Public Health Management of Invasive Group A Streptococcal Disease in the Northern Territory Guideline

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Contents

Acknowledgments

This document has been prepared by Centre for Disease Control (CDC), Department of Health, Northern Territory. Contributors to this document include (in surname alphabetical order):

- Robert Baird — Microbiologist and Infectious Diseases Physician
- Johanna Birrell — Public Health Registrar
- Rowena Boyd — Public Health Nurse Specialist and Epidemiologist
- Emma Childs — Public Health Nurse Specialist
- Pasqualina Coffey — Public Health Physician
- Heather Cook — Public Health Nurse Specialist
- Bart Currie — Infectious Diseases Physician
- Josh Francis — Paediatric Infectious Diseases Physician
- Laura Francis — Paediatric Nurse and Public Health Nurse Specialist
- Mary-Rose Godsall — Infection Prevention and Control
- Te-Yu Hung — Paediatric Infectious Diseases Physician
- Vicki Krause — Director of Centre for Disease Control
- Amy Legg — Specialist Infectious Diseases Pharmacist
- Kimberley McMahon — Public Health Nurse Specialist
- William Majoni — Director of Renal Medicine
- Peter Markey — Public Health Physician
- Mahesh Menon — Infectious Diseases Physician
- Nancy Merridew — Infectious Diseases Registrar, coordinated 2022 guideline updates
- Elizabeth Moore — Public Health Doctor; Aboriginal Medical Services Alliance NT
- Anna Ralph — Infectious Diseases Physician
- Matthew Pitman — Author and coordinator of original 2015 NT iGAS Guidelines
- Lesley Scott — Public Health Nurse Specialist
- Jennifer Yan — Paediatric Infectious Diseases Physician

General enquiries about this publication should be directed to:

- **Centre for Disease Control, Darwin**
  Department of Health, Northern Territory
  Mail: PO Box 40596, Casuarina, NT 0811
  Email: CDCsurveillance.darwin@nt.gov.au
  Phone: (08) 8922 8089

Key changes

Description
Version 1.0 – released 2015 • **Public health management of invasive group A Streptococcal infection, Northern Territory 2015** – DoH Digital Library: Public health management of invasive group A streptococcal infection
Version 2.0 – released 2022 • **Definitions** – Case definition for invasive group A Streptococcal (iGAS) disease updated to include probable cases – Severe iGAS definition updated to include endometritis post-partum • **Haemodialysis public health response** – Secondary antibiotic prophylaxis recommended after a primary iGAS episode

Guideline

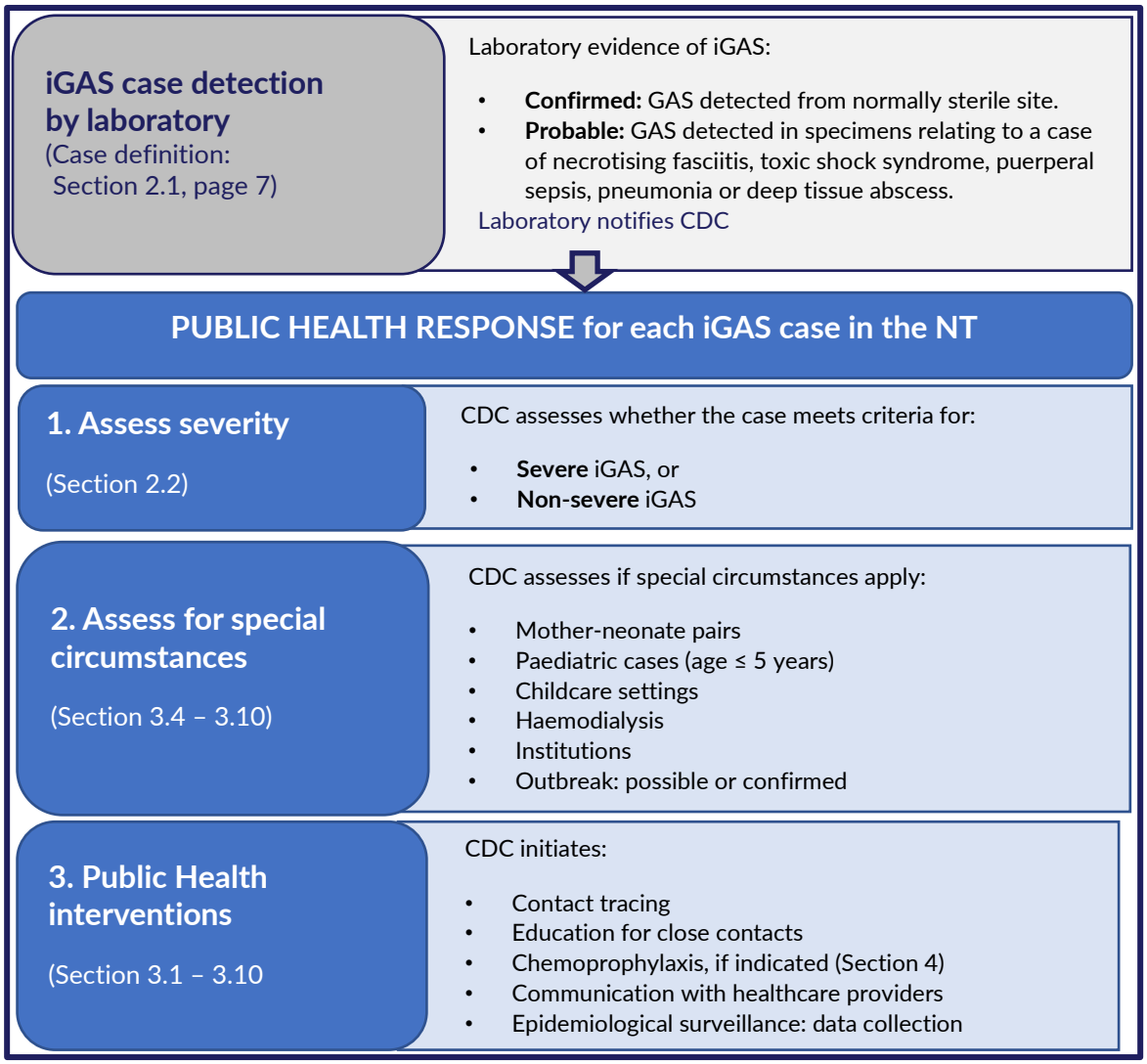
Background

Invasive group A Streptococcal (iGAS) infection is a rare but serious disease that occurs in a complex relationship with clinical and social determinants of health.

Public health responses to iGAS vary between jurisdictions. The release of this updated version of the Northern Territory (NT) iGAS public health management guidelines co-incides with iGAS becoming nationally notifiable in all Australian states and territories from July 2021.[1] iGAS has been notifiable in the Northern Territory since May 2011 and in Queensland since December 2015. An ongoing public health response to iGAS is supported by Australian surveillance data.[1-3]

The NT population is burdened by particularly high rates of group A Streptococcal (GAS)-related disease. These NT guidelines are based on local epidemiology, expert opinion and available local and international evidence (see Appendix). Dosing revisions in this document are in line with current Australian Therapeutic Guidelines and the Central Australian Rural Practitioners Association (CARPA) Standard Treatment Manual.

