NT Health Interim Guidelines

Clinical Management of Diphtheria in Primary Care in the Northern Territory

These interim guidelines are intended to support clinicians managing suspected and confirmed cases of diphtheria in the community. As the diphtheria outbreak evolves, guidance will be updated as necessary. This interim guidance recognises that increased medical support will be required for the evaluation of cases and prescribing of azithromycin, the increased use of azithromycin, and the resource requirements of regular review of suspected diphtheria patients in community in case of progression to severe disease. Processes are underway to support SSTP prescribing of azithromycin for Remote Area Nurses and Aboriginal Health Practitioners. Vaccination remains the most important measure to protect against severe diphtheria.

There are several different ways that a case of diphtheria might present or be detected in the primary healthcare setting in the Northern Territory. These include:

1. Respiratory diphtheria presentation
2. Cutaneous diphtheria presentation (most common)
3. Asymptomatic pharyngeal colonisation
4. Late complications of diphtheria, a significant contributor to diphtheria related mortality: cardiac (myocarditis, arrhythmias, dilated cardiomyopathy), renal failure, neuropathy

Importance of immunisation

While colonisation or infection with toxigenic *Corynebacterium diphtheriae* is possible in both fully vaccinated and inadequately vaccinated people, the risk of severe diphtheria disease is much higher in people who are inadequately vaccinated. People who are adequately vaccinated are unlikely to present with severe disease. Vaccination rates are variable across the Northern Territory, and with ongoing community transmission, there is a significant risk of exposure, colonisation, infection and severe disease for people who are inadequately vaccinated. **Respiratory diphtheria can be progressive and life-threatening in people who are inadequately vaccinated against diphtheria**.

"Inadequately vaccinated" applies to children who are not up to date with childhood immunisation recommendations (diphtheria toxoid containing vaccine at 2, 4, 6, 18 months, 4 years, 13 years) or an adult who has had < 3 diphtheria toxoid containing vaccines in their life or is > 10 years since their last diphtheria toxoid containing vaccine dose. A person who has diphtheria in the context of being inadequately vaccinated, should be vaccinated with an age-appropriate diphtheria toxoid containing vaccine after recovery.

1. Respiratory diphtheria

Respiratory diphtheria can present with slowly progressive pharyngeal symptoms. The classic presentations of pseudomembrane formation and progressive neck swelling are characteristic of severe diphtheria; but may not be the way that cases initially present. The first presentation may be with signs and symptoms of **pharyngitis** or **tonsillitis**.

Respiratory diphtheria should be considered in people (whether vaccinated or not) who present with typical signs and symptoms of **pharyngitis or tonsillitis with exudate.** People with a **known close contact**

with a diphtheria case or who are **inadequately vaccinated** have a higher probability of having diphtheria, and diphtheria should be considered even in the absence of exudate.

If respiratory diphtheria is suspected, the person should be **isolated** as effectively as is practical, and **contact and droplet precautions** used, particularly when collecting respiratory samples.

Inadequately vaccinated people with suspected symptomatic respiratory diphtheria may require admission to hospital for supportive management, antibiotics, and administration of diphtheria antitoxin (DAT). **Adequately vaccinated** people with suspected symptomatic respiratory diphtheria can usually be managed as an **outpatient** with supportive care and antibiotics. Daily or second daily **clinical reviews** are important to determine if DAT should be given based on warning signs including worsening pseudomembrane, progressive neck swelling or signs of sepsis or respiratory distress.

If toxin gene-positive *C. diphtheriae* infection is confirmed on laboratory testing for a person who is **not admitted to hospital,** the person should be **reviewed** urgently to assess clinical progress, and discussed with (paediatric or adult) infectious diseases on-call with a **low threshold for admission** to hospital if there is progression of symptoms despite antibiotics, or other clinical concerns.

Pseudomembrane: early pseudomembrane may be difficult to differentiate from standard pharyngeal or tonsillar exudate. Pseudomembrane development is due to direct toxin effects on tissue leading to cellular necrosis, and classically is more fibrous and adherent to the tissue, rather than purulent exudate which is easily removed by a swab. It coalesces in later disease to form a well demarcated grey white membrane. Disruption of significant pseudomembrane can cause bleeding and respiratory obstruction.

*Appendix A: Suspected **respiratory** diphtheria algorithm*

2. Cutaneous diphtheria

Cutaneous diphtheria might be suspected clinically because of a non-healing wound or ulcer (>2 weeks), or an ulcer of any duration in someone who has had contact with a known case of diphtheria. These lesions can begin as a pustule, developing into a superficial, sloughy ulcer with well-demarcated edges. It may also be diagnosed coincidentally based on a swab culture of a skin sore where toxin gene-positive *C. diphtheriae* is isolated in the laboratory.

Non-toxigenic strains of *C. diphtheriae* can also be isolated from wound swabs, however, these do not usually cause disease and do not require directed treatment, or contact tracing.

Toxin-mediated (i.e. severe) disease from cutaneous diphtheria is rare and most cases can be managed with antibiotics, without any need for hospital admission or administration of diphtheria antitoxin (DAT). However, cutaneous diphtheria can be severe if unrecognised and untreated in inadquately vaccinated people. DAT might be considered in some cases, where there is progression of a large wound (>2cm diameter) or suspected toxin-mediated systemic features, particularly in inadequately vaccinated people.

*Appendix B: Suspected **cutaneous** diphtheria algorithm*

3. Asymptomatic pharyngeal colonisation

Asymptomatic pharyngeal colonisation may be identified as a result of contact tracing, where asymptomatic close contacts may have pharyngeal swabs sent for laboratory testing.

*Appendix C: **Asymptomatic** pharyngeal colonisation algorithm*

4. Late complications of diphtheria

It is possible for late, toxin-mediated complications of diphtheria to present days, weeks or months after resolution of symptoms associated with untreated *C. diphtheriae* infection. These presentations are likely to be rare but should be considered if someone who is inadequately vaccinated presents with unexplained cardiac, renal or neurological disease.

People presenting with shortness of breath, chest pain, palpitations, unexplained tachycardia need a medical consult; perform clinical review, ECG and troponin and consider myocarditis secondary to diphtheria in differentials.

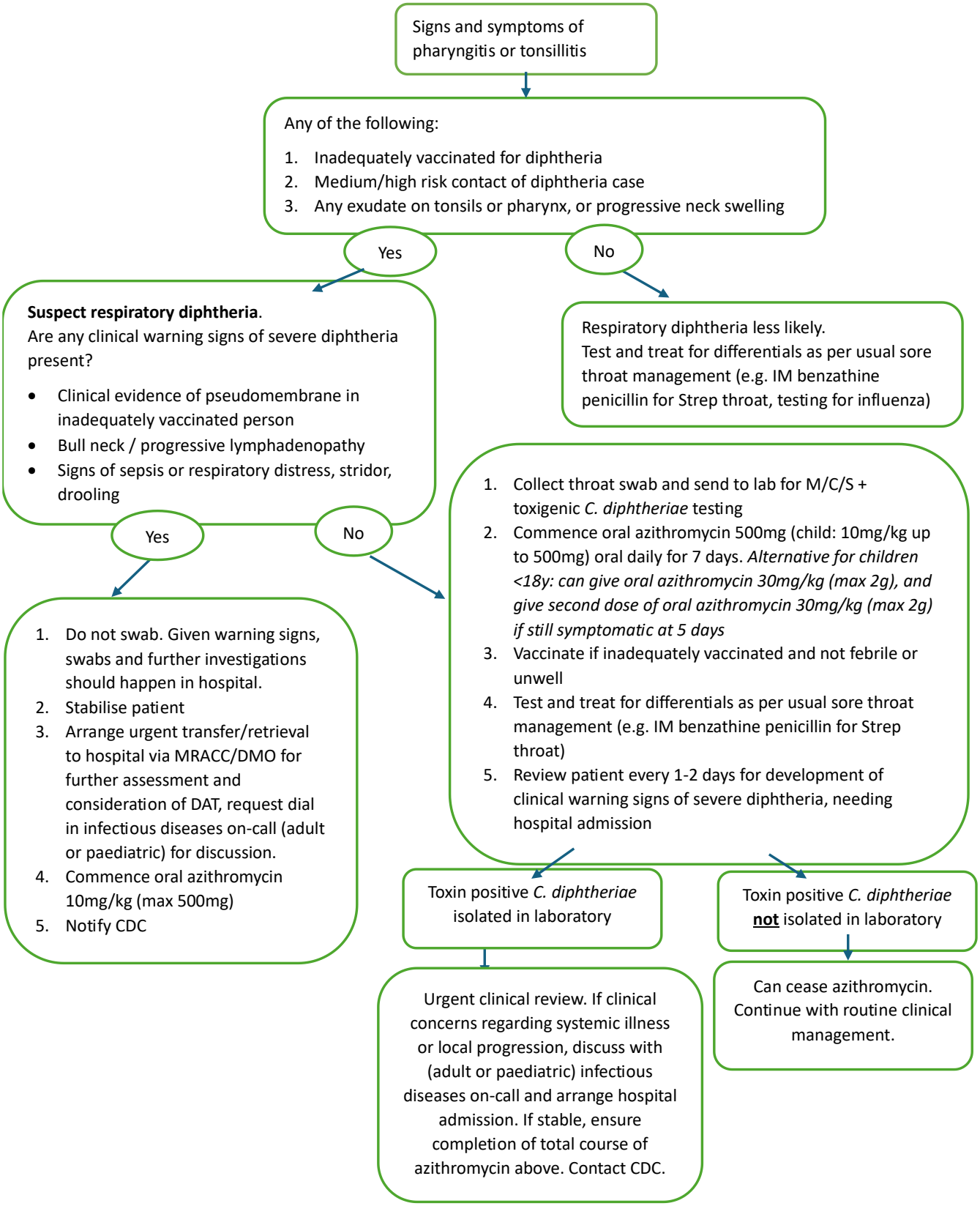
If a person who is inadequately vaccinated presents with signs and symptoms of myocarditis, acute renal failure, or new onset of neurological symptoms, consider the possibility of diphtheria. Discuss with (adult or paediatric) infectious diseases on-call and consider hospital admission for further investigations and management. Notify CDC.

