National enhanced surveillance of severe group A streptococcal disease

PROTOCOL

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Version: 1.5

Version Date: 20 February 2009

1. BACKGROUND

Several parts of the UK saw an increase in the number of severe group A streptococcal infections during December 2008[1]. Sudden increases in cases were identified in the North East and East of England, the latter seeing an unusually high case fatality rate (7 of 19 confirmed cases died). As a result of these increases, an IRIS Level 3 incident (3693) was declared on the 16th January 2009. Subsequent analysis of isolates submitted to the reference laboratory identified an increase in *emm*3 in January 2009[2], a GAS type associated with a higher case fatality rate than most other *emm* types[3].

Periodic upsurges in iGAS and rheumatic fever have been reported in many countries across Europe and North America since the 1980s[4]. The reasons behind these increases are poorly understood. The current increases being seen in the UK may be attributable to a natural cycle in disease incidence. However, the potential for changes in virulence of circulating strains or increased incidence in particular risk groups, as seen in the UK during the early 2000s[5], remain possible. The significant influenza activity in the UK during December 2008 may have contributed directly or indirectly to the current increase in iGAS by increasing transmission of GAS and/or rendering individuals with influenza more susceptible to secondary infection with GAS[6].

As part of the HPA response to the increases currently being seen in iGAS, national enhanced surveillance is being introduced to gain additional information to evaluate the public health management of these diseases. This will be the third period of enhanced surveillance in the UK. The first was introduced in 1994-97 in response to the cluster of necrotising fasciitis in Gloucester. The second, in 2003-04, formed part of Europe-wide initiative (Strep-EURO) and provided the evidence-base for the current public health guidance on the management of iGAS community contacts[7;8].

2. AIM AND OBJECTIVES

The aim of the enhanced surveillance is to evaluate as expeditiously as possible any changes in the epidemiology of severe group A streptococcal infections to inform public health guidance. Information obtained will be used to inform wider clinical and public health guidance, including, if appropriate, CMO cascade on diagnosis and treatment. This will be realised through the following objectives:

1. Identify any increases in risk of severe GAS infection in established or novel risk groups who might benefit from further advice, prophylaxis or other intervention

2. Identify potential improvements in the public health management of both individual cases and clusters and contact follow-up

3. Evaluate the epidemiology of severe GAS infection in relation to clinical, risk factor, outcome of cases and possible associations with microbiological characteristics.

4. Use the opportunity of enhanced surveillance to raise general clinical and public health awareness of this condition and recommended public health actions around individual cases.

3. METHODS

3.1. Case definition

Severe group A streptococcal infections are defined through the isolation of a group A streptococcus (*Streptococcus pyogenes*) from a site that is normally sterile (blood; cerebrospinal fluid; joint aspirates; pericardial/peritoneal/pleural fluids; deep tissue or abscess at operation or necropsy; bone) or from a non-sterile site in combination with a severe clinical presentation – streptococcal toxic shock, necrotising fasciitis, pneumonia, puerperal sepsis, septic arthritis, meningitis). This definition is a slight expansion on the definition of invasive disease (iGAS) which is limited to cases with sterile sites only.

3.2. Data collection

Enhanced surveillance questionnaires should be completed for all cases diagnosed by laboratories in England from specimens collected since the 1st January 2009.

Instructions for Microbiology Departments

Microbiology departments are requested to undertake the following at the point a case is diagnosed:

1. Notify the HPU of all cases that fit the case definition to initiate contact assessment according to existing national guidelines
2. Complete the first part of the surveillance form (yellow section), along with any identified risk factors in the blue section, available as a PDF file or MS Excel spreadsheet at http://www.hpa.org.uk/GAS/enhanced.surveillance
3. E-mail or fax the form to the HPU for completion of the remainder of the form.
4. Ensure the sterile site GAS isolate/s or those from other cases meeting the case definition are referred to SDRU for typing.

