Guidance for Community Treatment, Diagnosis, and Data Collection for Shigella Outbreak Edmonton Zone, Alberta Health Services (EI-2022-4111)

This guidance document was developed in response to the *Shigella* outbreak occurring among vulnerable residents of Edmonton and was updated following its reopening.

In addition to higher risk exposure settings (e.g., encampments in the inner city), high hospitalization rates and increased infection severity have been observed. Therefore, empiric treatment with antibiotics is justifiable for the outbreak duration as it is expected to shorten both the clinical course of disease (with expected resolution within 2-3 days) [1] and the period of fecal excretion of the bacteria once symptoms resolve.

Community agencies with appropriate medical oversight are encouraged to create and adopt protocols to reflect the below therapeutic guidance.

Please note: Therapeutic recommendations below are applicable **for this outbreak only** for vulnerable persons[1] suspected of having shigellosis[2] who meet the following criteria:

- Moderate to severe diarrhea (i.e., > 3 stools / 8h, fever) AND
- Stable and suitable for outpatient therapy

Collect a stool specimen or a rectal swab regardless of treatment (see 'Diagnosis' section).

Empiric Antibiotic Treatment Guidance for Adults[a,b]	
First Line therapy options	
Azithromycin[c] 1 g PO X 1 dose [2] [3]	Use azithromycin if allergic/intolerant of ciprofloxacin. **Single dose therapy** is preferred if: • risk of loss to follow-up • medication access concerns • adherence challenges
Ciprofloxacin[d] 500 mg PO bid X 3 days	Consider if severe vomiting, or intolerant/allergic to azithromycin *First dose PO then 5 additional doses to complete course*
Alternate regimen[e]: Consult ID if there are clinical concerns using first/second line therapy	
Cefixime 200 mg PO BID X 5 days	Use if allergic/intolerant to first line agents *First dose PO then 9 additional doses to complete course*
Antimotility agents for consideration	
Loperamide 4 mg PO X 1 then: 2 mg after each loose stool (max for d16 mg /day X 2 days)	Give 4 mg dose X 1 Issue 6 additional 2 mg tablets for day 1 If needed, issue 8 tablets for day 2

[1] For the purposes of the outbreak, a vulnerable person is defined as: having no fixed address, using an emergency shelter, addiction recovery site or supportive housing, reporting living on the street, receiving services from agency for vulnerable residents, reporting substance abuse and/or scavenging.

[2] Clinical illness is characterized by diarrhea, fever, nausea and sometimes toxaemia, vomiting, cramps [14].

Notes:

a. Most patients will have substantial resolution of symptoms over the first 24-48 hours of therapy. If symptoms do not resolve and treatment failure is suspected, repeat diagnostic workup including culture is advised.
b. Resistance to various antibiotics in *Shigella* isolates has been described. Ongoing surveillance of resistance patterns in the outbreak strain, *Shigella flexneri 3a*, is occurring. These antibiotic recommendations are interim and subject to review.
c. Azithromycin is appropriate for use for children (using weight-based dosing rather than the regimen above) and in pregnancy. It may be associated with a higher risk of post-dose, short-term nausea as compared to quinolones. It can be associated with a prolonged QT interval [4]. It is not highlighted as a clinically important interaction in opiate use addiction therapeutics.
d. If ciprofloxacin is used for treatment, it is necessary to assess drug-drug interactions with warfarin and anticonvulsants. Do not take with bismuth subsalicylate (Pepto-Bismol).
e. Trimethoprim-sulfamethoxazole (TMP/SMX) not recommended as alternative for empiric therapy due to greater than 70% resistance in outbreak strain.

Data Collection

For individuals who have been offered empiric therapy, it is recommended that the following information is collected and documented:

- Demographic information: name, date of birth, ULI
- Whether the individual is houseless or has no fixed address
- Exposure history: access to shelters and encampments (with approximate location), and which specific shelters have been accessed
- Underlying medical conditions such as immunocompromised state or pregnancy
- Symptom onset date
- List of symptoms
- Type of therapy that was administered
- Date and time therapy was administered
- Outcome: whether symptoms resolved or whether the individual re-presented to hospital or required additional medical care

Diagnosis

Establishing the diagnosis is still recommended in individuals who have been offered empiric therapy. In response to the outbreak, the following measures have been implemented to decrease barriers to timely diagnosis for the duration of the outbreak:

1. Laboratories are now releasing presumptive results from molecular testing rather than awaiting culture confirmation:
    - "*Presumptive POSITIVE PCR for Shigella species/Enteroinvasive E. coli (EIEC). In the context of the current outbreak with Shigella flexneri 3a, this positive PCR result likely represents a true positive for Shigella species. Please refer to the enteric culture for further results"*

2. Rectal swabs will be accepted for enteric bacteria testing for the duration of the outbreak only.
    - Bulk stool specimens remain the preferred method of collection as they provide the labs with more material for testing. However, in situations where providers are not able to collect the bulk stool specimen, a rectal swab can be used.
    - **Ensure epidemiological investigation number is marked on both the lab requisition and the specimen label (i.e. 2022-EI-4111).**

Antimotility Therapy

- Loperamide (Imodium®) in combination with antibiotics may double the cure rate at 24 hours [5], although there is not a lot of data specific to *Shigella* [6].
- A single small study in 1973 [7] raised a possibility of prolonged fever associated with diphenoxylate/atropine (Lomotil®) given without antibiotics in 7 patients, and no improvement in carriage over placebo.
- Some providers may avoid antidiarrheal medication in patients with evidence of dysentery (fever, bloody or mucous stools) unless antibiotics are also given.
    - Studies of loperamide use in infectious diarrhea have not revealed harms [8].
    - Loperamide is also often avoided when *C. difficile* is suspected.
- Patients taking loperamide should be cautioned not to exceed the maximum daily dose.

Supportive Therapies

Additional information on the use of oral rehydration and nausea medications to support individuals with severe diarrheal illness in the community is found below.

Oral Rehydration Solution (ORS):

Oral rehydration can reduce the risk of severe illness and dehydration from diarrhea. Because salt and glucose absorption are coupled in the small intestine, solutions that contain both stimulate fluid absorption, and are better than drinking water [9].

Oral rehydration is NOT suggested for people with more severe dehydration who need assessment for IV fluids, those who are unable to drink liquid (respiratory problems or unconsciousness), patients with shock (with low blood pressure) or inability to maintain ORS due to vomiting.

People with diarrhea (or those caring for them) may consider use of oral fluids that have additional simple electrolytes. Slowly sipping fluids may be better tolerated than drinking larger amounts. In initial rehydration, intake of one litre over 1-2 hours can be targeted and patients should take 1-2 cups minimum after each bowel movement [10]**.** For less severe illness, a goal of 3 to 4 litres over 24 hours may be sufficient. As a rule of thumb most recipes suggest about ½ tsp salt and some sugar containing fluid in every liter of solution, with examples following of “homemade” options. These examples have been suggested for patients with high volume small bowel fluid loss [11]. An alternate would be purchased oral rehydration solution packets - generally these are made for 1 packet in 1 L of water. Gatorade or sports drinks are recommended to be diluted/adjusted (see below).

World Health Organization based ORS Recipe

	1 litre	**4 litres (milk jug)**
Table salt (sodium chloride)	3/8 tsp	**1 ½ tsp**
Salt Substitute (potassium chloride)	¼ tsp	**1 tsp**
Baking soda (sodium bicarbonate)	½ tsp	**2 tsp**
Table sugar	2 tbsp + 2 tsp	**½ c plus 3 tbsp**
Add tap water to total	1 liter	**4 liters**
Optional: NutraSweet or Splenda-based flavoring of choice to taste [12]		

Other homemade rehydration options (which have been partially adjusted for anticipated sugar content of the juice):

Gatorade base
Choose any flavor, except red
2 cups Gatorade
2 cups water
½ tsp salt

Grape juice base
½ cup juice
3½ cups water
½ tsp salt

Apple juice base
1 cup of juice
3 cups of water
½ tsp salt

Nausea Medication

If people are experiencing nausea and vomiting that impairs their ability to hydrate themselves, or more importantly makes them unable to take any recommended oral treatments including antibiotics, antiemetic therapy should be considered. There are potential side effects to these medications so they should be reserved for people who cannot tolerate oral medications or fluids.

The main over the counter medication option is oral dimenhydrinate (Gravol®), which has been shown potentially useful in gastroenteritis in children, with a main side effect of sedation.

The main prescription-based option would be ondansetron (Zofran®), which has evidence for use in gastroenteritis with the need for oral rehydration [13]. Other commonly used options such as metoclopramide (Maxeran®) are not generally suggested for this use.

Potential Dosage Options

Medication	*Suggested Dosage*
Dimenhydrinate (Gravol®) *[over the counter]*	50 mg PO every 6 hours. Reassess after 4 doses May be given IV or SC by designated health care providers
Ondansetron (Zofran®) *[prescription]*	4 mg PO (orally disintegrating tablet) x 1 dose

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