2 Single case of iGAS: risk assessment and identification of contacts

2.1 Risk Assessment

Following a notification of iGAS infection, conduct a Public Health Risk Assessment (PHRA) on a case-by-case basis to:

a) Establish any potential sources of infection or contact with healthcare within the last 7 days prior to the onset of symptoms consistent with GAS
b) Establish if there are any settings or contexts that may require more detailed risk assessment to establish close contact and possible onward transmission
c) Details should be recorded on the enhanced surveillance form.

Examples of settings or contexts are identified below; however, this is not an exhaustive list and other settings may be identified through a PHRA:

- **Residential Care Facilities**: residents are **not** usually classified as close contacts unless they share a bedroom; however, a detailed risk assessment should be undertaken, see Chapter 5
- **Settings where individuals co-habit**: (for example, boarding schools, universities, hostels), see Chapter 6
- **Congregate settings**: Congregate settings refer to a range of facilities where people (most or all of whom are not related) live or stay overnight and use shared spaces (e.g., common sleeping areas, bathrooms, kitchens) such as: shelters, group homes and emergency accommodation including International Protection Accommodation Services (IPAS)(39).
- **Childcare facilities (CCF):** Children attending the same crèche, school or other childcare setting are **not** normally considered to be close contacts; however, it may be possible to define a group within this setting which fulfils the definition of close contact (for example, a childminder's home), see Chapter 4
- Acute hospital and maternity settings see here.

d) Long haul travel (8 hours or more) see Section 2.2
e) Identify close contacts (see Section 2.2)
f) Ascertain close contacts at high risk (Section 2.3)

Following the PHRA, advice should be given to contacts and antibiotic chemoprophylaxis offered where appropriate. Details should be recorded on the available incident management system.

2.2 Identify close contacts

Individuals meeting the definition of close contacts should be identified (see definition of close contact in Chapter 1). Contacts with more than 24 hours of continuous exposure to cases are at highest risk of infection and colonisation (40, 41). If any close contacts with signs and symptoms of possible GAS infection are identified, they should be referred for clinical assessment and treatment (Table 3, Table 4 and Algorithm 1) (42).

A PHRA may identify other close contacts, such as those with prolonged or intimate contact. Area Public Health Teams should exercise judgement in defining close contacts for cases who do not reside in the same household as the case. Criteria for identifying close contacts are outlined earlier in **Section 1.3.2**.

Situations which may require more detailed assessment include people living in the following settings:

- Congregate settings
- Complex household arrangements where people are reluctant to disclose information
- Hostels providing temporary accommodation for the homeless, see Chapter 6.

People travelling in prolonged close proximity, on long-haul vehicle or aircraft journeys (8 hours or longer) should also be considered when identifying close contacts (5). In these situations, consider:

1. The duration of exposure
2. Ventilation in the vehicle and

3. Whether the case was symptomatic during the journey.

Where the identity of individuals in prolonged close proximity to the case is known, treatment or prophylaxis for individual contacts may be possible and a risk assessment may be undertaken.

If the case undertook international travel, regardless of the length of the journey, ensure that the International Health Regulations (IHR) national focal point is notified. Please refer to International Aviation and Transport Authority (IATA) guidance for more information relating to air travel and communicable diseases.

2.3 Identify high risk contacts

Identify any close contacts considered high risk and eligible for antibiotic chemoprophylaxis (see Table 4).

2.3.1 Older persons (≥75 years)

The incidence of iGAS increases with age (43-45) and this risk is significantly elevated for cohabiting persons whose partner or spouse develops iGAS infection (6, 46). In couples over 75 years the secondary household risk of iGAS infection was estimated at 15,000 per 100,000 person-years (46). The guideline development group made a pragmatic decision to recommend antibiotic chemoprophylaxis for all older persons (75 years and above) who are household contacts of an iGAS case regardless of the nature of the relationship. In a residential care facility, only sharing a bedroom with a case is to a household, refer to Chapter 5 for further information.

