#### Travelers' diarrhea definitions

Mild (acute): diarrhea that is tolerable, is not distressing, and does not interfere with planned activities.

Moderate (acute): diarrhea that is distressing or interferes with planned activities.

Severe (acute): diarrhea that is incapacitating or completely prevents planned activities; all dysentery (passage of grossly bloody stools) is considered severe.

Persistent: diarrhea lasting ≥2 weeks.

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- Antimicrobial prophylaxis should not be used routinely in travelers (Strong recommendation, low/very low level of evidence).
- Antimicrobial prophylaxis should be considered for travelers at high risk of health-related complications of travelers' diarrhea (Strong recommendation, low/very low level of evidence).
- 3. Bismuth subsalicylate (BSS) may be considered for any traveler to prevent travelers' diarrhea (Strong recommendation, high level of evidence).
- When antibiotic prophylaxis is indicated, rifaximin is recommended (Strong recommendation, moderate level of evidence).
- Fluoroquinolones are not recommended for prophylaxis of travelers' diarrhea (Strong recommendation, low/very low level of evidence).

#### Therapy of mild travelers' diarrhea

- Antibiotic treatment is not recommended in patients with mild travelers' diarrhea (Strong recommendation, moderate level of evidence).
- 7. Loperamide or BSS may be considered in the treatment of mild travelers' diarrhea (Strong recommendation, moderate level of evidence).

#### Therapy of moderate travelers' diarrhea

- 8. Antibiotics may be used to treat cases of moderate travelers' diarrhea (Weak recommendation, moderate level of evidence).
- 9. Fluoroquinolones may be used to treat moderate travelers' diarrhea (Strong recommendation, moderate level of evidence. Qualifying Remarks: Emergence of resistance to this class of drug though without strong evidence of clinical failure outside of SEAsia, combined with the potential for adverse dysbiotic (reduction in diversity of intestinal microbiota) and musculos keletal consequences, contribute important uncertainties to the risk-benefit assessment and underlie a non-unanimous GRADE of this recommendation).
- Azithromycin may be used to treat moderate travelers' diarrhea (Strong recommendation, high level of evidence).
- 11. Rifaximin may be used to treat moderate travelers' diarrhea (Weak recommendation, moderate level of evidence). Qualifying Remarks: Caution should be exercised in provision of rifaximin as empirical therapy of moderate diarrhea in regions or itineraries in which high risk of invasive pathogens are anticipated.
- Loperamide may be used as adjunctive therapy for moderate to severe travelers' diarrhea (Strong recommendation, high level of evidence).
- Loperamide may be considered for use as monotherapy in moderate travelers' diarrhea (Strong recommendation, high level of evidence).

#### Therapy in severe travelers' diarrhea

- 14. Antibiotics should be used to treat severe travelers' diarrhea (Strong recommendation, high level of evidence).
- 15. Azithromycin is preferred to treat severe travelers' diarrhea (Strong recommendation, moderate level of evidence).
- 16. Fluoroquinolones may be used to treat severe, nondysenteric travelers' diarrhea (Weak recommendation, moderate level of evidence).
- 17. Rifaximin may be used to treat severe, nondysenteric travelers' diarrhea (Weak recommendation, moderate level of evidence).
- 18. Single-dose antibiotic regimens may be used to treat moderate or severe travelers' diarrhea (Strong recommendation, high level of evidence).

#### Follow-up and diagnostic testing

- Microbiologic testing is recommended in returning travelers with severe or persistent symptoms or in those who fail empiric therapy (Strong recommendation, low/very low level of evidence).
- 20. Molecular testing, aimed at a broad range of clinically relevant pathogens, is preferred when rapid results are clinically important or non-molecular tests have failed to establish a diagnosis (ungraded). Qualifying Remarks: No studies have been published as of yet which show that using these tests improves patient outcomes.

#### Additional consensus statements (ungraded)

- 21. There is insufficient evidence to recommend the use of commercially available prebiotics or probiotics to prevent or treat travelers' diarrhea.
- 22. Studies are needed on changes in the gut microbiome in travelers with and without diarrhea to darify the benefits and harms of current and novel preventive, diagnostic, and therapeutic approaches.
- 23. There is an incrementally increasing association between travel, travelers' diarrhea, and antibiotic use with the acquisition of multidrug-resistant bacteria. Pretravel counseling should include information about this risk, balanced against the benefits of antibiotic use.

### Prophylaxis

- Antimicrobial prophylaxis should not be used routinely in travelers (Strong recommendation, low/very low level of evidence).
- Antimicrobial prophylaxis should be considered for travelers at high risk of health-related complications of travelers' diarrhea (Strong recommendation, low/very low level of evidence).
- Bismuth subsalicylate (BSS) may be considered for any traveler to prevent travelers' diarrhea (Strong recommendation, high level of evidence).
- When antibiotic prophylaxis is indicated, rifaximin is recommended (Strong recommendation, moderate level of evidence).
- Fluoroquinolones are not recommended for prophylaxis of travelers' diarrhea (Strong recommendation, low/ very low level of evidence).

抗生剤の予防投与は原則ありません。 場合によりビスマス製剤を用いるようです。

# Therapy of Mild Travelers' Diarrhea

- Antibiotic treatment is not recommended in patients with mild travelers' diarrhea (Strong recommendation, moderate level of evidence).
- Loperamide or BSS may be considered in the treatment of mild travelers' diarrhea (Strong recommendation, moderate level of evidence).

