e.g. school class
- Household contacts

4.2 Confirmation of cluster

An evaluation should be undertaken to ascertain whether the cluster requires immediate public health action or just further investigation initially.

4.2.1 Confirmed cluster: requires immediate public health action

A confirmed cluster requiring immediate public health action is defined as:

The occurrence of at least two confirmed cases of serious pneumococcal disease of the same (or not yet determined) serotype in a closed setting with onsets within a two-week period.

In a cluster involving a single confirmed and a probable case, the serotyping of the probable case should be expedited to include/exclude a cluster.

Two weeks corresponds to the period of maximally elevated risk after the initial case (box 1). Outbreaks with longer intervals between the first and the final case have been described and their management should be discussed in conjunction with HPU, HPA Centre for Infections (Immunisation department and Respiratory and Systemic infection laboratory) or Health Protection Scotland as appropriate.

⁷ Sero-specific antigen detection in a cluster setting on e.g. urine specimen is available free-of-charge from the HPA Respiratory and Systemic Infection Laboratory.

BOX1: Risk of transmission - Evidence grade D

Of the 42 clusters of serious pneumococcal disease (involving at least 2 clinical cases) in closed settings found on reviewing the literature, 26 had sufficient data to elucidate an epidemic curve. Of these 26 clusters, 25 involved the same serotype. In these 25 outbreaks, the median outbreak size was 4 with a range of 2 to 46. 81% of all cases occurred within 14 days of onset of the index case, and 91% within the first 28 days. Serotypes/groups **most commonly** associated with clusters were 14 (7 clusters), 4 (5 clusters), 9, 1, and 9V, all causing 4 clusters each. Reported attack rates ranged from 0.18% – 66% (median 8.9%). No secondary transmission leading to serious pneumococcal disease in staff was reported in any of the outbreaks.

Table: Distribution of number of cases per cluster and length of outbreak

No. of cases in cluster	No. of clusters	Illness onset in contacts <i>(median and range in days after illness onset in index case)</i>
2 - 4	13	4 (1 – 95)
5 - 9	4	16 (10 - 58)
10 - 14	4	12.5 (5 – 20)
>15	4	20 (8 – 30)

4.2.2 Suspect cluster: requires further investigation, not immediate public health action

A suspect cluster is defined as:

Two or more probable cases or one confirmed and one or more probable in a closed setting with onset dates within a two week period

A suspect cluster requires further investigation to confirm or refute the diagnosis. Specific public health interventions are not required initially in this instance.

Further investigation for alternative diagnoses according to the clinical syndrome should be undertaken in discussion with the local microbiologist. This should include pneumococcal specific investigations (as listed in section 5) and consideration of specific testing for other infections as indicated by the clinical picture.

For pneumonia, testing for influenza (pneumococcal and influenza infection may occur concurrently), Q-fever, RSV, mycoplasma and legionella infection should be considered.

For meningitis and sepsis, testing for Hib and meningococcal and other bacterial infections or viruses as appropriate to the clinical and laboratory results should be considered.

4.2.3 Excluded clusters

A single case of IPD in a closed setting is not defined as a cluster. Similarly, when two (or more) cases occur which are subsequently found to be due to different serotypes, this is not defined as a cluster for the purposes of these guidelines.

5. Laboratory investigation

To guide the appropriate public health response, it is important that pneumococcal disease is rapidly confirmed, and that serotype information is quickly available. Hence, it is important that early liaison should occur between the responsible clinician with the local microbiologist to ensure that appropriate clinical samples are taken and with the reference laboratory to ensure that relevant samples are sent as soon as possible for serotyping.

Most clusters of serious pneumococcal infection will come to light following the isolation of *Streptococcus pneumoniae* from, or detection of pneumococcal antigen or DNA in a normally sterile site from one or more patients in the suspect cluster. Further investigation of possible related cases will be dictated in large part by their clinical presentation. To confirm pneumococcal disease, the following investigations should be performed wherever possible.