Figure 1. Flowchart of the NT Public Health Response to iGAS



Group A Streptococcus (GAS) clinical overview

Aetiology: GAS are bacteria that are also known as *Streptococcus pyogenes* and Streptococcal A (Strep. A). There are many different GAS strains or types (also known as *emm* types) and some are more likely to cause disease than others.

Colonisation: GAS is commonly present on the skin, upper respiratory, gastrointestinal, and anogenital tracts. When it lives on a person without causing disease, the person is said to be 'colonised' or have GAS 'carriage' and the person is not 'infected'. However, GAS can cause infection and a wide variety of clinical disease in humans – including for people who are usually healthy. The balance of GAS 'colonisation' versus 'infection' depends on:

- A person's comorbidities, immune status, and living conditions, and
- The particular strain of GAS involved and its ability to cause harm.

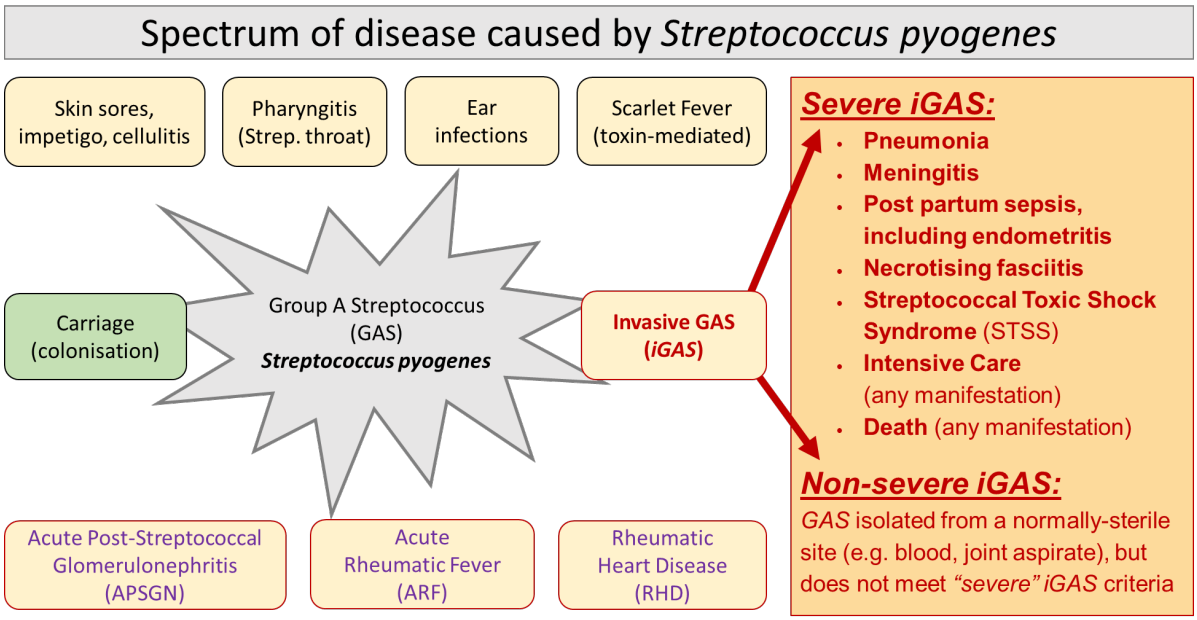
Mode of transmission: GAS can be acquired by direct skin contact, contact with respiratory secretions from an infected person's nose or mouth, large droplets when they cough or sneeze, or from discharge from skin sores or wounds. It can also be transmitted by direct contact with contaminated environment such as clothes, linen and surfaces.

Clinical features:

GAS can cause a wide variety of clinical manifestations (Figure 2), including:

- Non-invasive (superficial) infections such as pharyngitis and impetigo
- Scarlet and puerperal fever (toxin-mediated)
- Invasive disease (severe or non-severe) such as bacteraemia, deep tissue abscess, meningitis, necrotising fasciitis, endometritis, osteomyelitis and streptococcal toxic shock syndrome
- Post-streptococcal immunological complications such as acute rheumatic fever and acute glomerulonephritis.

Figure 2. Spectrum of disease caused by GAS



2. Definitions

2.1 Case definitions for iGAS

Confirmed case A confirmed case requires laboratory definitive evidence only. **Laboratory definitive evidence**: 1. Isolation of Group A Streptococci (*Streptococcus pyogenes*) by culture from a normally sterile site. OR 2. Detection of Group A Streptococci (*Streptococcus pyogenes*) by nucleic acid testing from a normally sterile site.
Probable case A probable case requires laboratory suggestive evidence AND clinical evidence. **Laboratory suggestive evidence**: Isolation or detection of Group A Streptococci (*Streptococcus pyogenes*) from a non-sterile site, such as a deep wound or deep tissue specimen, surgical biopsy, or post-mortem specimen, immediately at or in proximity to the site of infection. **Clinical evidence**: A compatible illness that requires hospitalisation, or surgery, or is associated with death. Compatible illnesses include: streptococcal toxic shock syndrome, necrotising fasciitis, puerperal sepsis, pneumonia with or without empyema, and deep tissue abscesses.

2.2 Case definitions for iGAS

Severe iGAS infection	iGAS infection presenting as pneumonia, meningitis, post-partum sepsis including severe endometritis❖, necrotising fasciitis, streptococcal toxic shock syndrome, or any manifestation requiring intensive care, or causing death.
Non-severe iGAS infection	iGAS infection that does not meet criteria for severe iGAS.

❖Endometritis post-partum has been added to the definition of *severe iGAS* in 2021 NT iGAS Guidelines. It excludes iGAS cases with a diagnosis of endometritis in the context of intrauterine device, which is considered an independent risk factor for infection, unless otherwise meeting severity criteria.

2.3 Contact definitions

Infectious period: from 7 days prior to the case becoming unwell with iGAS infection until 24 hours after the commencement of effective antibiotics.