軽症の場合は抗生剤投与はなく、場合によりロペミンかビスマス製剤を用います。

### Therapy of Moderate Travelers' Diarrhea

- Antibiotics may be used to treat moderate travelers' diarrhea (Weak recommendation, moderate level of evidence).
- 9. Fluoroquinolones may be used to treat moderate travelers' diarrhea (Strong recommendation, moderate level of evidence. Qualifying Remarks: Emergence of resistance to this class of drug though without strong evidence of clinical failure outside of SE Asia, combined with the potential for adverse dysbiotic (reduction in diversity of intestinal microbiota) and musculoskeletal consequences, contribute important uncertainties to the risk-benefit assessment and underlie a non-unanimous GRADE of this recommendation).
- Azithromycin may be used to treat moderate travelers' diarrhea (Strong recommendation, high level of evidence).
- 11. Rifaximin may be used to treat moderate travelers' diarrhea (Weak recommendation, moderate level of evidence). Qualifying Remarks: Caution should be exercised in provision of rifaximin as empirical therapy of moderate diarrhea in regions or itineraries in which high risk of invasive pathogens are anticipated.
- Loperamide may be used as adjunctive therapy for moderate to severe travelers' diarrhea (Strong recommendation, high level of evidence).
- Loperamide may be considered for use as monotherapy in moderate travelers' diarrhea (Strong recommendation, high level of evidence).

中等症の場合はロペミンのみで 経過をみることもある。 抗生剤としてジスロマックか シプロキサンを投与する場合もある。

Table 2. Acute diarrhea antibiotic treatment recommendations

Antibiotica	Dose	Treatment duration
Azithromycin <sup>c, d</sup>	1000 mg by mouth or	Single or 1-day divided <sup>b</sup>
•	500 mg by mouth	3 day course
Levofloxacin	500 mg by mouth	Single dose <sup>b</sup> or 3 day course
Ciprofloxacin	750 mg by mouth or	Single dose <sup>b</sup>
	500 mg by mouth	3 day course
Ofloxacin	400 mg by mouth	Single dose <sup>b</sup> or 3 day course
Rifaximin <sup>e</sup>	200 mg by mouth three times daily	3 days

<sup>\*</sup>Antibiotic regimens may be combined with loperamide, 4 mg first dose, then 2 mg dose after each loose stool, not to exceed 16 mg in a 24 hour period.

<sup>&</sup>lt;sup>b</sup>If symptoms are not resolved after 24 hours, continue daily dosing for up to 3 days.

<sup>&</sup>lt;sup>c</sup>Use empirically as first line in Southeast Asia and India to cover fluoroquinolone resistant Campylobacter or in other geographical areas if Campylobacter or resistant ETEC are suspected.

<sup>&</sup>lt;sup>d</sup>Preferred regimen for dysentery or febrile diarrhea.

Do not use if clinical suspicion for Campylobacter, Salmonella, Shigella or other causes of invasive diarrhea.

## Therapy in Severe Travelers' Diarrhea

- Antibiotics should be used to treat severe travelers' diarrhea (Strong recommendation, high level of evidence).
- Azithromycin is preferred to treat severe travelers' diarrhea (Strong recommendation, moderate level of evidence).
- Fluoroquinolones may be used to treat severe, nondysenteric travelers' diarrhea (Weak recommendation, moderate level of evidence).
- 17. Rifaximin may be used to treat severe, nondysenteric travelers' diarrhea (Weak recommendation, moderate level of evidence).
- 18. Single-dose antibiotic regimens may be used to treat moderate or severe travelers' diarrhea (Strong recommendation, high level of evidence).

重症例では先ずジスロマックを選択。 次にシプロキサン。

# Follow-up and Diagnostic Testing

- 19. Microbiologic testing is recommended in returning travelers with severe or persistent symptoms or in those who fail empiric therapy (Strong recommendation, low/very low level of evidence).
- 20. Molecular testing, aimed at a broad range of clinically relevant pathogens, is preferred when rapid results are clinically important or non-molecular tests have failed to establish a diagnosis (ungraded). Qualifying Remarks: No studies have been published as of yet which show that using these tests improves patient outcomes.

海外から帰国した人で症状が続いていたり、重症化していれば 便培養を実施する。

Pre-travel	Providers should consider the following in counseling the traveler:  (1) Definitions of travelers' diarrhea and severity classification  (2) Importance of oral rehydration through fluid and salt intake for all travelers' diarrhea  (3) Information on effectiveness of treatments for travelers' diarrhea and the risk of travel, travelers' diarrhea, and antibiotic use with the acquisition of multi-drug resistance bacteria.  (4) Provision of empiric treatment medications as indicated by itinerary and provider-traveler determination  (5) Intra- and post-travel illness follow-up recommendations					
	Self-determination of Illness Severity					
During Travel	Mild Diarrhea that is tolerable, is not distressing, and does not interfere	Moderate Diarrhea that is distressing or interferes with planned activities	Severe Diarrhea that is incapacitating or prevents planned activities			
	with planned activities		Non-dysentery	Dysentery*		
	<u>May</u> use loperamide or bismuth subsalicylates	<u>May</u> use loperamide alone or as an adjunct to antibiotics	May use loperamide as adjunct to antibiotics			
		±	+			
		May use antibiotic (Table 2)	Should use antib	piotic (Table 2)		
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avel	Acute travelers' diarrhea should be treated empirically as above.					
Post-travel	Microbiologic testing is recommended in returning travelers with severe or persistent symptoms or in those who fail empiric therapy					
	Multiplex molecular diagnostics are preferred in patients with persistent or chronic symptoms					