5.1 Culture

Culture of *Streptococcus pneumoniae* from blood, CSF or any other normally sterile site represents the optimal confirmation method for serious pneumococcal disease. In addition to antimicrobial susceptibility testing, all isolates should be sent to an appropriate reference laboratory for serotyping as soon as possible, and if appropriate, further molecular characterisation to assess strain relatedness.

Blood culture

Blood for culture should be obtained from all cases sufficiently unwell to be admitted to hospital. A number of factors influence the sensitivity of blood culture including recent antibiotic treatment, volume of blood collected, and the bacterial load. It is important to note that only 20 to 25% of lobar pneumonia cases will yield a positive blood culture. If blood cultures appear to contain pneumococci, but are negative on subculture, an aliquot of the "negative" blood culture may be tested for pneumococcal antigen, for example with the Binax™ test (if from person 2 or more years of age), and if positive referred to an appropriate reference laboratory for serotype-specific antigen detection.

CSF culture

Where possible CSF should be obtained for culture in cases of clinically suspected pneumococcal meningitis. Culture negative samples with a high index of suspicion of pneumococcal disease (e.g. as suggested from microscopy) may be tested for pneumococcal antigen, for example with the Binax™ test and also referred to an appropriate reference laboratory for pneumococcal PCR and/or serotype specific antigen detection.

Aspirate from other normally sterile sites (e.g. joint or pleural fluid)

Culture of pneumococci from these sites confirms invasive infection. Culture negative samples with a high index of suspicion of pneumococcal disease (e.g. as suggested from microscopy) should be referred to an appropriate reference laboratory for pneumococcal PCR and/or serotype specific antigen detection.

Sputum

A positive culture of sputum for *S. pneumoniae* is not on its own adequate for a diagnosis of pneumococcal pneumonia; it should be interpreted in the context of the clinical picture, the quality of the specimen, and the methods used for sputum processing in the individual laboratory. Growth of *Streptococcus pneumoniae* in significant numbers from a purulent sample from patients with signs and symptoms of pneumonia is usually significant and may potentially guide further management.

Nasopharyngeal swabs

Nasopharyngeal swabs of cases can provide supportive evidence of pneumococcal infection. However, positive cultures are not confirmatory of pneumococcal disease, since carriage occurs and is particularly common in young children (up to 50% in the age group 1 to 4 years).

Swabs should be taken and transported using standard methods.

Nasopharyngeal swabs collected from healthy contacts of cases within the cluster, for example members of the same school class or crèche group, is not part of the routine public health management of these clusters, but on occasion may help guide further management (see section 7).

Antimicrobial susceptibility testing

All pneumococcal isolates obtained from patients known or suspected to be involved in the cluster should be subjected to antimicrobial susceptibility testing including the agents suggested for antimicrobial prophylaxis within these guidelines.

5.2 Non-culture diagnostic tests

Urinary antigen detection - Immunochromatographic assay

The immunochromatographic rapid urinary antigen test (BINAX™) has been shown to be a rapid, sensitive and specific tool diagnostic tool for pneumococcal pneumonia and IPD in adults and older children ^{60;61 62;63 64}.

However, the clinical utility of the test is reduced in younger children as the positive predictive value is lower. A positive antigen test in this group may merely reflect pneumococcal carriage ^{65 66-68}.

In cases where the urinary antigen test is positive and there are no positive cultures available for serotyping, subsequent serotype specific antigen detection should be undertaken on the urine as soon as possible at an appropriate reference laboratory. This allows serotyping of culture negative cases.

PCR

PCR-based assays for the detection of specific DNA sequences of *S pneumoniae* are available at reference and some NHS laboratories in the UK. These can be used on CSF, blood and fluids from other normally sterile sites. As noted above positive results on blood samples from younger children (<2 years) must be interpreted with caution and in the context of clinical observations and other investigations.

5.3 Serotyping of *Streptococcus pneumoniae*

Rapid ascertainment of serotype is an important tool to confirm or exclude a suspected cluster, to assess the relatedness of cases within a cluster and thus inform public health management.