In other settings such as congregate settings, settings where individuals co-habit, crèche, school or other childcare settings, acute hospitals, high risk close contacts may be identified through a PHRA. Refer to the appropriate sections in this guideline.

Recommendation 1: Offer antibiotic chemoprophylaxis to all older (75 years and above) household contacts of the case.

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2.3.2 Pregnancy, post-partum period and neonates

Signs of severe sepsis in women ≥37 weeks of pregnancy or with a history of recent childbirth, particularly with confirmed or probable GAS infection, should be regarded as an obstetric emergency (47, 48). A recent systematic review reported a pooled incidence of iGAS infection in pregnancy of 0.12 per 1,000 live births from 9 studies conducted in high income countries (49).

Women with puerperal sepsis acquire their infection from children in the household or other contacts (50, 51). The majority of iGAS infections in the post-partum period are reported in the 28 days after giving birth (85%) and can be severe for both mother and baby (51, 52). A UK study reported that the risk of iGAS is increased by approximately 80-fold within 28 days post-partum as compared to other women aged 15 to 44 (53) and US surveillance data report a 20- fold increase in bacteraemia and developing septicaemia (52). This highlights the importance of suspecting iGAS in a maternity patient presenting with sepsis and providing immediate support, including early administration of intravenous antibiotics.

Babies born to infected or colonised mothers may become colonised at birth (54). Swabbing of ears, nose, and umbilicus should be considered for babies born to iGAS-infected mothers. Maternal and neonatal infection can arise on the same day but the median onset times are 2 days postpartum (interquartile range (IQR) 0 to 5 days) for mothers and 12 days (IQR 7 to 15 days) for neonates (53). Whilst the increased risk within mother-baby pairs is likely due to transmission at birth, a small proportion of these neonates may acquire infection from the household or other close contact rather than the mother in the days following delivery.

Recommendation 2: Offer antibiotic chemoprophylaxis to all women from ≥37 weeks of pregnancy up to 28 days after giving birth who are close contacts of the case.

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Recommendation 3: Offer antibiotic chemoprophylaxis to neonates up to 28 days after birth where the mother or any close contact develops iGAS infection.

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2.3.3 Chickenpox and influenza

Chickenpox (or Varicella) is a risk factor for development of iGAS infection in children, with the highest risk 4 to 5 days after onset of rash (range 2 to 14 days) (55, 56). Clusters of chickenpox and iGAS co-infection have previously been identified in Ireland, as outlined in a 2016 study by Ó Maoldomhnaigh et al. (57). In this study, of 10 children admitted to hospital with iGAS infection, 7 also had active chickenpox co-infection. A year later, in 2017, a similar cluster was identified in the same hospital, with 6 of 13 children with iGAS presenting with chickenpox co-infection (58). Evidence suggests that offering antibiotic chemoprophylaxis to a household contact who develops chickenpox with active lesions within the 7 days prior to diagnosis of iGAS in the index case or within 48 hours after commencing antibiotics by the iGAS case, if exposure is ongoing, may reduce the risk (59).

Influenza is also a recognised risk factor for iGAS infection (60-63) but as there is limited evidence regarding the impact of influenza on secondary household transmission of iGAS, antibiotic chemoprophylaxis is not currently recommended. (Also see Section 2.3.2).

Although other illnesses and host factors have been associated with an increased risk of sporadic iGAS infection there is limited evidence to recommend antibiotic chemoprophylaxis (64, 65).

Recommendation 4: Offer antibiotic chemoprophylaxis to a close contact who has developed chickenpox with active lesions within the 7 days prior to diagnosis of iGAS in the index case, or within the 48 hours after commencing antibiotics by the iGAS case if exposure ongoing.