Close contacts include all of the following:

- ***Airway exposure****:* anyone directly exposed to the case's nasopharynx, including bystander cardiopulmonary resuscitation (CPR), ambulance, nursing and medical staff involved in suctioning the airway, inserting airway adjuncts, or tracheal intubation during their *infectious period*
- ***Bed contact****:* shared bedding with the case during their *infectious period*
- ***Carers****:* family, friends, or staff who helped the case with their activities of daily living during their *infectious period*
- ***Direct contact****:* anyone whose mucous membranes or non-intact skin has been in direct contact with a case's nasal or pharyngeal secretions or open skin lesion, during their *infectious period* (common in young children playing together)
- ***Homeless contact****:* anyone who spent at least 24 hours in close proximity to a homeless case of iGAS during their *infectious period*
- ***Household contact****:* anyone who spent at least 24 hours in the same house as a case of iGAS during their *infectious period*
- ***Mother-neonatal pairs****:* if either a mother or baby develops iGAS in the neonatal period (i.e. onset of illness within the first 28 days post-partum) then the other is deemed a close contact
- ***Sexual or intimate contact****:* anyone who has had sexual relations, or other intimate contact, with a case during their *infectious period.*

Other definitions:

- ***Childcare setting:*** includes group or institutional child care centres (day care), family or home day care (including informal arrangements) and pre-schools.[10]
- ***Childcare setting contact****:* any child, staff member, or child carer (paid or unpaid) who has spent at least 4 hours at the same *childcare setting* as a case of iGAS infection during their *infectious period.* There is no requirement to have attended at the same time as the case.
- ***Haemodialysis unit contact***: patients and patient-care staff that attended the same Dialysis Unit as a case of iGAS during their *infectious period*
- ***Institution:*** residential facility including, but not limited to, nursing homes, residential hostels, homeless shelters, prisons, alcohol mandatory treatment centres, and military barracks
- ***Institutional contact:*** any residents or *patient-care staff* at an *institution* where at least 1 case of *iGAS* has been identified within the last 3 months
- ***Patient-care staff***: employees of an institution who assist residents with personal activities of daily living such as washing, mobilising, dressing and toileting, during their *infectious period*

2.4 Epidemiology of iGAS in the NT

iGAS became notifiable in the NT in May 2011. NT iGAS surveillance data demonstrates that between 1 May 2011 and 30 April 2021 there were 692 cases notified, an average of 69 cases per year (range 56 to 85) of which 380 (55%) were female. The case fatality rate was 6% (40/692). Molecularly-confirmed clusters (outbreaks) were detected on 4 occasions during the 10 year period.

511 (74%) of iGAS notifications occurred in Indigenous Australian people, with an incidence 8 times higher than non-Indigenous people in the NT (Table 1). A high proportion of people with iGAS have at least one risk factor for disease, with previous research in the NT identifying pre-existing chronic medical conditions in 66% of cases; most commonly type 2 diabetes mellitus and kidney disease.[2]

Figure 3 shows case frequency by age group and ethnicity. iGAS incidence in the Indigenous Australian population was higher for children under 5 years old, followed by a steadily increasing incidence from 30 years of age. For non-Indigenous people the incidence was highest in those aged over 70 years.

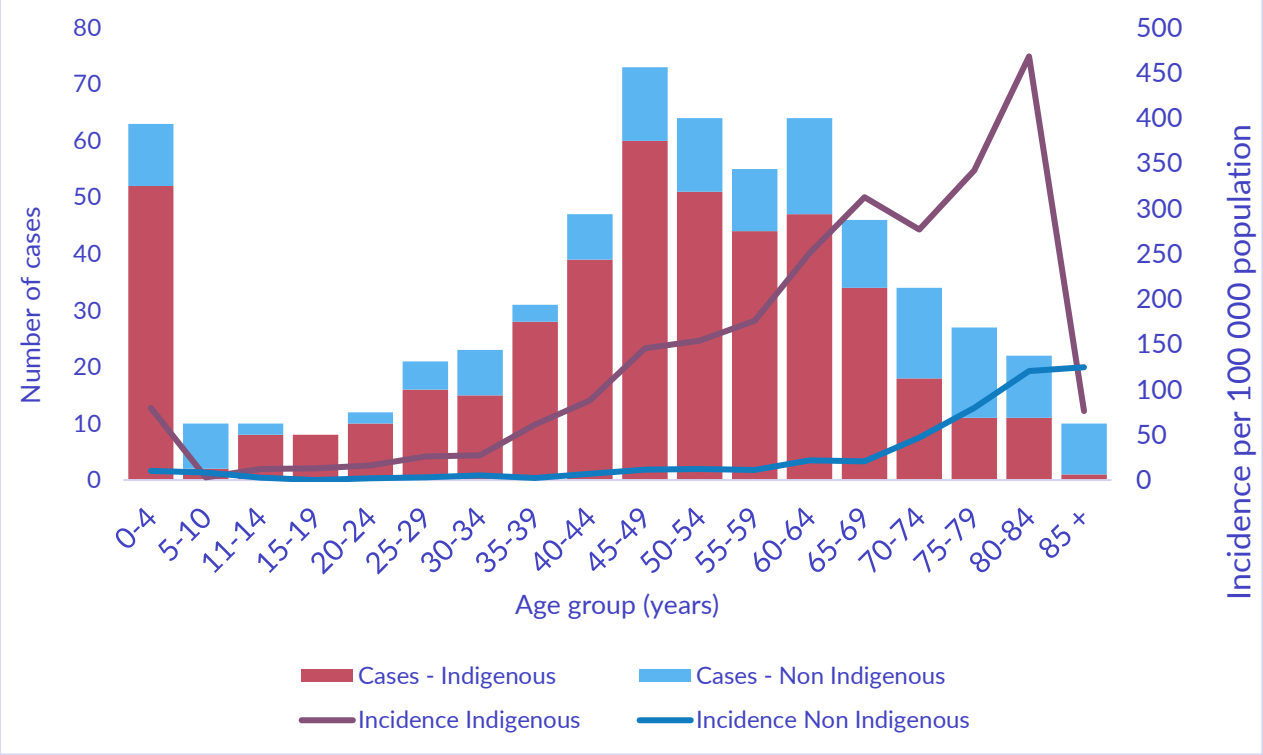
Table 1. Case numbers and incidence of iGAS infection in the NT, 1 May 2011 to 30 April 2021

Population	***n***	**Incidence (per 100,000 person-years)**	**95% confidence interval**
NT overall	692	31	29-33
- Indigenous Australians	511	87	80-95
- Non-Indigenous Australians	181	11	9-13
NT dialysis population	133	1668	1397-1977
- Top End region	52	1164	870-1527
- Central Australia region	81	2041	1621-2537

These data likely underestimate total cases. From 2011 to late 2016 only a confirmed case definition was used in the NT, requiring isolation of GAS from a sterile site. Recognising a lack of sensitivity in the surveillance system to capture cases of necrotising fasciitis (if GAS was not isolated from a sterile site) a probable case definition was added in the NT from October 2016, encompassing laboratory suggestive and clinical evidence. The probable case definition has been updated in this 2022 version of the guideline.

Severity of iGAS disease has been recorded for cases notified in the NT since 2017, with 27% of notifications (approximately 20 cases per year) classified as *severe iGAS*.

Figure 3. Frequency (bar graph) of cases and incidence (line graph) of iGAS by age group and Indigenous status in the NT, 2012 to 2020



2.5 Prevention of iGAS

iGAS and other diseases caused by GAS may be preventable through action on the social determinants of health and primordial, primary and secondary prevention measures. Table 2 sets out a holistic approach to preventing and improving outcomes from iGAS.