Serotype identification of pneumococcal isolates is undertaken at reference laboratories in the UK. If a cluster is being considered, the relevant person at the national reference laboratory should be rapidly informed to expedite serotype investigations.

Serotype information may also be obtained from non-culture positive specimens including CSF, other normally sterile body fluids and pneumococcal antigen positive urine.

At least one bacterial and/or antigen positive isolate from each case should be sent to a reference laboratory for serotyping. Such laboratories will be able to undertake further molecular characterisation as necessary. It is important to ensure the reference laboratory is informed of the despatch of outbreak/incident related specimens and samples to ensure prioritisation on arrival.

In addition, through the programme of enhanced surveillance for paediatric empyema, culture-negative empyema fluid from children aged 0-16 years with suspected pneumococcal pneumonia should be sent to the HPA Meningococcal Reference Unit for PCR testing. Pneumolysin PCR -positive extracts will be forwarded to the Respiratory and Systemic Infection Laboratory, Colindale, for autolysin PCR confirmation and serotype-specific antigen detection.

6. Public health management of a cluster

The following applies to situations when a cluster has been identified that fits the definition as set out in 4.2.1.

Public health interventions to prevent further cases should be offered to close contacts (as defined in section 3.3) that are part of the same closed setting. This may include information provision, offering chemoprophylaxis, vaccination and implementing infection control measures. To optimise their impact, the measures should be instituted rapidly and ideally simultaneously. Interventions should not be delayed unduly while awaiting the results of serotyping.

6.1 Define close contacts

As outlined in section 3.3

6.2 Provide information

It is important to provide information to all concerned. Explain what the situation is, and that close contacts are at a possibly increased risk of infection. Explain that they need to be aware that if they develop particular symptoms suggestive of pneumococcal infection they should contact or attend relevant health care services. Information should explain that antibiotics with or without vaccine reduce the risk of disease, but do not guarantee 100% protection. See appendix for information sheet and standard letter.

6.3 Infection control measures (Level of evidence D, box 2)

BOX 2: Infection control - Level of evidence: D

In published outbreaks, infection control measures have been instituted including isolation of patients, cohorting and reinforcement of hand washing^{8-14 19}. In only one outbreak¹² were these interventions used in isolation; the outbreak terminated seven days after infection-control measures were commenced, with a further 5 cases occurring in the intervening period.

For non-residential settings such as schools there are no grounds to close classes or exclude contacts. For residential settings or hospitals, the Infection Team controlling the incident will need to consider closure to new admissions until control measures are in place. Infection control measures should include:

Isolation

In care home settings, most residents are already cared for in single rooms. Wherever possible staff should either be allocated to the ill or the well. If possible, patients should be kept in single rooms for the first 24 hours after antibiotic treatment has commenced (Grade D – expert opinion).

Cohorting

Cohorting of cases in acute hospital situation and in settings such as nursing homes or prisons where single rooms may not be available should be used.

Hand and respiratory hygiene practice

Good hand and respiratory hygiene should be encouraged, including for relatives and visitors.

Respiratory protection:

Facemasks are not necessary for routine care, but should be used for activities, which produce aerosols such as chest physiotherapy (Grade D-expert opinion only). Non-sharing of respiratory devices such as spacers and nebulisers should be reinforced.

6.4 Antimicrobial prophylaxis (Level of evidence D, box 3,4)

BOX 3: Antimicrobial prophylaxis in cluster reports - Evidence grade D

In 13 published outbreaks, an antibiotic intervention was used where the impact is detailed^{8-14;16;17;22-25}. In all reports there were no control subjects and the timing of antibiotics varied from within 6 days of the first case to two months after the last case.

Prophylaxis of contacts with rifampicin-containing regimes^{9;10;14;22;24;37}, azithromycin^{11;25}, penicillin^{16;17;23} and erythromycin^{8;13} have been used. Additional agents in rifampicin based regimes included quinolones^{9;10} or clindamycin²² or mupirocin^{10;14} – and were for multiple resistant organisms.