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Table 3 Summary of public health actions for close contacts of iGAS cases in household settings

Risk assessment of household contact	Defined as	Action required
A) High-risk	• older persons (≥75 years) • pregnant women ≥37 weeks • women within 28 days after giving birth • neonates (up to 28 days old) • individuals who develop chickenpox with active lesions within 7 days prior to diagnosis of iGAS in the index case or within 48 hours after commencing antibiotics by the iGAS case, if exposure ongoing	Offer chemoprophylaxis only to high-risk contacts. Administer as soon as possible (within 24 hours) and not beyond 10 days after iGAS after date of diagnosis of index case. Provide household with '*Information leaflet for contacts of patients with Invasive Group A Streptococcal infection (iGAS)*
B) Symptomatic: iGAS symptoms*	Symptoms suggestive of iGAS	Urgent referral to secondary medical care for immediate medical assessment Provide household with *Information Leaflet for Contacts of Patients with Invasive Group A Streptococcal infection (iGAS)*

	If 2 or more confirmed or probable iGAS cases (in previous 30 days) are identified in the household setting	Offer chemoprophylaxis to entire household ASAP Provide household with *Information Leaflet for Contacts of Patients with Invasive Group A Streptococcal infection (iGAS)*
C) Symptomatic: GAS symptoms**	Symptoms suggestive of localised GAS infection	Refer symptomatic close contact for clinical assessment and treatment (*GP assessment and treatment if GAS suspected).* Provide household and close contacts with *Information Leaflet for Contacts of Patients with Invasive Group A Streptococcal infection (iGAS)* Provide GP with copy of Guidance for General Practitioners and others on the management of infections caused by Group A Streptococcus
D) All other close contacts	Those not reporting symptoms at the time of the risk assessment and not in a high-risk group.	Provide *Information leaflet for contacts of patients with Invasive Group A Streptococcal infection (iGAS)* to advise all other close contacts to be alert to the signs and symptoms of GAS infection and seek medical attention if they develop a febrile illness or any clinical manifestation of GAS within 30 days after diagnosis of index case. In this situation, consider chemoprophylaxis for any asymptomatic close contacts based on PHRA (other asymptomatic household close contacts may be offered chemoprophylaxis following PHRA and taking account of current epidemiological situation)

* High fever, severe muscle aches or localised muscle tenderness increasing pain, swelling and redness at site of wound, unexplained diarrhoea, or vomiting.
** Sore throat, fever, minor skin infections, scarlatiniform rash.

2.4 Antibiotic chemoprophylaxis

2.4.1 Recommended prophylactic antibiotic regimens for close contacts

Phenoxymethylpenicillin (penicillin V) or Amoxicillin are the drugs of choice for adults and children with no history of penicillin allergy. It has been in use for the prevention of acute rheumatic fever following GAS pharyngitis for over 50 years and has a favourable tolerability, safety, and cost profile (66-70). To our knowledge there have been no published reports of penicillin-resistant GAS isolates.

For those who are penicillin allergic, macrolides remain the option of choice and where susceptibilities are available, these should be reviewed to ensure the prescribed agent remains active. Clinicians should check for potential significant interactions with other prescribed medications.

In penicillin allergy, clarithromycin is the recommended option for non-pregnant adults, children, and infants <6 months of age. This is based on expert consensus and available evidence. For example, a 2001 study demonstrated that 10 days of clarithromycin was more effective than 5 days of azithromycin in the eradication of group A Streptococcus (71). Furthermore, there is evidence that azithromycin favours the development of antibiotic resistance when compared to clarithromycin (72). For those who are penicillin allergic and either pregnant or within 28 days of giving birth, erythromycin is recommended due to more robust safety data for this agent in pregnancy and the post-partum period compared to newer macrolides (73, 74). For close contacts in the first trimester of pregnancy, a 5-day course of azithromycin may be considered as an alternative based on decision of the prescribing clinician.

See Table 4 for information on Choice of agent for treatment of Group A Streptococcus (GAS) or chemoprophylaxis for a contact of invasive Group A Streptococcus (iGAS).

2.4.2 Time to clearance following antibiotics

There is relevant evidence that antibiotic treatment achieves a high rate (>90%) of clearance of pharyngeal GAS 24 hours after initiation of therapy (75). This evidence supports the recommendations provided in subsequent chapters, that individuals with GAS pharyngitis should isolate for at least 24 hours after starting antibiotic treatment. The systematic review also found that GAS was cultured from the pharynx of 9% of patients on routine follow-up after completion of antibiotics (75).