Instructions for HPUs

HPUs should reconcile notifications made directly to them from microbiology laboratories with copy reports and cases identified through LabBase. HPUs should complete the following steps:

1. Co-ordinate the completion of surveillance forms
2. Complete HPU section of surveillance forms (blue part)
3. Ensure the patient's vital status at 7 days is completed in the yellow section if blank
4. Enter questionnaire data on the HPA web-portal https://www.hpawebservices.org.uk/iGASsurveillance/
5. Keep a unit line-list and file of completed forms for an audit trail and reconciliation of local data with national isolates

To assist HPUs in keeping track of all cases arising in their HPU, copies of typing reports on all iGAS isolates submitted to SDRU will be passed to them. CfI will also provide a line list all iGAS isolate referrals, along with typing and patient details, since 1st January 2009 to each HPU. This list will include details of the laboratory where the

initial isolate was obtained allowing the HPU to allocate forms correctly to referring hospital microbiology departments.

3.3. Use of the HPA web-portal

For access to the web portal, each HPU Director should send the name and e-mail address of individual/s who require access to Theresa.lamagni@hpa.org.uk. On first logging on to the web portal, users should change their password to one of their own choice through the 'My Profile' section of the web site. All users should ensure that their password is at least eight characters in length and contain at least one upper and lower case character, digit and punctuation character. The number of logging attempts is restricted to a maximum of three attempts after which the account is locked and can only be reset by contacting the helpdesk. Account holders should not pass on their logon details to other individuals and should ensure that their username and password are kept secure.

To enter a new questionnaire

Select 'New' from the Surveillance menu on the home page. The questionnaire can be entered directly online using your mouse or tabbing through to move between fields. Any questionnaire sections that are not applicable do not need to be completed and can be skipped by progressing to the next section. Clicking the Finish link displayed on the last questionnaire section (Risk Factors) will display a confirmation page with a unique code e.g. 6a50fb02-4d66-4f56-a598-a23f16c8d78e that should be copied and kept for future reference. This can easily be done by selecting the code with the mouse (position the mouse cursor at the beginning of the code, hold down the left mouse button and move the mouse to the right until the entire code is selected). Once selected, click the right mouse button and select 'Copy' to copy the code and paste it in a separate document for future reference.

To edit a questionnaire

To edit or complete a previously started questionnaire, select Edit from the Surveillance menu and the search web page will be displayed. All questionnaires that have been created are initially displayed in a list on the page. If there are more than 10 questionnaires in the list, the list will be divided into a number of pages which can be accessed by clicking on the page number displayed at the bottom of the page. To select a particular questionnaire to edit, locate the questionnaire in the list and click the 'Select' link associated with the questionnaire. To more quickly locate the questionnaire, enter the code in the field labeled 'Code' and click the 'Search' button. The % special character is a wildcard character that is used to specify any number of characters. The following table lists two typical searches using the wildcard character and the expected search results.

Code field	Search results
%	All questionnaires
019%	All questionnaires assigned a unique code beginning with 019

3.4. Notes on completion

i) PATIENT DETAILS

• Report number/CoSurv ID - please indicate the unique LabMod record number associated with this case.

• SOUNDEX - this is a code based on the patient's surname e.g. L265 to help maintain confidentiality. Please provide the SOUNDEX code if you are able to do so or leave blank for the HPU to complete. The MS Excel version of the questionnaire has an inbuilt function for generating SOUNDEX codes.

• Date of hospital admission - please give the date the patient was admitted to hospital during this hospital stay

• Location at time of onset - please indicate where the patient was at the time they developed symptoms of iGAS and if their own home, the number of household members in total, and the number of children aged less than 16 years.

ii) ISOLATE DETAILS

Please provide full details for all specimens from which group A streptococci were isolated.

iii) CLINICAL DETAILS

• Post-mortem diagnosis - please indicate if iGAS infection was only confirmed through specimens taken post mortem.

• Non-focal bacteraemia - bacteraemia in the absence of any identified primary focal site of infection.

• Multi-organ failure - altered organ function (2 or more systems) such that homeostasis cannot be maintained without intervention.

• Hypotensive shock - systolic blood pressure ≤ 90mm Hg.

• Renal impairment - two-fold elevation of age-adjusted creatinine level (or higher).

• DIC - disseminated intravascular coagulation.

• Liver impairment - raised sGOT, sGPT or two-fold elevation of bilirubin levels (or higher).