Table 2. Holistic approach to iGAS prevention

Primordial prevention: healthy skin	Skin sores, scabies, and tinea are very common in the NT and cause a large burden of primary disease and secondary complications. Varicella zoster virus (VZV) causes chickenpox and shingles, which predispose to iGAS[10] and are preventable through vaccination. Healthy skin guidelines: • National Healthy Skin Guideline: for the Prevention, Treatment and Public Health Control of Impetigo, Scabies, Crusted Scabies and Tinea for Indigenous Populations and Communities in Australia;[4] • Recognising & Treating Skin Infections: A visual clinical handbook;[5] • Healthy Skin Program - Guidelines for Community Control of Scabies, Skin Sores Tinea and Crusted Scabies in the NT;[6]
Primordial prevention: environmental and social practices	Optimisation of social determinants of health and access to health hardware. • Households: support healthy living practices, including washing people, regular washing of clothes and bedding, and reducing the negative impacts of overcrowding

	• Institutions: adhere to infection control protocols for hand hygiene, cleaning and laundry
Primary prevention	Measures that treat skin and throat infections to prevent iGAS. • Prompt medical review and treatment if unwell • Optimisation of comorbidities
Secondary prevention – haemodialysis patients	Haemodialysis patients who have been diagnosed with iGAS infection are at high risk of future recurrence[7]. Long-term, year-round secondary antibiotic prophylaxis is recommended for haemodialysis patients after an episode of iGAS infection: • Top End haemodialysis patients - **sulfamethoxazole 800mg + trimethoprim 160mg orally three times a week after haemodialysis** • Central Australian haemodialysis patients – **amoxicillin 500mg orally daily[8]**
Transmission precautions	Transmission precautions are recommended during the first 24 hours after an iGAS case first receives effective antibiotics. During that timeframe, all people (including healthcare workers and visitors) attending the case or entering their environment should adopt droplet AND contact precautions (goggles, mask, gown, and gloves).
Education	Education for the general public and for clinicians to recognise GAS symptoms, signs, and risk factors.
Chemoprophylaxis	Antibiotics may be prescribed for *close contacts* of a person with iGAS, to prevent secondary cases.
(Screening tests for *GAS* carriage is <u>not</u> indicated in healthy people and risks harm)	In asymptomatic people there is no role for testing for GAS carriage because GAS is part of normal human microbiome. If detected in this context, healthy individuals may end up being inappropriately treated to eradicate a mild colonising GAS strain. This can risk opportunistic recolonisation with a pathogenic GAS strain, adverse reactions to antibiotics and antimicrobial resistance.

3. Public Health response

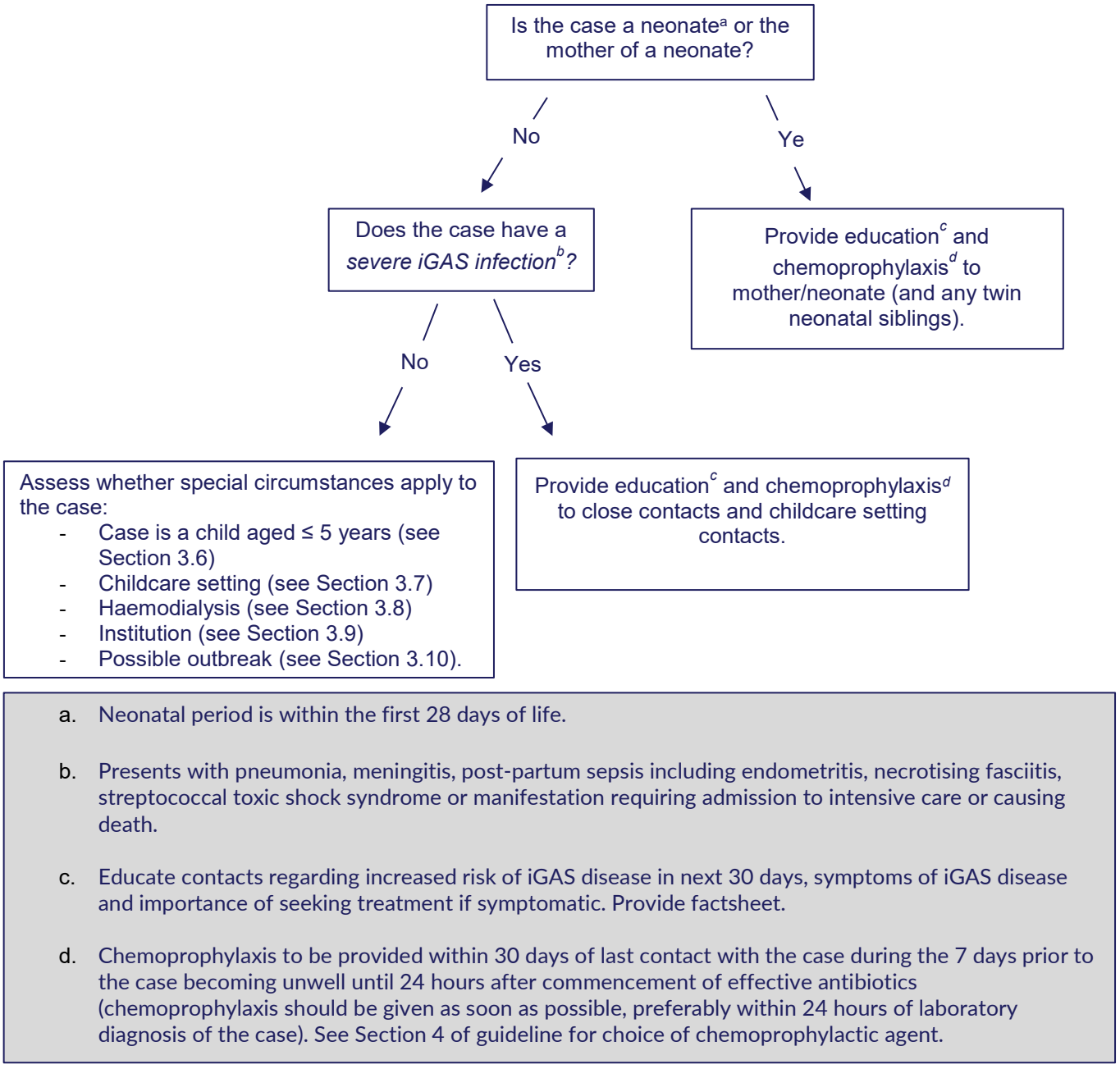
3.1 Overview table and flowchart

Table 4. Overview of NT public health response to an iGAS case

Case severity	Public health response: for all cases of iGAS (confirmed or probable), initiate within 1 working day of notification:
***Severe* iGAS** (Section 3.3)	→ Due to potential for virulent strains, contact trace and offer chemoprophylaxis and education to all *close contacts*
Non-severe iGAS (Section 3.4)**: assess whether special circumstances apply to the case:**	
Mother-neonate pairs (Section 3.5)	→ High risk for transmission; managed as for *severe iGAS*
Children aged ≤ 5 years (Section 3.6)	→ Liaise with Paediatric Infectious Diseases to consider contact tracing for education and chemoprophylaxis
Childcare setting (Section 3.7)	→ Liaise with childcare facility to identify all childcare setting contacts

Haemodialysis (Section 3.8)	→ Liaise with renal team, consider long-term secondary prophylaxis
Institution (Section 3.9)	→ Liaise with facility management
Outbreak (Section 3.10)	→ Consider an outbreak response if there are 2 or more cases of iGAS (regardless of severity) within 30 days in a childcare setting, haemodialysis unit, or other context; or 3 months in an institution.
Non-severe iGAS, if Special Circumstances not identified (Section 3.4)	→ CDC provides education to the case (or the person responsible), who informs their contacts. Primordial and social measures apply (Table 2). Contact tracing for *chemoprophylaxis* generally not indicated.

Figure 3. Flowchart for the public health management of iGAS disease in the NT



a. Neonatal period is within the first 28 days of life.

b. Presents with pneumonia, meningitis, post-partum sepsis including endometritis, necrotising fasciitis, streptococcal toxic shock syndrome or manifestation requiring admission to intensive care or causing death.

c. Educate contacts regarding increased risk of iGAS disease in next 30 days, symptoms of iGAS disease and importance of seeking treatment if symptomatic. Provide factsheet.

d. Chemoprophylaxis to be provided within 30 days of last contact with the case during the 7 days prior to the case becoming unwell until 24 hours after commencement of effective antibiotics (chemoprophylaxis should be given as soon as possible, preferably within 24 hours of laboratory diagnosis of the case). See Section 4 of guideline for choice of chemoprophylactic agent.

3.2 Education for contacts of iGAS (any severity)

Education about GAS-related disease should be provided in all cases, given the high burden of GAS clinical disease in the NT. Advise the following:

- *Close contacts* (as defined in Section 2.3) are at increased risk of developing *iGAS* and other *GAS*-related disease in the 30 days after their date of exposure to the case during the infectious period (or for 3 months if the case is associated with an *institution).* Explain symptoms, advise seek urgent medical review if they arise. Supply iGAS Factsheet (Section 5).
- **Symptomatic contacts**: any contact who reports symptoms of iGAS, regardless of the case's severity, should be advised to seek immediate medical review and state that they have been exposed to iGAS
- Consider whether iGAS antibiotic chemoprophylaxis is indicated (Figure 3).

3.3 Severe iGAS

For all cases of severe iGAS:

- Complete mandatory surveillance form
- Identify and follow up all *close contacts*; it may be necessary to seek assistance from local primary care clinicians and/or facility management
- Provide education to the case (or their responsible person) and each of their *close contacts* (see Section 3.2)
- *Chemoprophylaxis* (see Section 4) should be offered to all asymptomatic *close contacts* of a case of *severe iGAS.* The CDC is responsible for coordinating chemoprophylaxis, but may seek assistance from other healthcare providers if necessary. If one *household contact* receives chemoprophylaxis, all of their household contacts should ideally be treated with chemoprophylaxis to prevent re-colonisation by an untreated household contact.

3.4 Non-severe iGAS – assess for special circumstances

For cases of non-severe iGAS:

- Complete mandatory surveillance form
- Provide education (see Section 3.2) to the case (or their responsible person / facility management), who is then delegated to disseminate information to their *close contacts*
- Chemoprophylaxis (see Section 4) for *close contacts* of non-severe iGAS
    - Recommended for *mother-neonatal pairs* (see Section 3.5)
    - Considered for:
        - Cases in children aged 5 years or younger (see Section 3.6)
        - Childcare settings (see Section 3.7)
        - Institutions (see Section 3.9)
        - Outbreaks (see Section 3.10)

3.5 Mother-neonatal pairs with iGAS

If either a mother or baby develops *iGAS* in the neonatal period (i.e. onset of illness up to and including the first 28 days post-partum), then follow up is as for *severe iGAS* (regardless of *iGAS case severity*):[9, 10]

- Provide education (see Section 3.2) to the case (or their responsible person) and each of their *close contacts*
- *Chemoprophylaxis* (see Section 4) should be offered to the asymptomatic member of the *maternal-neonatal pair* (and any twin neonatal siblings). The CDC is responsible for coordinating chemoprophylaxis, but may seek assistance from other healthcare providers if necessary. If one *household contact* receives *chemoprophylaxis*, all of their household contacts should ideally be treated with *chemoprophylaxis* to prevent re-colonisation by an untreated household contact.

3.6 Children aged 5 years and younger with iGAS

There is a high incidence of iGAS in children aged under 5 years of age in the NT, with associated severe complications.[2-3, 9, 11-12]

If *non-severe iGAS* is diagnosed in a child age 5 years or younger, but older than 29 days (for neonates see Section 3.5):

- Public health to liaise with Paediatric Infectious Diseases to consider *close contact* tracing for *chemoprophylaxis* (see Section 4), which CDC will coordinate if advised by paediatric team
- Provide education (Section 3.2) to the case (or their responsible person), who is then delegated to educate any *close contacts*.

3.7 Childcare settings

Outbreaks have occurred in NT childcare centres, but are rare. Young children of childcare age are typically exposed to respiratory secretions by sharing toys, tactile play, and because they frequently place objects in their mouth. Note: there is no specific public health iGAS response for older children attending schools, as no increased risk has been demonstrated.

For all iGAS cases that attended a childcare setting during their *infectious period*:

- Provide education (Section 3.2) to all *childcare setting contacts* (or their responsible person)
- *Chemoprophylaxis* (see Section 4)
    - If a person with *severe iGAS* has attended a *childcare setting* during their *infectious period*, offer chemoprophylaxis to all asymptomatic *childcare setting contacts* as soon as possible if it can be given within 30 days of last attendance at the childcare setting by the case.
    - If a person with *non-severe iGAS* has attended a *childcare setting* during their *infectious period*, liaise with Paediatric Infectious Diseases to consider chemoprophylaxis for *childcare setting contacts*.

3.8 Haemodialysis units

There is a very high incidence of iGAS among haemodialysis patients in the NT (2,205 per 100,000-person-years in the dialysis population, 95% CI 1080-3999).[2] Furthermore, dialysis patients who experience a primary iGAS episode of are at high risk (16%) of future recurrence.[7]

The underlying reasons are poorly understood. Contributing factors may include relative immunocompromise from chronic renal failure and high rates of concurrent risk factors such as diabetes mellitus, peripheral vascular disease and chronic skin conditions. Patients living with renal failure are also prone to developing severe complications from iGAS, in part due to multisystem comorbidities and frailty.

Dialysis Unit healthcare staff may be exposed to GAS in the course of patient care, including via respiratory transmission and direct contact with skin sores when assisting patient transfers to dialysis chairs and needling fistulae. Haemodialysis in-centre and inpatient dialysis is under the remit of NT Infection Prevention and Control Unit protocols. However, Public Health can provide support for education and contact tracing.

If a haemodialysis patient or dialysis unit staff member is diagnosed with iGAS:

- **Public health response (CDC):**
    - Complete mandatory surveillance form
    - Apply relevant section 3.3 or 3.4 (for *severe* vs *non-severe iGAS*)
    - Review surveillance database to identify possibility of an outbreak (section 3.10) that may require an extended response
    - Notify Dialysis Unit Nurse Manager and the primary nephrologist named on the request form of the iGAS case and they will also notify the Renal Nursing and Medical Directors
    - Support an educational response within the Dialysis Unit and supply the iGAS Factsheet for distribution (Section 5)
- **Renal team to promote iGAS awareness among renal patients and staff:**
    - Irrespective of whether an outbreak is occurring, all *patient-care staff* and other patients that attend the same Dialysis Unit should be informed of their increased risk of iGAS infection in the next 30 days, the symptoms of iGAS infection and the importance of seeking medical attention promptly should these occur. This process can be coordinated by the Dialysis Unit and local Infection Prevention and Control Unit
    - Encourage monthly (ongoing) skin integrity check for all dialysis patients
    - Diagnose, treat, and cover all sores with clean dressings

- **Renal team to consider long-term secondary antibiotic prophylaxis for case**:
    - Top End haemodialysis patients – sulfamethoxazole 800mg + trimethoprim 160mg orally three times a week after haemodialysis
    - Central Australian haemodialysis patients – amoxicillin 500mg orally daily.

3.9 Institutions

When *iGAS* occurs in an *institutional* resident or worker, the CDC and facility management must work closely together to assess risks for *close contacts*, identify possible outbreaks, then tailor and coordinate the public health response. Institutions vary substantially, for example according to:

- Housing capacity
- Interactions between residents, inmates, staff, and visitors
- Residents' level of independence or need for assistance with activities of daily living
- Residents' frailty and medical comorbidities
- Staff movement between areas
- Cleaning protocols – environmental, linen, laundry, personal hygiene
- Meal services and food protocols.

If a resident or worker in an *institution* is diagnosed with iGAS:

- Complete mandatory surveillance form
- Apply relevant section 3.3 or 3.4 (for *severe* vs *non-severe iGAS*)
- Review surveillance database and information from facility management to identify possibility of an outbreak (section 3.10) that may require an extended response
- All *institutional contacts* should be informed of their increased risk of iGAS infection in the next 3 months, the symptoms of iGAS infection and the importance of seeking medical attention promptly should these occur (supply iGAS Factsheet for distribution, Section 5). This process can be coordinated by the institution's management.

3.10 Outbreaks

Outbreak definitions:

- ***Confirmed iGAS outbreak***: 2 or more epidemiologically-linked cases of iGAS infection that occur within 30 days, or within 3 months in *institutions*, and are identical on molecular (*emm*) typing of the isolates
- ***Possible iGAS outbreak***: 2 or more epidemiologically-linked cases of iGAS infection that occur within a 30 day period (or up to 3 months in institutional settings), where the iGAS strains have not yet been confirmed as identical on molecular typing or confirmation is not possible due to isolates being unavailable

It is preferred to first confirm an iGAS outbreak through molecular typing and then initiate a public health response. However, a public health response may be initiated in *possible iGAS outbreak* situations if there is strong epidemiologic suspicion of GAS transmission.

In the setting of a *confirmed* or *possible iGAS outbreak*, the CDC may convene an outbreak control team, involving management staff from an affected facility (childcare / haemodialysis / institution / other) and primary care. Outbreaks in Dialysis Units and Hospitals will require input from the NT Health Infection Prevention and Control team.

The response may include:

- Primordial prevention:
    - Review of health hardware, infection control, laundry and hygiene practices
- Primary prevention:
    - Education of staff and residents about GAS and iGAS
    - Check for and treat skin lesions and throat infections
    - Optimisation of comorbidities
- Other:
    - Microbiology consultation to coordinate molecular typing of bacterial isolates
    - Consider chemoprophylaxis for close contacts
    - Media releases and other public communication

4. Antibiotic chemoprophylaxis

Antibiotic *chemoprophylaxis* for *close contacts* of *iGAS* is recommended in some situations (Section 3.3-3.10). If indicated, *chemoprophylaxis* should be administered as soon as possible, ideally within the first 24 hours of the *case*'s *iGAS* diagnosis, but can be offered up to 30 days of last contact – the earlier the better to prevent a secondary case of *iGAS*. Do **not** wait for *iGAS* isolate antibiotic susceptibility results. Empiric chemoprophylaxis recommendations below are in keeping with current Therapeutic Guidelines and CARPA Standard Treatment Manual.[13-14] At the doses below, no dose adjustments are needed for renal impairment.

The CDC and Aboriginal community-controlled organisations can prescribe and provide chemoprophylaxis for free. *Close contacts* may have to pay costs through other primary care practices. See Administering Bicillin | Rheumatic Heart Disease Australia (rhdaustralia.org.au) for administration advice.

First line: Benzathine benzylpenicillin, pregnancy category A

The NT recommends benzathine benzylpenicillin (long acting) as a single weight-based injection, which bypasses issues of potential non-compliance and is generally well-tolerated:

Patient Weight	Benzathine* Benzylpenicillin single intramuscular dose	Volume of dose from pre-filled** syringe
neonate and child 6 kg or less	0.3 million units	0.6 ml
child 6 kg to less than 12 kg	0.45 million units	0.9 ml
child 12 kg to less than 16 kg	0.6 million units	1.2 ml
child 16 kg to less than 20 kg	0.9 million units	1.7 ml
adult or child 20 kg or more	1.2 million units	2.3 ml
**Benzathine benzylpenicillin is long acting (also known as LA Bicillin); do not confuse this drug with benzylpenicillin (which is short acting and therefore ineffective for the prophylaxis)* ***All preparations contain the same concentration of benzathine benzylpenicillin*		

OR, if benzathine benzylpenicillin is considered clinically unsuitable, consider:

Second line: Cefalexin, pregnancy category A

Patient Weight	Cefalexin oral dose	Frequency & Duration
Neonate or child less than 25 kg	25 mg/kg up to 1 g	12-hourly for 10 days
Adult or child 25 kg or more	1 g	12-hourly for 10 days

OR, if benzathine benzylpenicillin and cefalexin are contraindicated for clinical reasons of allergy (immediate severe hypersensitivity or delayed severe hypersensitivity), then consider:

Third line: Azithromycin, pregnancy category B1

Patient Weight	Azithromycin oral dose	Frequency & Duration
Child	12 mg/kg up to 500 mg	daily for 5 days
Adult	500 mg	daily for 5 days

Notes:

- **Clindamycin** is no longer recommended for *iGAS close contact chemoprophylaxis*.

- Chemoprophylaxis number needed to treat (NNT) is challenging to estimate. For England, where iGAS incidence is 3 per 100,000 population per year, the theoretical NNT of iGAS household close contacts, assuming 100% effectiveness was: overall = 271; mother-neonate pairs = 50; and couples aged ≥75 years = 82.[9]

5. Forms, education and other resources

Complete the following forms for each iGAS case.

Name of document	Public Health to complete	Form location
iGAS data collection form	For all cases	Page 19 of this document
Notification of a notifiable disease	For all cases	DoH Digital Library: Reporting of notifiable diseases by doctors form (nt.gov.au)
iGAS contact tracing and chemoprophylaxis prescription		Public Health Response - All Documents
***Severe* iGAS Letter to primary healthcare notifying of case**	For all *severe iGAS* cases	Public Health Response - All Documents
***Non-Severe* iGAS Letter to primary healthcare notifying of case**	For all *non-severe iGAS* cases	Public Health Response - All Documents
Letter to GP, notifying of chemoprophylaxis	For all *close contacts* who have received chemoprophylaxis	Page 20 of this document
The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (3rd edition)	Reference guide for administration of benzathine benzylpenicillin	ARF RHD Guidelines 3rd Edition (rhdaustralia.org.au) (pages 173-183)

iGAS educational resources:

Name of document	Comment	Form location
Education factsheet iGAS - pictorial	Educational resource for cases and contacts	DoH Digital Library: Invasive Group A Streptococcus (iGAS) infection (nt.gov.au)
Education factsheet iGAS Detailed	Educational resource for cases and contacts	Group A streptococcal - NT.GOV.AU Group A streptococcal disease Jan 2016.pdf (nt.gov.au)

5.1 Mandatory iGAS data form: all cases

CASE DEMOGRAPHICS			
First Name:		Surname:	
HRN:	Date of birth:	Phone:	
Indigenous status (circle) Aboriginal / Torres Strait Islander / Other (specify):			
Place(s) of residence in 7 days prior to onset of symptoms			
Details of childcare setting, haemodialysis unit, and institution(s) – if applicable			
Date of symptom onset:			
DETERMINE CASE SEVERITY, and OTHER INDICATIONS FOR ACTION			
Assess ALL of the following; circle answers (do not leave blank)			**Public Health Action**
CASE confirmed diagnosis or outcome	Intensive Care Unit admission	Yes / No	If **YES to any** then this is a case of ***SEVERE iGAS;*** **chemoprophylaxis recommended for all *close contacts.*** See Section 3.3
	Meningitis	Yes / No	
	Necrotising fasciitis	Yes / No	
	Pneumonia	Yes / No	
	Post-partum sepsis, including severe endometritis	Yes / No	
	Streptococcal Toxic Shock Syndrome	Yes / No	
	Died	Yes / No	
Mother-neonatal cases	Is the case a neonate (defined as a baby aged 28 days or younger)	Yes / No	If **YES to either** then **chemoprophylaxis recommended.** See Section 3.5
	Is the case a mother who gave birth in the last 28 days	Yes / No	
Paediatric	Is the case a child aged 5 years or younger (but not a neonate, see above), with non-severe iGAS?	Yes / No	If YES, then liaise with Paediatric Infectious Diseases, Section 3.6
Childcare Settings	Did the *case* attend a childcare setting during the *infectious period* – either as a child or as a carer (paid or unpaid)?	Yes / No	If **YES** then see Childcare Setting Section 3.7
Haemo-dialysis	Is the case a haemodialysis patient?	Yes / No	If **YES** then see Haemodialysis Section 3.8
	Does the *case* work at a haemodialysis centre?	Yes / No	
Institution	Does the *case* live in an *institution?*	Yes / No	If **YES to any** then see Institution Response Section 3.9
	Does the *case* work at an *institution* and help residents with activities of daily living (e.g. showering, dressing)	Yes / No	
Outbreak	Are 2 or more cases (regardless of severity) linked in the last 30 days?	Yes / No	If **YES then see Outbreak** Section 3.10

5.2 Letter: Advice to GP regarding chemoprophylaxis

Centre for Disease Control
Postal Address: PO Box 40596 Casuarina
NT 0811
Tel: 0889228044
Fax: 0889228310
eMail: cdcdarwin.ths@nt.gov.au
Our Ref:

Date: _____/_____/_____

Dear Doctor

Your patient _____ has been contacted by the Centre for Disease Control (CDC) as part of contact tracing following exposure to an infectious case of invasive Group A Streptococcal disease (iGAS).

They were given the following medication and appropriate advice on

Date: _____/_____/_____

Medication: _____

Dose: _____

Route: _____

People who have close contact with an infectious case of invasive Group A Streptococcal disease are at increased risk of disease in the 30 days following exposure. Your patient has been advised to seek medical care should they develop a sore throat, skin sores, or other symptoms suggestive of infection especially within the next month.

Sincerely

Centre for Disease Control

CDC contact numbers

Darwin	8922 8044
Alice Springs	8951 9505
Katherine	8973 9049
Nhulunbuy	8987 0357
Tennant Creek	8962 4259

6. Appendix: Background to guidelines

6.1 Public health response to household contacts'

i. Evidence for treatment of household contacts and international guidelines

Chemoprophylaxis for household contacts of iGAS infection is controversial. A Canadian study found a rate of iGAS infection in household contacts of index cases of 2.94 per 1000 household contacts.[15] A subsequent United States (US) study found a rate of 0.66 cases per 1000 household contacts.[16] Taking both of these studies into account, the US Centers for Disease Control and Prevention in 2002 published a statement that did not endorse routine chemoprophylaxis for household contacts due to low risk of infection and lack of data on efficacy of chemoprophylaxis in the household contact setting.[17] However, they stated that health care providers may choose to offer chemoprophylaxis to household contacts if they had additional risk factors for acquiring iGAS infection such as age over 65, certain comorbidities or Indigenous ethnicity. The Public Health Agency of Canada (PHAC) in 2006 responded to the same studies by issuing a public health response guideline for close contacts of iGAS infection[18] but restricted their response to household contacts of severe iGAS cases.

Unpublished data from the United Kingdom (UK) demonstrated 5 household clusters of iGAS infection in 2003; 3 of these were mother-neonate pairs. On this basis, the UK Health Protection Agency in 2004 issued a public health response for household contacts restricted to mother-neonate pairs, stating that the number of non-mother-neonate household contacts needed to treat to prevent 1 case of iGAS was more than 2000.[19] The rigor with which these UK case-contact pairs were identified is difficult to determine as the data remain unpublished. Furthermore, in explaining their public health response, the Health Protection Agency did not address the discrepancy in proportion of clusters that were mother-neonate pairs in the UK study compared to the US and Canadian studies in which no such clusters were identified.

The Canadian estimate is similar to the US estimated rate of meningococcal infection in meningococcal household contacts of 4.2 per 1000 household contacts.[20] The background community prevalence rates of iGAS infection per 100,000 persons per year in the published Canadian and US studies were 2.4 and 3.5 respectively.[15-16] Assuming infection risk is confined to the first 30 days after exposure, the calculated incidence rate ratios in household contacts are 1492 and 229 respectively. In Australia, a study in the state of Victoria identified 3 cases of iGAS infection in household contacts of index cases over a two and a half year period.[11] The incidence rate of iGAS disease in contacts was 2011 (95%CI 645 – 6268) times higher than the population incidence in Victoria. That is, household contacts are at up to a 2011-fold risk of acquiring iGAS in the first month after diagnosis of the index case compared to the general community in temperate areas.

ii. Implications for household contacts in the Northern Territory

The Northern Territory (NT) currently has an incidence rate of iGAS infection of around 28/100,000 persons per year, about 10 times the rate in temperate regions.[2] North Queensland had an overall incidence rate of 15.9/100,000 persons per year from 1996-2001 (calculated from published Indigenous and non-Indigenous rates).[21] There are no data on rates of iGAS infection with the same strain in household contacts in tropical regions and it is not known if the same high incident rate ratio of infection in household contacts to infection in the general community applies in the tropics as was found in the studies from temperate regions. The high community incidence rate in the NT suggests a high force of infection due to factors such as crowding, poor hygiene and skin lesions; the same factors would apply to household contacts and thus the incidence rate ratio may be similar. Assuming a moderate 800-fold incidence rate ratio, the rate of infection in household contacts would be 1.9%. If chemoprophylaxis were 90% efficacious, the number of contacts needed to treat (NNT) to prevent 1 case of iGAS infection would be 58.

However, previous studies in the NT and Queensland have demonstrated a much more diverse range of iGAS genotypes than is seen in temperate areas suggesting less clonality and thus potentially a greater proportion of cases that are sporadic rather than transmitted directly from another case of iGAS

infection.[2,11,21] Furthermore, high rates of sporadic GAS exposure may lead to higher rates of immunity and less household transmission than the above calculations would suggest. A more confident estimate of the incidence rate ratio in the NT would require further epidemiologic studies and molecular typing of iGAS strains in regions of high endemicity. If the incidence rate in household contacts in the NT were similar to temperate regions at 0.2%, and if chemoprophylaxis were 90% efficacious, the NNT would be 556. The actual NNT may be somewhere between 58 and 556.

Between May 2011 and November 2021, there were 5 recognised epidemiologically and molecularly linked iGAS infection clusters in the NT. Actual numbers may be greater than this if epidemiologic links were not identified.

iii. Targeting subgroups of household contacts

Considering the frequency and severity of iGAS infections in the NT,[2,22] the NT Centre for Disease Control (CDC) has resolved to devise a public health response to cases of iGAS infection based on the limited available evidence. These NT guidelines are modelled in part on the Canadian guidelines. However, there are some theoretical and practical differences.

The Canadian guideline restricted a public health response to contacts of severe cases of iGAS infection for 2 reasons: firstly, the rate of iGAS infection in contacts, 0.066 to 0.29%, was considered to be low, requiring a high NNT, and, secondly, they suggested that the manifestation of iGAS infection in index and contact is usually the same. Thus it seemed reasonable to target those contacts who stood to gain the most from prevention of iGAS, i.e. contacts of severe cases.

However, evidence for identical manifestation of iGAS infection in community-dwelling index cases and contacts is limited to the 2 published studies from the US and UK in which only 3 of 5 (60%) index-contact pairs had the same manifestation.[15-16] Moreover, data from nursing home and military outbreaks confirm that the same strain of GAS can cause varying clinical manifestations with varying severity in different patients.[23-26]

The NT guideline restricts public health response to contacts of severe cases of iGAS infection for different reasons. Firstly, there are about 64 iGAS infections per year in the NT of which about 15 are severe. Australian Bureau of Statistics 2011 census data report an average 2.9 people per household in the NT with 4.2 per household for Indigenous people. However, overcrowding is a risk factor for GAS infection. Therefore, assuming 5 close contacts per case, that 0.2 to 1.9% of contacts are infected and that chemoprophylaxis is 90% efficacious, 58 to 63 of the 64 annual cases would be sporadic, 1 to 5 would be preventable cases in contacts and 0 to 1 would be household transmissions due to chemoprophylaxis failure respectively. Thus, if one were to target all sporadic iGAS infections, a public health response would be required on average every 5.8 to 6.3 days respectively. While much of the contact tracing work would fall to different remote clinics, this quantity of work is currently beyond the level of resources of the NT CDC. Secondly, while a single iGAS strain may cause varying manifestations and severity of illness, a strain which has already caused severe iGAS infection has already demonstrated its capacity to cause severe disease unlike a strain which has only to date caused non-severe iGAS infections. On this basis it is reasonable to restrict a response to contacts of patients with severe iGAS infection. This would reduce the number of public health responses to about 14 to 15 per year or, on average, once every 24 to 26 days.

Adopting the US CDC approach of restricting response to household contacts with additional risk factors for infection, including Indigenous ethnicity, would likely not significantly reduce the number of public health responses required as NT residents have high rates of comorbidity, 77% of those with iGAS infection are Indigenous[2] and if one household member has an additional risk factor then all household contacts would need antibiotics to prevent recolonisation after completion of chemoprophylaxis.

In the circumstance of iGAS disease occurrence in a mother or neonate, the NT guideline recommends chemoprophylaxis regardless of disease severity in the index case. This is based on unpublished UK data which identified transmission between 3 mother-neonate pairs.[19] Additionally the NT guidelines recommend chemoprophylaxis of all neonates from multiple birth pregnancies following iGAS infection in mother or neonatal siblings. This recommendation is based on an identified transmission in 2011 between

one neonatal pair in the NT where iGAS infection occurred in neonate twins with onset of infection separated by 2 days.[27] Also taken into consideration was the intensive nature of the close contact between mother and newborns and immaturity of the neonatal immune system.

iv. Definitions of close contacts

The definition of a household contact in the NT guideline, being anyone who has spent at least 24 hours in the same household as the case during the 7 days prior to the case becoming unwell until 24 hours after commencement of effective antibiotics, is the same as that used in the US CDC 2002 iGAS statement[17] while the Canadian guideline uses 20 hours as the cut-off.[18] The 24 hour duration is based on a study demonstrating much higher rates of iGAS strain carriage in those who spent at least 24 hours versus those who spent 12 to 24 hours with the case in the 7 days preceding hospitalisation (27% vs 1.8%).[28] Carriers in this study usually but not always lived in the same household. Considering the prevalence of homeless persons in the NT, the NT guideline includes a definition for homeless contacts, not found in the US or Canadian guidelines, being anyone who has spent at least 24 hours in close proximity to the homeless case during the 7 days prior to the case becoming unwell until 24 hours after commencement of effective antibiotics.

The Canadian guidelines limit a public health response to the first 7 days after last contact with the iGAS case based on an argument that most close contacts who become infected do so within the first 7 days of last contact.[18] However, in the prospective Australian, Canadian and US studies, of 6 definite household case-contact pairs for whom there is information available on the interval between infections, only 3 had an interval of 7 or less days.[15] The other 3 pairs had intervals of 8, 15 and 21 days.[11,15-16] Consequently, the NT guidelines recommend chemoprophylaxis up to 30 days following last contact with a case where that contact was during the period from 7 days prior to onset of symptoms until 24 hours after commencement of effective antibiotics. While the increased risk of iGAS disease in contacts lasts for 30 days, the highest risk is likely to exist within the first 7 days post-exposure. Therefore chemoprophylaxis should be given as soon as possible following diagnosis. While evidence of transmission of iGAS infection between direct and sexual non-household contacts is limited, these are included in the NT guideline on theoretical grounds as in the Canadian guideline.

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