CATMAT statement on international travellers and typhoid: From guidelines to practice

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Disclaimer
- Points of view expressed in this presentation are my own and do not necessarily reflect CATMAT’s or PHAC’s opinions/policy

Objectives
- At the end of this session, participants will be able to:
  - Summarize key points of the CATMAT statement on prevention of typhoid in travellers
  - Discuss pros and cons of the GRADE approach
  - Integrate patients’ and practitioners’ values and preferences into the decision making process

Clinical vignettes
Organized tour in Asia

- Rosemary, 67 years old and her husband Georges, 70 years old
- Going on a 3 weeks organized tour of South East Asia
- Vietnam, Cambodia and Laos
- Mainly hotels, will spend 3 days on a cruise of the Mekong
- Rosemary takes Losec® for an ulcer

Would you vaccinate them against typhoid fever?

- Yes
- No

Safari in Africa

- Mitchell, 45 years old, is going with a group to Kenya and Tanzania
- They will ascend Mount Kilimanjaro and then go on a 2 week-safari

Would you vaccinate him against typhoid fever?

- Yes
- No

VFR to India

- Anjali, 5 years old, is going with her mom to India
- Will visit her grandmother in Bombay for 4 weeks

Would you vaccinate her against typhoid fever?

- Yes
- No
VFR to Mexico

- Sara, 6 years old, is going with her mom to Mexico City for 4 days
- Will be staying with her mom’s family

- Will you vaccinate her against typhoid fever?
  - Yes
  - No

Volunteer in Haiti

- Andrew, 27 years old, is going to Haiti for 3 months
- He is volunteering with an NGO and will teach English to schoolchildren
- Will be staying in Port au Prince with some trips outside the capital

- Would you vaccinate him against typhoid fever?
  - Yes
  - No

- Have you read CATMAT’s statement on typhoid fever?
  - Yes
  - No

- Are you familiar with the GRADE approach?
  - Yes
  - No
Key points of the statement

What is GRADE?
- Grading of Recommendations Assessment, Development and Evaluation
- Method developed in 2004 by an international group of health professionals, researchers and guideline developers
- Goal: to overcome problems related to inconsistent rating of evidence and confusion with different rating systems
- Systematic reviews
- Structured, transparent
- Rates the quality of evidence and grades the strength of recommendations

What is GRADE?
- Considers balance between
  - Benefits/harms
  - Values/preferences of patients
- Used or endorsed by at least 70 organizations, including WHO, Uptodate and Cochrane Collaboration

Summary of the statement
- Typhoid vaccine
  - Moderately effective (~50%)
  - Well tolerated with very low risk of serious adverse events
  - Moderate confidence in the estimate of effect for vaccine efficacy
- Predictor of typhoid risk in travellers
  - Strongest predictor: destination of travel
  - Estimated risk: 1/3,000 South Asia (high risk)
  - 1/50,000–100,000 Sub-Saharan Africa, North Africa and the Middle East, or South America (intermediate risk)
  - < 1/300,000 Caribbean and Central America (low risk)
  - Moderate confidence in the baseline estimates of typhoid risk by destination

Other risk factors
- Children
- Visiting friends and relatives (VFRs),
- Presence of achlorhydria or use of acid suppression therapy
- Longer duration of travel
- May increase the risk of contracting typhoid but magnitude of incremental risk unclear
- Confidence in the effect estimates (quality of the data) very low

Values and preferences
- No data on the values and preferences of travellers/practitioners regarding the use of typhoid vaccine for prevention of typhoid
- Assumption: majority of Canadian travellers would consider the threshold of 1/10 000 (absolute risk of typhoid) worth it to get the vaccine
- Among destinations for which data are available, travel to South Asia only region where risk exceeded this threshold
Summary of recommendations

- Vaccine recommendations: conditional
- What does it mean?
  - Providers should discuss with the traveller the anticipated benefits and harms (including financial costs) associated with vaccination, and help the traveller reach a decision that is consistent with his/her values and preferences.
  - Available injectable polysaccharide vaccines do not protect against enteric fever (paratyphoid) caused by Salmonella paratyphi.
  - Current evidence not sufficient to recommend oral typhoid vaccine (Ty21a) for protection against paratyphoid.

CATMAT suggests that typhoid vaccine (Ty21a or Vi polysaccharide vaccine) be used for Canadian travellers visiting South Asia*; Conditional recommendation, moderate confidence in estimate of effect.