Recommendation 5: Contacts of iGAS cases who have GAS pharyngitis or pharyngeal carriage should isolate for at least 24 hours after starting antibiotic treatment.

SIGN grading B

Recommendation 6: Contacts of iGAS cases who have other presentations of GAS infection should isolate for at least 24 hours after starting antibiotic treatment.

Good practice point

Table 4 Choice of agent for treatment of Group A Streptococcus (GAS) or chemoprophylaxis for a contact of invasive Group A Streptococcus (iGAS)

Group	Drug	Dose	Duration
Adult first line			
All adults ≥18 years	Phenoxymethylpenicillin (Penicillin V) or Amoxicillin	500mg PO every 6 hours 500mg PO every 8 hours	10 days 10 days
Adult second line (penicillin allergy)			
Adults including non-pregnant women	Clarithromycin*^	250mg PO every 12 hours	10 days
Pregnant women and mothers within 28 days of giving birth***	Erythromycin*^	500mg PO every 6 hours	10 days
Child first line[3]			
Infant 1 to 11 months**	Amoxicillin	125mg PO every 8 hours	10 days
Child 1 to 4 years	Amoxicillin	250mg PO every 8 hours	10 days
Child 5 to 17	Amoxicillin	500mg PO every 8 hours	10 days
Child second line (penicillin allergy)			
Birth to 6 months	Clarithromycin*^	7.5 mg/kg PO every 12 hours	10 days
6 months to 17 years	Clarithromycin*^	7.5 mg/kg PO every 12 hours to a maximum of 250mg every 12 hours	10 days
Adolescents (under 18 years) who are pregnant or within 28 days of giving birth***	Erythromycin*^	As per pregnant women dosing above – if very low body weight, consider lower dose and consult a pharmacist.	10 days

* Where susceptibilities are available, these should be reviewed to ensure the prescribed agent remains active.
** Please seek specialist advice for dosing for premature infants
*** Azithromycin may be considered as an alternative in 1st trimester of pregnancy, on advice of the prescribing clinician
^ Clinicians should check for potential significant interactions with other prescribed medications and discuss with a local microbiologist if macrolides are not felt to be appropriate.

3 For the Management of invasive and non-invasive Group A Streptococcal infection for mothers and neonates within 28 days of delivery, see here.

2.4.3 Contact communication and antibiotic chemoprophylaxis

Probable and confirmed cases of iGAS infection should be notified by telephone promptly to the Medical Officer of Health and Area Public Health Teams in and out of hours so that public health actions can be taken as soon as possible, ideally within 24 hours.

Priority must be given to identifying and assessing close contacts, providing them with Information leaflet for contacts of patients with Invasive Group A Streptococcal infection (iGAS) and arranging antibiotic chemoprophylaxis for high-risk contacts (Table 4). No contact screening is necessary.

Recommendation 7: Offer antibiotic chemoprophylaxis promptly (within 24 hours, and not beyond 10 days after date of diagnosis in the index case) to high-risk contacts, without screening.

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2.4.4 Timing of administration of chemoprophylaxis

Chemoprophylaxis should be commenced as soon as possible, within 24 hours. The risk to close contacts is highest immediately following exposure and elevated for the first 10 days after iGAS diagnosis[4] in the index case (7, 46, 76) although cases have also been reported up to 28 days later (45, 46).

Recommendation 8: Chemoprophylaxis should be commenced as soon as possible (within 24 hours) after eligible contacts are identified and not beyond 10 days of diagnosis in the index case. Advise GPs to maintain low threshold of suspicion for 30 days in all close contacts. When a contact is deemed eligible for chemoprophylaxis, the full course should always be completed.

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[4] As the existing evidence base comprises studies centered on hospital admission or diagnosis date, rather than exposure date, we use diagnosis date to define the period of highest risk of transmission.

For the full reference list scan the QR code below: