

## SURVEILLANCE REPORT

# Shigella Antimicrobial Resistance

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## Introduction

This report describes antimicrobial susceptibility testing (AST) results from Public Health Ontario (PHO) for *Shigella* species, with a focus on multidrug-resistant (MDR) and extensively drug-resistant (XDR) cases. PHO routinely performs AST on *Shigella* isolates identified at PHO as well as isolates submitted by other laboratories with a request for confirmatory identification, AST, and/or subtyping surveillance. This report covers *Shigella* AST from January 2018 to March 2023.

# Background

Shigella infection (shigellosis) is a common cause of bacterial gastroenteritis in Canada and worldwide. Typical symptoms include diarrhea, abdominal cramping, nausea, vomiting, and fever.<sup>1,2</sup> Known risk factors include exposure to untreated water, poor food sanitation, or anal-oral contact. The following groups may be at greater risk of symptomatic infection: young children, travelers, and men who have sex with men (MSM).<sup>2,3</sup> Moderate to severe infections may require treatment with antibiotics. Currently recommended antibiotics include azithromycin, fluoroquinolones (e.g. ciprofloxacin), third-generation cephalosporins (e.g. ceftriaxone), trimethoprim-sulfamethoxazole (TMP-SMX), and ampicillin.<sup>1,3</sup>

There has been growing concern related to drug-resistant strains of *Shigella* circulating worldwide. Early in 2022, the United Kingdom Health Security Agency<sup>4</sup> and World Health Organization<sup>5</sup> issued communications noting an increase of XDR *Shigella sonnei* cases in the UK and Europe, which were first observed in the UK during 2018.<sup>4</sup> In June 2022, the Pan American Health Organization released an alert of potential risk of the strain circulating in Latin America and the Caribbean.<sup>6</sup> The United States Centers for Disease Control and Prevention (CDC) issued a similar advisory in February 2023, stating the proportion of XDR *Shigella* infections had increased from zero percent of cases in the United States in 2015 to five percent of cases in 2022.<sup>7</sup> Investigations are ongoing to better characterize the impact of XDR *Shigella* infections, and this report provides an update on the current situation in Ontario.

## **Definitions**

#### Multidrug-resistant (MDR) Shigella:

For this report, we have defined MDR *Shigella* as resistant to three or more of the five established antibiotics used to treat *Shigella* infections: azithromycin, fluroquinolones (e.g. ciprofloxacin), third-generation cephalosporins (e.g. ceftriaxone), TMP-SMX, and ampicillin.

#### Extensively drug-resistant (XDR) Shigella:

For this report, we used the CDC's definition of XDR *Shigella*, defined as resistant to all five established antibiotics used to treat *Shigella* infections: azithromycin, ciprofloxacin, ceftriaxone, TMP-SMX, and ampicillin.<sup>7</sup>

# **Highlights**

- In Ontario, the proportion of MDR shigellosis cases was stable from 2018 to 2022 at approximately 50%.
- The proportion of XDR shigellosis cases increased from 1.0% in 2018 to 6.6% in 2022. In the first three months of 2023, the proportion of XDR cases was 9.1% (6/66).
  - This increasing trend in XDR has been observed only in Shigella sonnei.
- More XDR cases were observed in males (27) compared to females (12); however, the proportion of shigellosis cases with XDR was the same for males and females at 3.6% (27/740 and 12/332, respectively).
- Overall, most *Shigella* isolates in Ontario were resistant to TMP-SMX (76.6%) or ampicillin (66.7%), and a significant proportion of isolates were resistant to azithromycin (43.3%), ciprofloxacin (33.9%), or ceftriaxone (17.6%).
- Nearly half (43.6%) of XDR shigellosis cases reported travel (17/39). Of the cases reporting travel, 52.9% (9/17) travelled to Pakistan. Among the XDR cases not reporting travel, 40.9% (9/22) indicated anal-oral contact.

## **Test Results**

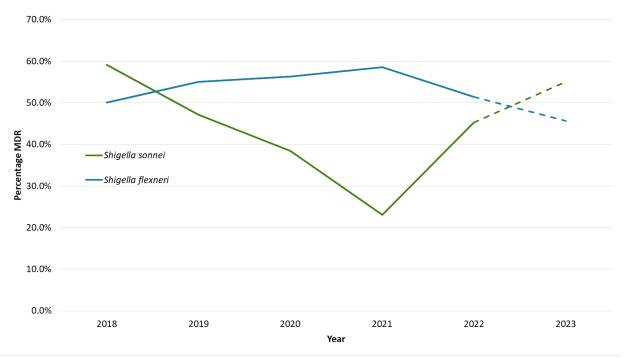
Table 1. Number and proportion of shigellosis cases identified as MDR or XDR by year, January 1, 2018 to March 31, 2023

Year	Number of cases	Number of MDR cases (percentage)	Number of XDR cases (percentage)
2018	292	153 (52.4%)	3 (1.0%)
2019	248	122 (49.2%)	5 (2.0%)
2020	155	75 (48.4%)	10 (6.5%)
2021	96	47 (49.0%)	0 (0.0%)
2022	228	109 (47.8%)	15 (6.6%)
2023*	66	32 (48.5%)	6 (9.1%)
Total	1,085	538 (49.6%)	39 (3.6%)

**Note:** \*Partial year, includes data up to March 31, 2023. Excludes isolates where partial AST results were available (n=13).

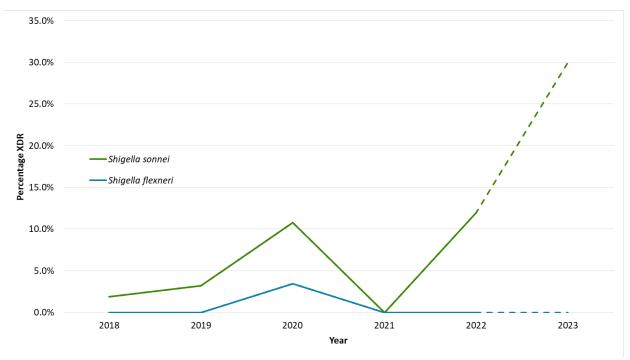
Data source: Public Health Ontario Laboratory Information Management System

Figure 1. Proportion of shigellosis cases identified as MDR by species and year, January 1, 2018 to March 31, 2023



**Note:** Dashed line indicates a partial year including data up to March 31, 2023. *Shigella boydii* and *Shigella dysenteriae* were excluded due to low numbers. Excludes isolates where partial AST results were available (n=13). **Data source:** Public Health Ontario Laboratory Information Management System





**Note:** Dashed line indicates a partial year including data up to March 31, 2023. *Shigella boydii* and *Shigella dysenteriae* were excluded due to low numbers. Excludes isolates where partial AST results were available (n=13). **Data source:** Public Health Ontario Laboratory Information Management System

Table 2. Number and proportion of shigellosis cases identified as MDR or XDR by sex, January 1, 2018 to March 31, 2023

Sex	Number of cases	Number of MDR cases (percentage)	Number of XDR cases (percentage)
Female	332	81 (24.4%)	12 (3.6%)
Male	740	453 (61.2%)	27 (3.6%)
Unknown	13	4 (30.8%)	0 (0.0%)
Total	1,085	538 (49.6%)	39 (3.6%)

**Data source:** Public Health Ontario Laboratory Information Management System. Excludes isolates where partial AST results were available (n=13).

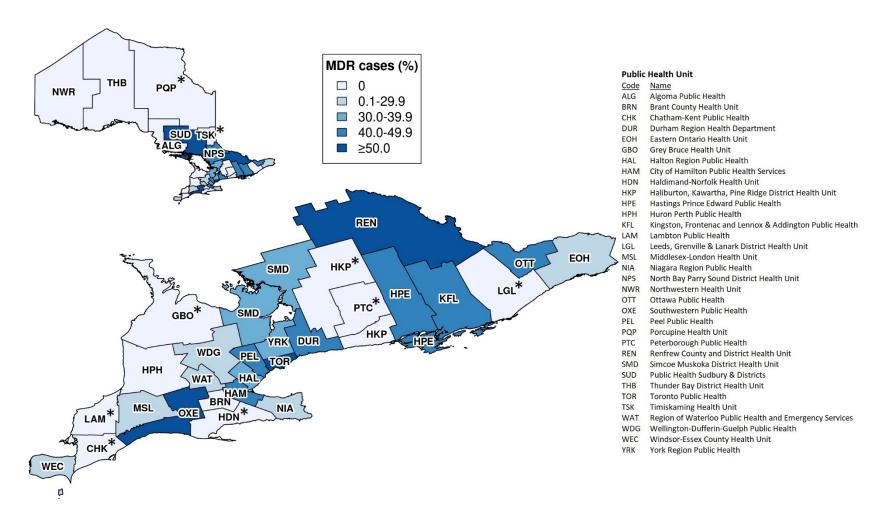
Table 3. Number and proportion of shigellosis cases identified as MDR or XDR by age group, January 1, 2018 to March 31, 2023

Age group	Number of cases	Number of MDR cases (percentage)	Number of XDR cases (percentage)
Ages: 0 – 9	123	44 (35.8%)	8 (6.5%)
Ages: 10 – 19	42	12 (28.6%)	2 (4.8%)
Ages: 20 – 64	849	454 (53.5%)	27 (3.2%)
Ages: 65 and over	70	27 (38.6%)	2 (2.9%)
Total	1,084	537 (49.5%)	39 (3.6%)

**Note:** Excludes one record with a missing date of birth. Excludes isolates where partial AST results were available (n=13).

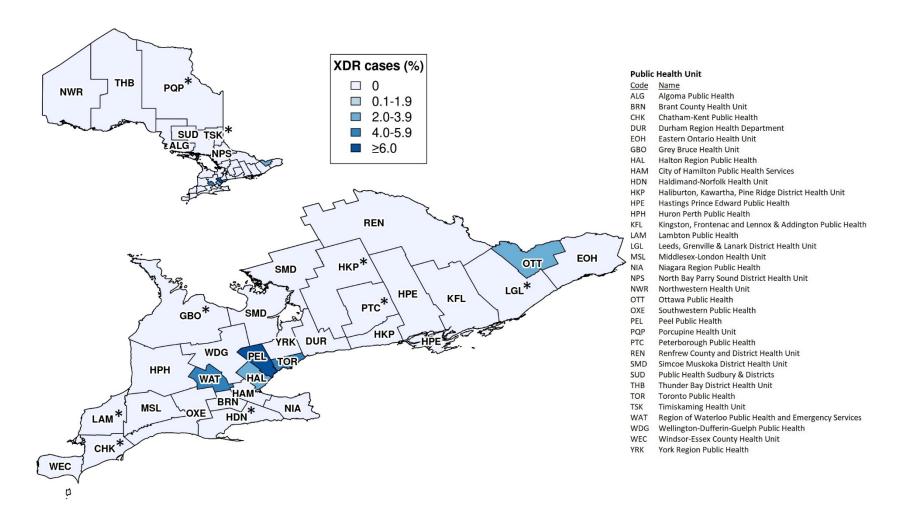
**Data source:** Public Health Ontario Laboratory Information Management System

Figure 3. Proportion of shigellosis cases identified as MDR by public health unit, January 1, 2018 to March 31, 2023



**Note:** \*Data were suppressed for public health units with fewer than five shigellosis cases. There were no shigellosis cases from Timiskaming Health Unit or Porcupine Health Unit. Public health unit was assigned using patient postal code or ordering provider postal code if patient postal code was missing. **Data source:** Public Health Ontario Laboratory Information Management System

Figure 4. Proportion of shigellosis cases identified as XDR by public health unit, January 1, 2018 to March 31, 2023



**Note:** \*Data were suppressed for public health units with fewer than five shigellosis cases. There were no shigellosis cases from Timiskaming Health Unit or Porcupine Health Unit. Public health unit was assigned using patient postal code or ordering provider postal code if patient postal code was missing. **Data source:** Public Health Ontario Laboratory Information Management System

Table 4. Number and proportion of *Shigella* isolates with resistance to azithromycin by species, January 1, 2018 to March 31, 2023

Shigella species	Number of isolates	Number resistant to azithromycin	Percentage resistant to azithromycin
Shigella sonnei	549	219	39.9%
Shigella flexneri	514	253	49.2%
Shigella boydii	28	3	10.7%
Shigella dysenteriae	5	0	0.0%
Total	1,096	475	43.3%

**Note:** Excludes one isolate without species-level identification. Excludes one isolate without a result for azithromycin.

Data source: Public Health Ontario Laboratory Information Management System

Table 5. Number and proportion of *Shigella* isolates with resistance to ceftriaxone by species, January 1, 2018 to March 31, 2023

Shigella species	Number of isolates	Number resistant to ceftriaxone	Percentage resistant to ceftriaxone
Shigella sonnei	550	157	28.5%
Shigella flexneri	514	32	6.2%
Shigella boydii	28	4	14.3%
Shigella dysenteriae	5	0	0.0%
Total	1,097	193	17.6%

Note: Excludes one isolate without species-level identification.

Data source: Public Health Ontario Laboratory Information Management System

Table 6. Number and proportion of *Shigella* isolates with resistance to ciprofloxacin by species, January 1, 2018 to March 31, 2023

Shigella species	Number of isolates	Number resistant to ciprofloxacin	Percentage resistant to ciprofloxacin
Shigella sonnei	549	196	35.7%
Shigella flexneri	514	174	33.9%
Shigella boydii	28	1	3.6%
Shigella dysenteriae	5	0	0.0%
Total	1,096	371	33.9%

**Note:** Excludes one isolate without species-level identification. Excludes one isolate without a result for ciprofloxacin.

Data source: Public Health Ontario Laboratory Information Management System

Table 7. Number and proportion of *Shigella* isolates with resistance to trimethoprim-sulfamethoxazole (TMP-SMX) by species, January 1, 2018 to March 31, 2023

Shigella species	Number of isolates	Number resistant to TMP-SMX	Percentage resistant to TMP-SMX
Shigella sonnei	550	478	86.9%
Shigella flexneri	514	336	65.4%
Shigella boydii	27	23	85.2%
Shigella dysenteriae	5	3	60.0%
Total	1,096	840	76.6%

**Note:** Excludes one isolate without species-level identification. Excludes one isolate without a result for TMP-SMX. **Data source:** Public Health Ontario Laboratory Information Management System

Table 8. Number and proportion of *Shigella* isolates with resistance to ampicillin by species, January 1, 2018 to March 31, 2023

Shigella species	Number of isolates	Number resistant to ampicillin	Percentage resistant to ampicillin
Shigella sonnei	544	274	50.4%
Shigella flexneri	510	432	84.7%
Shigella boydii	27	17	63.0%
Shigella dysenteriae	5	1	20.0%
Total	1,086	724	66.7%

**Note:** Excludes one isolate without species-level identification. Excludes isolates without results for ampicillin (n=11).

Data source: Public Health Ontario Laboratory Information Management System

# **XDR Shigellosis Cases**

Table 9. Distribution of XDR shigellosis cases by public health unit, case characteristics, and travel status, January 1, 2018 to March 31, 2023

	Percentage of travel-related XDR shigellosis cases (n=17)	Percentage of XDR shigellosis cases who did not report travel (n=22)	Percentage of all XDR shigellosis cases (n=39)
Diagnosing public health unit			
Toronto Public Health	58.8% (10/17)	63.6% (14/22)	61.5% (24/39)
Peel Public Health	29.4% (5/17)	18.2% (4/22)	23.1% (9/39)
Ottawa Public Health	0.0% (0/17)	9.1% (2/22)	5.1% (2/39)
Halton Region Public Health	5.9% (1/17)	0.0% (0/22)	2.6% (1/39)
Lambton Public Health	5.9% (1/17)	0.0% (0/22)	2.6% (1/39)
Peterborough Public Health	0.0% (0/17)	4.5% (1/22)	2.6% (1/39)
Region of Waterloo Public Health and Emergency Services	0.0% (0/17)	4.5% (1/22)	2.6% (1/39)
Age and sex			
Age range	1–70	1–81	1–81
Median age	27.0	32.5	29.0
Proportion of males	58.8% (10/17)	77.3% (17/22)	69.2% (27/39)
Risk factors			
Anal-oral contact	29.4% (5/17)	40.9% (9/22)	35.9% (14/39)
Close contact with a case	0.0% (0/17)	9.1% (2/22)	5.1% (2/39)
Sex with same sex*	20.0% (2/10)*	28.6% (4/14)*	25.0% (6/24)*

**Note:** Travel and risk factor information was not provided for all cases. Travel-related refers to cases who reported travel within four days prior to symptom onset. \*Data for the risk factor of "sex with same sex" is only collected by Toronto Public Health. Denominators for this risk factor were therefore derived from Toronto Public Health cases (n=24).

Data source: Integrated Public Health Information System (iPHIS)

Table 10. Distribution of travel-related XDR shigellosis cases by travel destination, January 1, 2018 to March 31, 2023

Travel destination	Number of cases	Percentage
Pakistan	9	52.9%
USA	2	11.8%
India	1	5.9%
Mexico	1	5.9%
Venezuela	1	5.9%
Caribbean (multiple countries)	2	11.8%
Europe (multiple countries)	1	5.9%
Total	17	100%

**Note:** Travel-related refers to cases who reported travel within four days prior to symptom onset.

Data source: Integrated Public Health Information System (iPHIS)

## **Technical Notes**

#### **Data Sources**

- Antimicrobial susceptibility testing data for *Shigella* isolates were extracted from the Public Health Ontario Laboratory Information Management System on April 6, 2023 at 1:00 p.m.
- Data for cases with XDR *Shigella* were extracted from the integrated Public Health System (iPHIS) on April 10, 2023 at 11:30 a.m.

# Methods and Data caveats: Public Health Ontario Laboratory Information Management System

- PHO routinely performs AST on *Shigella* isolates submitted by community and hospital laboratories, which should encompass most if not all confirmed shigellosis cases in the province.
- PHO performs AST according to the current guidelines from the Clinical and Laboratory Standards Institute (CLSI).<sup>8</sup>
- Drug resistance was determined using the minimum inhibitory concentration (MIC) breakpoints defined in the CLSI M100-ED33:2023.8
- To assign a date for each isolate, sample collection date was used if available; otherwise, login
  date was used. The earliest date available was then assigned as the index date for each case,
  and repeat isolates were considered part of the same case if the same species was identified
  within 90 days of the index date. If the index date was more than 90 days apart, they were
  counted as a separate case.

- Maps were generated using PHO's Easy Maps tool, available from the following link: <u>PHO Easy Maps 2.0</u>. Public health unit was assigned using patient postal code, where available, or ordering provider postal code if patient postal code was missing.
- XDR Shigella cases were linked to data from the Integrated Public Health Information System (iPHIS) using health card number and/or first name, last name, and date of birth.

# Methods and Data caveats: Integrated Public Health Information System (iPHIS)

- iPHIS is a dynamic disease reporting system that allows ongoing updates to data previously entered in the system. As a result, data extracted from iPHIS represent a snapshot at the time of extraction and may differ from previous or subsequent reports.
- Risk factor information was collected from iPHIS. The information is consistent with the standardized Ontario Investigation Tool for Shigellosis used across PHUs during case interviews.
  - Data for the risk factor of "sex with same sex" is only collected by Toronto Public Health.
- Travel-related refers to cases who reported travel within four days prior to symptom onset.
- Age represents the age of the case at the time of illness. Age extracted from iPHIS was rounded to the nearest whole number.
- Diagnosing public health unit refers to the case's public health unit of residence at the time of illness onset or report to public health and not necessarily the location of exposure.

## References

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### Citation

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