• Soft tissue necrosis - fasciitis, myositis or gangrene.

• Streptococcal toxic shock syndrome (STSS) – defined as 'Isolation of a group A streptococcus with hypotension (systolic BP ≤ 90mm Hg) and two or more of the following: renal impairment, coagulopathy, liver abnormalities, acute respiratory distress syndrome, extensive tissue necrosis, erythematous rash'.

• Admitted to ITU/HDU - please indicate if the patient has as a result of this infection been admitted to an intensive care/therapy unit, high dependency or level 2 dependency unit.

• Surgical intervention - please indicate if the patient underwent any surgical procedure/s as a result of this infection, including exploratory surgery.

• Outcome - Please indicate the patient's vital status at exactly 7 days after the initial GAS isolation. Please include the date of death where applicable.

iv) RISK FACTORS

Please tick any that apply, noting any other possible risk factors, including disease or treatment-related immunosuppression.

• Hospital acquired infection - defined as infection occurring 48 hours after hospital admission (including time in originating hospital in the case of transfer).

• Upper respiratory tract infection - please indicate if the case had signs and symptoms of an upper respiratory tract infection, what kind of infection, whether a GP was consulted and if antibiotics were prescribed (for treatment of infection, not for prophylaxis). Influenza-like illness is defined by fever over 38ºC, myalgia and respiratory symptoms.

• Any other risk factor - please select or type in any other potential risk factor (acute or chronic).

• Pre-admission use of analgesics/antipyretics - please indicate whether the patient took any analgesics/antipyretic preparations in the 48 hours prior to admission with iGAS. Use of these agents has been associated with development of severe iGAS presentations although an aetiological link remains unproven.

• Close contacts - close contacts are defined as someone who has had prolonged close contact with the case in a household type setting during the 30 days before onset of illness e.g. living and/or sleeping in the same household, pupils in the same dormitory, boy/girlfriends, HCW directly exposed to larger particle droplet/secretions from the respiratory tract of a case.

3.5. Assistance with surveillance programme

HPUs should contact Theresa Lamagni at the Centre for Infections for general assistance with the surveillance programme. For technical support on the web-based data capture system please call the ISD helpdesk on 020 8200 1566 or e-mail developmenthelpdesk@hpa.org.uk. In the event that the iGAS surveillance website encounters a problem, the website will display a page with detailed error information (Page Name, Page State, Error Message and Stack Trace). This information should be forwarded to helpdesk as soon as possible. Please copy the information by pressing the 'Alt' and 'Prt Sc' buttons simultaneously and then paste in an email message.

3.6. Data analysis and dissemination

Regular data analyses will be undertaken by the Centre for Infection to update clinical and health protection staff on the current situation. In-depth analyses will be performed to generate hypotheses and suggest public health actions. Results will be disseminated through a number of means, including the *Health Protection Report*, peer-review papers and conference proceedings. The efforts of reporters will be acknowledged in all publications.

3.7. Criteria for cessation of enhanced surveillance

The incident management team will keep under continual review the need for this enhanced surveillance programme. Factors that will be taken into account include: trends in disease incidence, the severity of the presentations, the identification of novel risk factors, changes in clustering patterns.

4. ETHICAL AND CONFIDENTIALITY ISSUES

4.1. Security of patient-identifiable information

Collection of patient data for this surveillance initiative falls within the HPA's Patient Information Advisory Group (PIAG) approval to process patient-identifiable information for the purposes of infectious disease surveillance, in accordance with Section 60 of the Health and Social Care Act 2001. This allows NHS organisations to disclose identifiable patient information to the HPA without the explicit consent of the patient concerned while remaining within the confines of the Data Protection Act. Annual applications are made by the HPA to PIAG for continued permission to process patient identifiable information.

The enhanced surveillance web portal is deployed using SSL and can only be accessible via a secure HTTP connection. This means that all data communications between the user's internet browser and the HPA web portal is encrypted and cannot be viewed by an unregistered user.

4.2. Maintenance of confidentiality and anonymity of data

The HPA has in place a number of security measures to prevent unauthorised or unlawful access to personal data held on site. All HPU and CfI staff handling surveillance data will to 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 only be removed as soon as practicable and in accordance to Caldicott data retention policy.

All electronic data will be held in password-protected files and all paper documents locked in filing cabinets.

5. INCIDENT MANAGEMENT TEAM

Robert George, CfI (chair)
Androulla Efstratiou, CfI
Theresa Lamagni, CfI

David Dance, RMN
Bharat Patel, RMN
Tim Wreghitt, RMN

Joe Kearney, LaRS (deputy chair)
Pat Nair, LaRS
Christopher Williams, LaRS
Paul Davison, LaRS
Isabel Oliver, LaRS
Mark Reacher, LaRS
Gareth Hughes, LaRS

Incident Lead - Mike Catchpole

6. REFERENCES

1. HPA. Group A streptococcal infections: update on seasonal activity, 2008/09.*Health Protection Report [serial online]* 2009; 3(2) http://www.hpa.org.uk/hpr/archives/2009/news0209.htm#igas)

2. Lamagni TL, Efstratiou A, Dennis J, Nair P, Kearney J, George R et al. Increase in invasive group A streptococcal infections in England, Wales and Northern Ireland, 2008/09. *Euro Surveill* 2009; 14(5).

3. O'Loughlin RE, Roberson A, Cieslak PR, Lynfield R, Gershman K, Craig A et al. The epidemiology of invasive group A streptococcal infection and potential vaccine implications: United States, 2000-2004. *Clin Infect Dis* 2007; 45(7):853-862.

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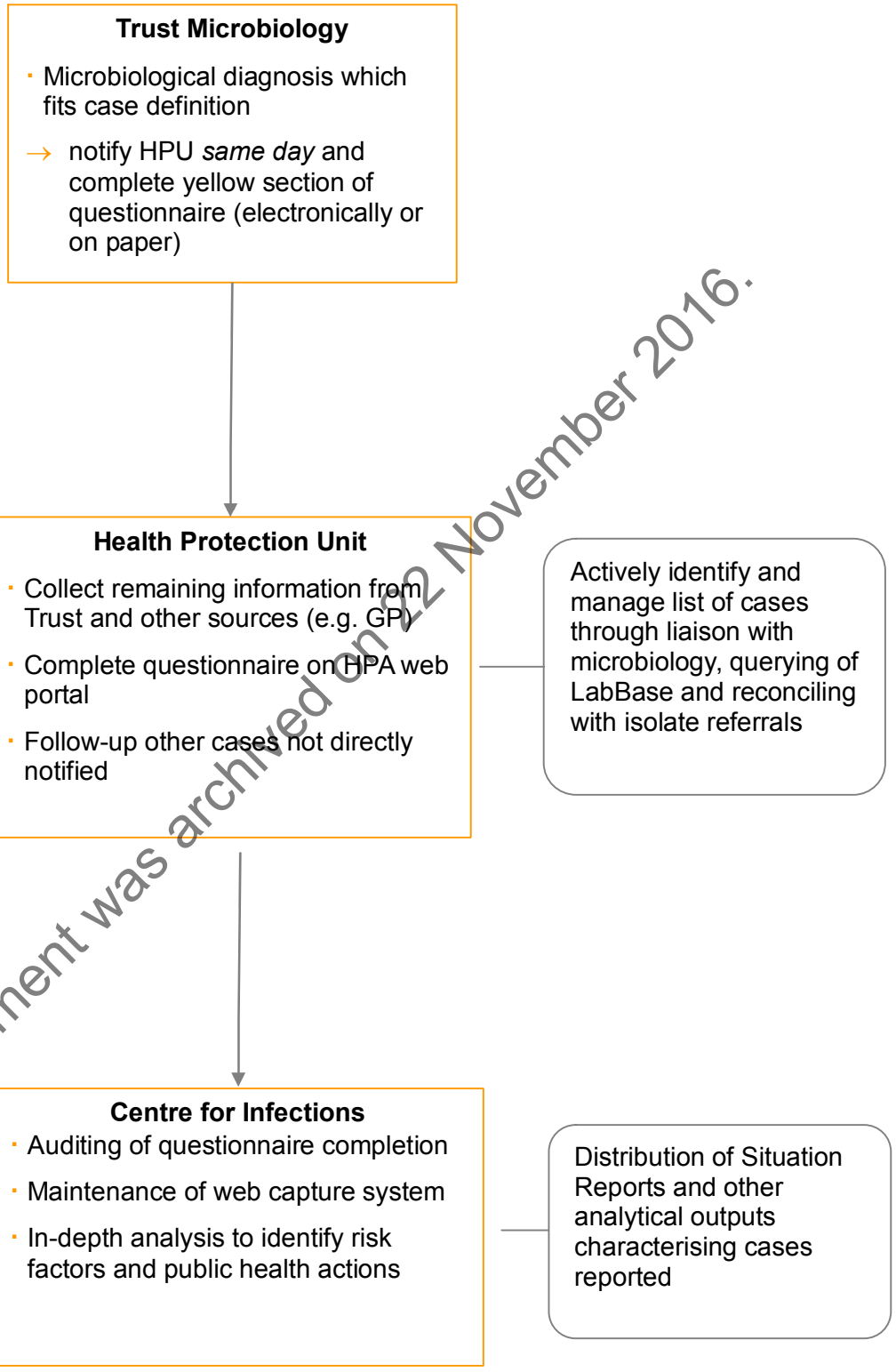
5. Lamagni TL, Neal S, Keshishian C, Hope V, George RC, Duckworth G et al. Epidemic of severe *Streptococcus pyogenes* infections in UK injecting drug users, 2003-04. *Clin Microbiol Infect* 2008; 14(11):1002-1009.

6. HPA. Influenza activity is increasing across the UK.*Health Protection Report [serial online]* 2008; 2(51)http://www.hpa.org.uk/hpr/archives/2008/news5108.htm#flu)

7. Lamagni TL, Neal S, Keshishian C, Alhaddad N, George R, Duckworth G et al. Severe *Streptococcus pyogenes* Infections, United Kingdom, 2003-2004. *Emerg Infect Dis* 2008; 14(2):201-209.

8. Health Protection Agency Group A Streptococcus Working Group. Interim UK guidelines for management of close community contacts of invasive group A streptococcal disease. *Commun Dis Public Health* 2004; 7(4):354-361.

ANNEX A – Enhanced surveillance flow chart



ANNEX B – Enhanced surveillance questionnaire

NATIONAL ENHANCED SURVEILLANCE OF SEVERE GROUP A STREPTOCOCCAL INFECTION

IN STRICT CONFIDENCE

Please tick boxes or write in the white space(s) provided (see notes overleaf)

Yellow sections to be completed by the Microbiology Department

YOUR NAME: **HOSPITAL:** **DATE:**

Blue sections to be completed by the Health Protection Unit

NAME: **HPU:** **DATE:**

i) PATIENT DETAILS

Report number/CoSurv ID:
Patient's initials: **SOUNDEX (of surname):**
Laboratory ref/code: **NHS number:**
Date of birth (dd/mm/yyyy): **Hosp. number:**
or **Age** years/months/days: **Sex:** ☐ Not known ☐ Male ☐ Female

Post code of residence: **Occupation:**

Ethnicity: ☐ Not known ☐ White ☐ Black Caribbean ☐ Black African
☐ Indian/Pakistani/Bangledeshi ☐ Mixed ☐ Other (please specify) ►

Date of hosp. admission: **Date of onset:**

Location at time of onset:
☐ Not known ☐ Other hospital ☐ Residential/nursing home
☐ Hostel ☐ Own home ☐ Other (specify) ►
Number in household? ► *Of these, number <16y*

ii) ISOLATE DETAILS

Date of specimen/s

Group A streptococci isolated from:
☐ Blood
☐ CSF
☐ Joint
☐ Peritoneal fluid
☐ Pleural fluid
☐ Sputum
☐ Tissue
☐ Abscess (site) ►
☐ Wound (site) ►
☐ Other (specify) ►

Isolate/s sent to HPA Streptococcus and Diphtheria Reference Unit?
☐ Not known ☐ No ☐ Yes

iii) CLINICAL DETAILS

☐ Clinical details not known

Diagnosis made at post mortem only?
☐ Not known ☐ No ☐ Yes

Focus of infection:
☐ Non focal bacteraemia ☐ Cellulitis ☐ Erysipelas ☐ Infection of injecting site
☐ Abscess ☐ Other wound infection
☐ Myositis ☐ Necrotising fasciitis (site) ►
☐ Puerperal sepsis ☐ Other genital tract infection ►
☐ Septic arthritis ☐ Peritonitis ☐ Meningitis ☐ Pneumonia ☐ Empyema
☐ Scarlet fever ☐ Pharyngitis/tonsilitis ☐ Other presentation ►

Symptoms: ☐ Fever ☐ Vomiting ☐ Diarrhoea
☐ Pain (specify site) ►
☐ Other symptoms ►

Degree of severity:
☐ Not known ☐ Renal impairment ☐ Liver impairment ☐ Multi-organ failure
☐ Respiratory distress ☐ Erythematous rash ☐ Hypotensive shock ☐ DIC
☐ Soft-tissue necrosis ☐ Streptococcal toxic shock syndrome ☐ Admitted to ITU/HDU
☐ Other (please specify) ►

Clinical management:
Antibiotic treatment (post admission) ☐ Not known ☐ None given
☐ Yes ► ☐ penicillin ☐ clindamycin ☐ macrolides ☐ cephalosprins ☐ other
Intravenous immunoglobulin used for treatment? ☐ Not known ☐ No ☐ Yes
Surgical intervention? ☐ Not known ☐ No ☐ Yes (please specify) ► ☐ debridement ☐ amputation ☐ other

Outcome (at 7 days after GAS isolation):
☐ Not known ☐ Dead ► ☐ GAS infection was main cause of death
☐ Alive ☐ GAS infection contributed to death (not main cause)
☐ GAS did not contribute to death
☐ cause of death not known
► date of death:

iv) RISK FACTORS

☐ Risk factor information not known

Chronic comorbidities:
☐ No underlying illness/predisposing factors
☐ Diabetes ☐ Malignancy ☐ Chronic respiratory condition
☐ Steroid use ☐ Dementia ☐ Chronic heart disease
☐ Homeless ☐ Alcoholism ☐ Chronic renal disease
☐ Injecting drug user ☐ Immunosuppression

Acute risk factors (within 14 days of iGAS onset):
☐ Skin lesion/wound ► ☐ trauma (penetrative) ☐ surgery
☐ trauma (blunt) ☐ line infection
☐ pressure sore ☐ injection site
☐ varicella (chickenpox) ☐ eczema
☐ impetigo/erysipelas ☐ skin ulcer
☐ Other lesion/wound ►
☐ Childbirth ► date
☐ Other pregancy related risk factor (e.g. miscarriage)

Was this infection hospital acquired?
☐ Not known ☐ No ☐ Yes

Upper respiratory tract infection?
(within 14 days of iGAS onset)
☐ Yes (specify reason and if GP consulted) ☐ No ☐ Not known
GP consult?
☐ Pharyngitis/tonsilitis ☐
☐ Scarlet fever ☐
☐ Influenza-like illness ☐ ► ☐ lab confirmation of viral infection?
► *Specimen date:*
☐ Other (specify) ►

Were antibiotics prescribed? ☐ Not known ☐ No ☐ Yes

Any other risk factor?

Pre-admission use of analgesics/antipyretics
(48 hours before admission):
☐ Yes (please specify) ☐ No ☐ Not known
☐ paracetamol ☐ ibuprofen ☐ aspirin
☐ other (please specify) ►

Was *this* case a close contact of other case(s) of GAS disease (within 30 days of onset)? e.g. strep throat, iGAS
☐ Yes (please specify) ☐ No ☐ Not known
specify relationship e.g parent
☐ household contact ►
☐ other contact ►

Had *this* case received antibiotic prophylaxis?
☐ Not known ☐ No ☐ Yes ► date
Date of onset/specimen of *linked* case: ►
Clinical presentation of *linked* case:
☐ non invasive GAS (specify) ►
☐ invasive GAS (specify) ►

Total number of close contacts identified in association with *this* case?
How many contacts given chemoprophylaxis?

Additional information