In terms of preventing further cases: where rifampicin^{24;37} or penicillin^{16;17;23} alone was given, no further cases after administration were detected. Further cases occurred in both outbreaks where azithromycin prophylaxis was employed^{11;25} and one of two where erythromycin was used¹³.

More research needs to be undertaken on the most appropriate choice, dose and duration of chemotherapy for the management of these clusters.

BOX 4: Antimicrobials in pneumococcal carriage studies - Evidence grade C

There are 15 published studies with data on the impact of antibiotics on nasopharyngeal pneumococcal carriage mainly in the context of acute otitis media^{3-6 26-35 36}. In 6 studies, azithromycin was used^{4;26;29;30;33;34}, in 3 ceftriaxone^{27;31;32} and 7 amoxicillin or co-amoxiclav^{3;5;6 27-30}. Follow-up was 10 days to 3 weeks. There were no such studies for rifampicin alone.

For the studies with amoxicillin or co-amoxiclav (n=7), carriage rate was reduced by a median of 86% (range 67-100%). For the studies with azithromycin (n=6), carriage was reduced by a median of 79% (range 67%-100%). For the three studies with ceftriaxone, carriage rate was reduced by a median of 24% (range 4-55%).

Aim

The aim of antimicrobial prophylaxis is to significantly reduce carriage of the outbreak serotype amongst close contacts and thus interrupt transmission in the group. It may also provide individual protection against serious disease amongst close contacts that may be in the incubation phase.

The aim is for antibiotic chemoprophylaxis to provide some initial protection until vaccination, (where indicated and given simultaneously), takes effect.

Indications

Chemoprophylaxis should be offered to close contacts of clusters in the following categories:

- (a) Close contacts (see case definition in section 3.3) in the closed setting where the cluster has occurred (nursery, ward, residential home, household etc). If defining a specific sub-group is not possible, prophylaxis can be offered to all in the institution.

- (b) Those who have had prolonged close contact with one of the cluster cases in a household-type setting (see case definition in section 3.3), where the cluster occurred in a closed setting outside of that household.
- (c) For health care workers in a hospital or other health care setting whose mouth or nose is directly exposed to large particle droplets/secretions from the respiratory tract of a case during acute illness until completed 24 hours of systemic antibiotics. General medical or nursing care of cases is not an indication for prophylaxis.

The Working Group recognised that identifying those who are defined as close contacts will require HPU staff to use their judgement in defining close contacts.

Timing

Antimicrobial prophylaxis should be offered as soon as possible (ideally within 24 hours) to close contacts of cluster cases as defined in section 2.5, regardless of vaccination status.

It may be offered to close contacts up to fourteen days after the onset of illness in the last case in the cluster.

Choice of antimicrobial

The choice of antimicrobial prophylaxis must always be guided by the in vitro susceptibility of the bacteria isolated and the target population (age, pregnancy etc). Most laboratories will not test for amoxicillin susceptibility in pneumococci, but this can be inferred readily from the penicillin result. Azithromycin susceptibility can be inferred from the results of erythromycin susceptibility testing. Rifampicin susceptibility should also be requested if this is not included in the routine set.

No antimicrobials are licensed for this purpose. Recommendations have been made based on a review of the literature of the use of antibiotics in the management of clusters (box 3) and in clearance of carriage (box 4). Providing the organism is penicillin sensitive, amoxicillin is recommended as first line choice therapy. Azithromycin (assuming macrolide sensitivity is confirmed) and rifampicin are second-line alternatives.

Information should be provided to close contacts about what management is recommended and its rationale. This should include explaining that antibiotic prophylaxis is not fully protective.

Prophylaxis for the cases

Cases should complete standard recommended antibiotic therapy to treat their disease. On the basis of the literature review of antibiotic effectiveness in reducing pneumococcal carriage, such standard therapy, should clear pneumococcal carriage and additional antimicrobial prophylaxis will not be required.

Prophylaxis Regimens for Contacts

Amoxicillin

Adults and >12 years 500mg BD orally for 7 days

Children 5-12 years 250 mg BD orally for 7 days
Children up to 5 years 125 mg BD orally for 7 days

A twice daily regime rather than thrice-daily is recommended as the former has both demonstrated effectiveness and is more operationally practical. In those individuals with penicillin allergy or a resistant strain, alternatives should be guided by in vitro susceptibility testing and include rifampicin or azithromycin.

Azithromycin

Adult 500mg OD orally for 3 days
Child >6 m 10mg/kg OD (max 500mg) orally for 3 days

As the prevalence of macrolide resistance amongst invasive pneumococcal isolates in the UK is greater than 10%, it is important to ascertain antimicrobial resistance pattern before offering azithromycin.

Rifampicin

Adults and children over 12 years of age 600mg OD orally for 4 days
Children 1-12 years 20 mg/kg OD orally for 4 days
Infants under 12 months of age 10mg/kg OD orally for 4 days

Rifampicin is recommended in the case of penicillin and macrolide resistance and/or penicillin allergy. It can be used in all age groups. Rifampicin is contraindicated in the presence of jaundice or known hypersensitivity. Interactions with other drugs, such as anticoagulants, phenytoin, and hormonal contraceptives should be considered. Side effects should be explained including staining of body fluids and contact lenses.

In clusters caused by multiply resistant *S pneumoniae*, combination prophylaxis should be considered in consultation with the local microbiologist.

Pregnancy

All three options can be used in pregnancy. As always, any drug should be used with caution in pregnancy, as there is a limited evidence base for safety. Rifampicin should be avoided in the later stages of pregnancy. For azithromycin, there is no evidence of harm in the foetus in animals; however, it should only be used in pregnancy when no adequate alternative is available.

6.5 Vaccination (Level of evidence, boxes 4 and 5)

Two types of pneumococcal vaccine are presently licensed in the UK, which include a variable number of capsular serotypes: the 23-valent-pneumococcal polysaccharide vaccine (PPV) and the 7-valent pneumococcal conjugate vaccine (PCV). PCV is now included in the routine childhood immunisation schedule and for children up to and including 5 years of age who are at increased risk of IPD or pneumococcal pneumonia (DoH GREEN BOOK).

PPV offers protection against the following serotypes;

1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F

PCV offers protection against the following serotypes;

4, 6B, 9V, 14, 18C, 19F, 23F

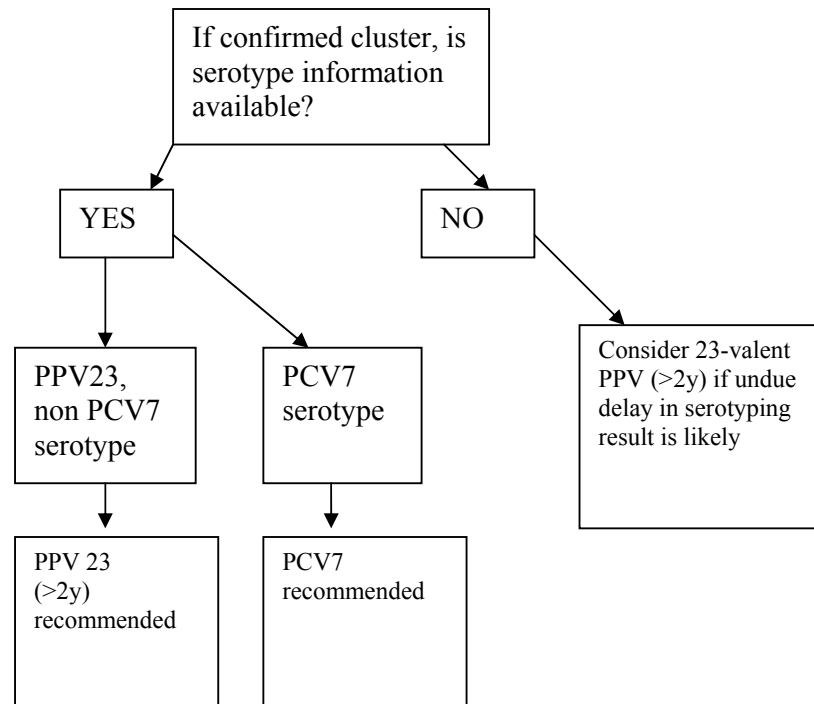
Phase 3 clinical trials have demonstrated that 7-valent PCV is efficacious against IPD and pneumonia^{69;70}. Introduction of PCV into the routine childhood programme in the United States has had a significant impact on IPD due to vaccine-serotypes in children and adults^{71;72}. New conjugate vaccines containing additional serotypes (10 and 13-valent) are likely to be licensed in the near future.

All children (2 years or more of age) and adults falling into a group at higher risk of pneumococcal disease, including all those over 65 years of age are recommended a single dose of PPV. Several meta-analyses of both RCTs (Fine 1994) and observational studies^{73;74} have demonstrated that PPV is effective against IPD. Evaluation of the effectiveness of the PPV programme in the elderly in England has indicated that protection wanes after approximately two years.

In the management of a cluster, PPV or PCV will not provide protection in the first 10-14 days following vaccination. Simultaneous antimicrobial prophylaxis is thus required to clear carriage for this intervening period.

The following algorithm outlines the recommendations for vaccination following identification of a cluster of pneumococcal cases requiring public health action:

Flow chart for action in confirmed cluster



In addition, it is important to ensure that all individuals (both cases and contacts) are vaccinated appropriately with pneumococcal vaccine (either conjugate and/or polysaccharide) according to their age and risk status.

6.5.1 7-valent pneumococcal conjugate vaccine

BOX 4: Pneumococcal conjugate vaccine and clusters: Level of evidence D

No published evidence of effectiveness of PCV in a pneumococcal cluster setting.

Unvaccinated close contacts in a cluster due to a 7-valent vaccine preventable serotype of *S pneumoniae* should be offered pneumococcal conjugate vaccine as soon as possible after diagnosis has been confirmed and up to fourteen days after the date of onset of the last case in the cluster. For those over 5 years of age, PCV is not specifically licensed and will need to be prescribed on a named patient basis.

In those who are partially vaccinated according to the current national guidelines, the remainder of the PCV course should be administered according to age and risk status.

Two groups should be offered a further booster, as there is evidence of reduced protection from UK national surveillance data (personal communication E Miller, HPA) for the following:

- Children who have received a single dose of PCV in the second year of life;
- Children aged 4-12 months who have received a full primary course, but not yet received a booster dose in the second year of life.

6.5.2 23-valent pneumococcal polysaccharide vaccine (PPV)

BOX 5: Pneumococcal polysaccharide vaccine and clusters: Level of evidence D

There are seven published clusters in which 23-valent PPV was given^{9;11;13;15-17 19}. In five of these, antibiotics were also administered^{9;11;13;16;17}. Of these five, in three there were further cases within one and 14 days of the intervention^{11;13;17}. In one cluster¹⁷, PPV was given alone initially; within three days of PPV, four further cases occurred and chemoprophylaxis was then undertaken. In another cluster¹³, those receiving only PPV were four times more likely to develop pneumonia within two weeks than those who additionally received antibiotics.

In the two clusters in which PPV alone was given^{15 19} further cases occurred from one day after vaccination to approximately 2/3 weeks after vaccination.

There was no intentional revaccination of individuals in any reports

Unvaccinated close contacts (institutional setting and household) over two years of age of a confirmed cluster due to either:

- a 23-valent (but non-7-valent) vaccine serotype or
- an unknown serotype (due to inability to type)

should be offered a single dose of PPV up to fourteen days after the onset of illness in the last case in the cluster.

Those individuals who have already received a dose of PPV more than two years previously should be offered a further dose of PPV.

Children under the age of 2-years should not be offered PPV vaccine. Not only is PPV vaccine effectiveness reduced; there is evidence that polysaccharide vaccines administered at this age result in hyporesponsiveness to subsequent doses⁷⁵.

7. Swabbing of close contacts

Consideration may be given to nasopharyngeal swabbing of contacts (those who are to receive prophylaxis) pre- and post-intervention to inform the evidence base regarding the effectiveness of these interventions. However, chemoprophylaxis should not be delayed while awaiting swabbing results.

Information from swabbing of close contacts may also inform possible repeat antimicrobial prophylaxis in individuals who are still culture positive.

8. Surveillance and communication

Initial detection of clusters will often be by parties outside the HPA, NPHS or HPS. They could include local microbiology laboratory, local education authority, local GPs, A&E doctors, paediatricians, physicians and prison services. It is important they are aware of the public health importance of these clusters and the need to report and liaise with the local Health Protection team and/or hospital Infection Control Team to ensure investigation and interventions are appropriately undertaken.

With the formation of an Outbreak Control Team (OCT) with a clear lead person within HPA, NPHS or HPS, the OCT should follow the standard HPA/HPS guidelines for outbreak response.

In subsequent communication it will be important to consider relevant parties including the PCT, SHA, local authority, local education authority, Commission for Social Care Inspection, local GPs, A&E, paediatricians or physicians etc.

Information on the cases and the setting should be reported by the responsible HPU and returned to the regional epidemiologist and HPA Centre for Infections or Health Protection Scotland. Reporting of these incidents will be important to inform the future development of these guidelines. See appendix for the proforma.

Laboratories should also report all confirmed cases as per the CDR Reporting Guidelines.

Appendix

Membership of HPA working group

Dr Richard Pebody (Chair)	HPA Centre for infections
Dr Chikwe Ihekweazu	PH SpR
Dr Marina Basarab	PH SpR
Dr Alex Doroshenko	PH SpR
Dr Deborah Wilson	PHMEG Nominee
Dr Isabel Oliver	RE nominee
Dr Bharet Patel	Regional Microbiologist
Dr David Dance	RMN/AMM nominee
Ms Sarah Brill	Community ICN nominee
Dr Mary Slack	SRMD RSIL
Dr Martin Donaghy	Director, Health Protection Scotland
Dr Robert George	Director SRMD-RSIL and Chair of HPA Pneumococcus and Hib Forum

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Table 1: levels of evidence

Available at [www.sign.ac.uk/guidelines/fulltext50/section 6.html](http://www.sign.ac.uk/guidelines/fulltext50/section%206.html)

1++	High quality meta analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies. High quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2-	Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3	Non-analytical studies e.g. case-reports, case series
4	Expert opinion

Grades of recommendation

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1++, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

Reporting form for cluster in closed setting

Section 1: Cluster details

Location/name of premises _____

Total number and clinical features of cases:

	Total no.	Meningitis	Pneumonia	Bacteraemia	Empyema	Other
Confirmed cases						
Probable cases						
Possible cases						

Date of onset: First case __/__/__

Last case __/__/__

Have any of the confirmed cases been serotyped? , If yes, what serotype(s) _____

Section 2: Type of setting (tick as appropriate)

- Child day-care Care home
Pre-school Hospital
School Prison
Household Military establishment

Other closed setting (please describe) _____

Section 3: Population at risk and action taken (tick as appropriate)

Number of persons in the establishment _____

Antibiotics given If yes, date __/__/__ How many? __ Name _____

PPV given If yes, date __/__/__ How many? __

PCV given If yes, date __/__/__ How many? __

How many pneumococcal cases occurred after the intervention? _____

Section 4: Nasopharyngeal swabbing of contacts (tick as appropriate)

Undertaken before If yes, date __/__/__ How many swabbed? __

If yes, how many were positive for *Streptococcus pneumoniae*? _____

Undertaken after If yes, date __/__/__ How many swabbed? __

If yes, how many were positive for *Streptococcus pneumoniae*? _____

How many were positive for the cluster serotype _____

Section 5: Additional comments

Form completed by: _____ Position: _____ Date: __/__/__

PLEASE RETURN FORM TO RICHARD PEBODY, HPA CENTRE FOR INFECTIONS

APPENDIX 2:

Example of letter to adult contact or parent of child contact if antibiotics and/or vaccination needed

Dear parent/guardian/student/resident/patient

Re Pneumococcal infection in x school/prison/care home

I am writing to inform you that x cases of meningitis/pneumonia/bacteraemia, probably/definitely caused by the pneumococcal bacteria have been identified within the school/nursery/class/prison/wing/care home. An information leaflet about pneumococcal infection is included with this letter.

The risk of this infection being passed on is likely to be extremely low. Activities should continue as normal and there is no reason to keep children away from nursery/school. As a precaution and in accordance with national expert advice, we will be offering preventive antibiotics and vaccination to other people/children in the nursery/school/class/prison/care home who have had prolonged contact with the cases since 2 days before date of the first case became unwell.

We have arranged for children/patients/residents to receive antibiotics/vaccination

at

on

Please could you complete and sign the enclosed (parental) consent form (and the child should be accompanied by a responsible adult to collect the medication and return it to ... by xx/xx/200x. I also enclose an information sheet.

If you/your child develop/s symptoms as described in the leaflet, please contact your doctor and show them this letter.

For further information, please contact the local HPU.

Yours sincerely,

Consultant in Health Protection

Enc. Consent form
 Information leaflet on pneumococcal disease
 Information sheet on antibiotic
 Information of pneumococcal immunisation

Example information leaflet for Pneumococcal Disease

This leaflet is for people and parents/carers of children who may have had close contact with a person who has serious pneumococcal disease when two or more linked cases have been identified.

What is pneumococcal disease?

Pneumococcal disease is a term used to describe the range of infections which can be caused by a bacterium called *Streptococcus pneumoniae*.

How do you catch it?

The bacteria which cause pneumococcal infections can be spread by close contact with someone who is carrying the bacteria when that person coughs or sneezes. They can also be spread by direct contact with respiratory secretions from an infected person, such as used paper tissues.

Some people can carry the bacteria in the backs of their noses and throats without ever becoming ill while others can go on to develop a pneumococcal infection. It is not known why it only affects some people but it is known that some groups of people are more at risk than others of developing it. These groups include:

- the very young or the very old
- people with a chronic illness such as diseases of heart, lung, kidneys or liver
- people without a spleen or with a damaged spleen
- people whose immune system is not working properly

What kind of infections do the bacteria cause?

The bacteria can cause a variety of infections ranging from sinusitis and ear infections to more serious illnesses such as pneumonia, meningitis and blood-poisoning.

Can you catch a pneumococcal infection from close contact with someone at home or school who has it?

The vast majority of people who come into contact with someone with a pneumococcal infection remain well and symptom-free. It is extremely rare for healthy people to catch the infection from a relative or a member of their household.

Why are close contacts being offered antibiotics?

When two or more cases of pneumococcal infection are identified in people living in the same house or who attend the same school or nursery class, there is evidence that close contacts may be at a slightly increased risk of developing the infection. As a precautionary measure, in these circumstances close contacts are offered information, antibiotics and sometimes immunisation.

Can people be immunised against pneumococcal disease?

All children born after September 2004 have routinely been offered a vaccine against certain types of pneumococcal disease. In addition, anyone aged 65 or older or anyone who is in one of the at-risk groups listed above is routinely offered a vaccine to protect against certain types of pneumococcal disease.

The vaccines only protect against certain types of pneumococcal disease. When two or more cases of pneumococcal disease are identified in a household, school or other closed environment, vaccine together with antibiotics will be offered to close contacts if it is effective against the particular type of pneumococcal disease identified.

What are the symptoms of pneumococcal disease?

Most people come into contact with the bacteria which can cause pneumococcal disease every so often and remain well. Developing a serious pneumococcal infection after coming into contact with an infected person is very rare. However, if you or your child develop any of the following symptoms in the next two weeks you should seek medical attention and show the letter and this leaflet to the doctor or nurse advising you. The symptoms to watch out for are:

- a severe cough
- shortness of breath
- chest pains
- confusion or drowsiness
- a severe prolonged headache
- stiff neck, aversion to light
- fever
- seizures

For further information please contact:

[insert HPU contact details]

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