5. Alternate options for antibiotic treatment

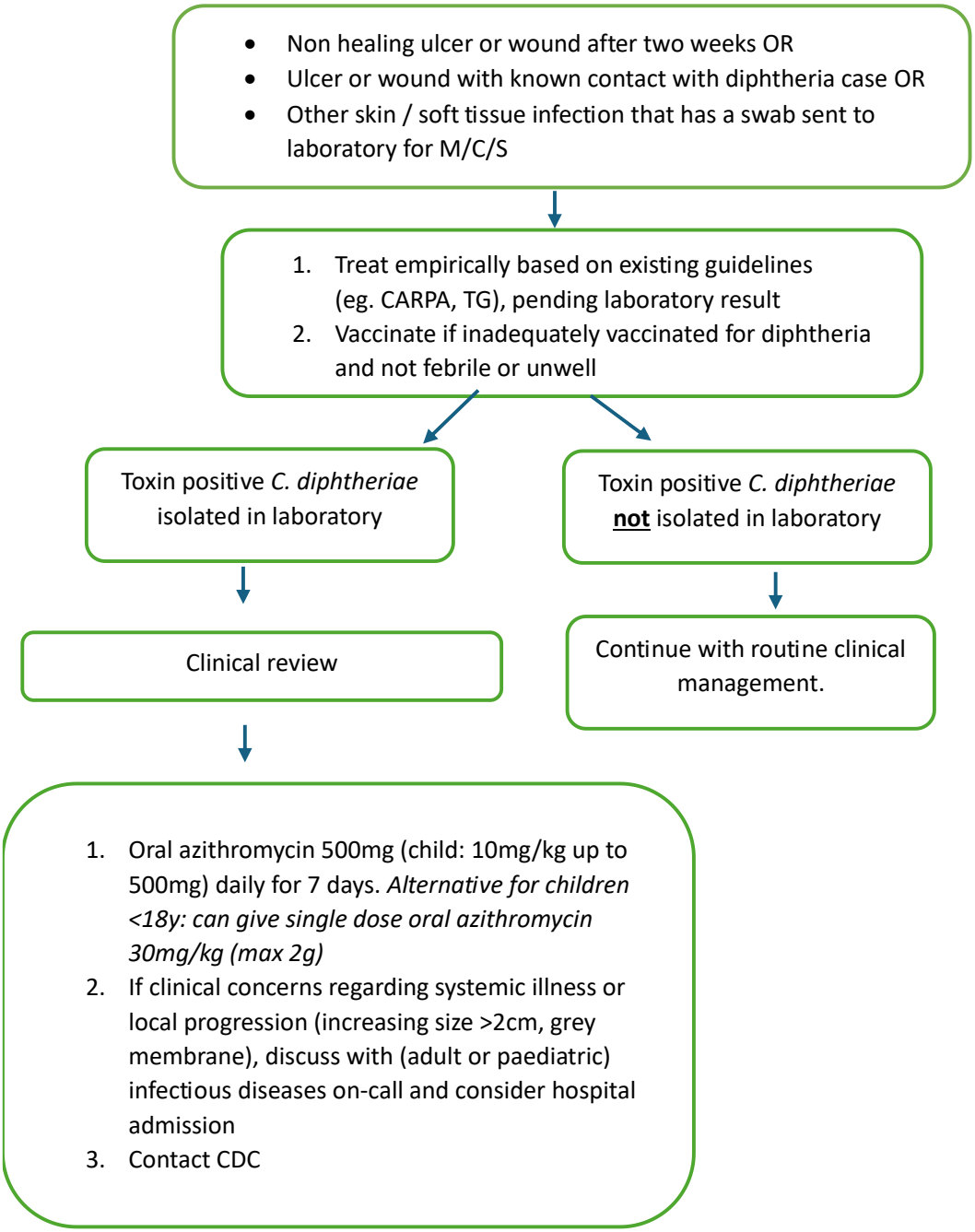
Azithromycin is the preferred first-line treatment for cases of confirmed cutaneous diphtheria and suspected respiratory diphtheria. Penicillin is not recommended due to decreased antibiotic susceptibility in the diphtheria strain causing this outbreak.

In case of allergy, contraindication (e.g. long QT) or unavailability of azithromycin, use **doxycycline**
Adult: doxycycline oral 200mg for first dose, then continue 100mg bd for total 7 days
Children: doxycycline oral 2mg/kg per dose (rounded to nearest 25mg) bd for 7 days

Appendix A: Suspected respiratory diphtheria algorithm



Appendix B: Suspected cutaneous diphtheria algorithm



Appendix C: Asymptomatic pharyngeal colonisation algorithm