* South Asia includes Afghanistan, Pakistan, India, Nepal, Bangladesh, Maldives, Sri Lanka, Bhutan. More than 90% of cases of typhoid among travellers were reported from India, Pakistan and Bangladesh.

CATMAT suggests that typhoid vaccine (Ty21a or Vi polysaccharide vaccine) not be used for Canadian travellers visiting destinations other than the South Asia; Conditional recommendation against (immunization), moderate confidence in estimate of effect.

The decision of whether or not to use typhoid vaccination for destinations other than South Asia might be influenced by:

- Other factors associated with risk of travel associated typhoid such as pediatric travel, visiting friends and relatives, longer duration of travel, the presence of achlorhydria or use of acid suppression therapy.
- Patient preferences.

What is typhoid fever?

Caused by Salmonella enterica subsp. enterica serovars Typhi
- Exposure through ingestion of contaminated water or food
- Humans are the only reservoir
- Incubation period usually 8-14 days but can vary from 3 to over 60 days
- Infectiousness: generally from the first week of infection until symptoms have resolved
- 10% of untreated individuals excrete the bacilli for three months or more
- 2% to 5% of untreated individuals become asymptomatic chronic carriers

Most cases and deaths (more than 90%) occur in Asian countries, predominantly in South Asia.
- Incidence in high income countries is low (<15/100,000 persons per year), cases are most often associated with travel
- Average of 127 cases per year in Canada from 1999 to 2011 mean annual incidence of 0.39/100,000
Clinical course
- Ranges from mild illness with low-grade fever to severe systemic disease
- Non-specific symptoms: fever, headache, abdominal pain, nausea, vomiting, malaise, anorexia, bradycardia, splenomegaly, cough, rose spots, constipation
- Complications: abdominal perforation and extra intestinal infection that can be fatal
- Hospitalization in North America and Europe is common (75%-90%) with a mean length of stay ranging from 6–10 days
- Case fatality rate
  - 10% for untreated cases in low income settings
  - <1% for patients receiving care in high income countries

Destination as a risk factor

So, what do these recommendations say to us as practitioners? How does GRADE translate into real life?

Debating the GRADE approach
- Current experience with applying the GRADE approach to public health interventions: an empirical study
  - Rehfuess EA, Aki AA. BMC Public Health 2013, 13:9
- Semi-structured interviews with individuals/groups that have applied the GRADE approach and with representatives of groups that actively decided against its use
  - 18 interviews
  - 15 in-depth responses

Pros and cons of the GRADE approach
- Explicit
- Transparent
- Rigorous
- Objective

What works well
- Current experience with applying the GRADE approach to public health interventions: an empirical study
- Semi-structured interviews with individuals/groups that have applied the GRADE approach and with representatives of groups that actively decided against its use
- 18 interviews
- 15 in-depth responses
Challenges reported
- Complexity of public health interventions
- Choice of outcome and outcome measures
- Ability to discriminate between different types of observational studies
- Use of non-epidemiological evidence
- GRADE terminology
- GRADE and guideline development process

Suggestions
- Refine and revise, where appropriate, current terminology and definitions
- Pragmatic guidance on application of the GRADE approach
- Potential modification to the existing scheme for rating the quality of evidence

Values and preferences for typhoid vaccine
- No study on willingness to pay for travellers
- Vaccine probably cost effective for residents of endemic areas
- Cannot be extrapolated to travellers
- No data describing non-economic based values and preferences of travellers related to typhoid prevention

Existential quandary
- The human brain needs certainties
- Beliefs, values, preferences, personal experiences are all part of our decision-making process
- Prone to errors, biases
- That’s why we all want guidelines and we want them to be clear, simple and prescriptive
- But…..What do we believe in when there is no God?
Let’s get back to basics

- What?
- Who?
- Where?
- How long?
- What for?

What is typhoid and where is the risk?
- Typhoid is a disease of poverty, of poor access to drinking water and sanitation
- Humans are the only reservoir
- Paucity of direct evidence on risk level
- What indirect evidence can we use to help inform our patients?
  - Where can we find these informations?
  - CIA World Fact Book
  - World Bank Data

Risk stratification by income level

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<thead>
<tr>
<th>World Bank Income group</th>
<th>Cases per 100,000 travellers</th>
<th>Cases per 100,000 local residents</th>
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<tbody>
<tr>
<td>Low income</td>
<td>2.1</td>
<td>2.3</td>
</tr>
<tr>
<td>Lower-middle</td>
<td>0.3</td>
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</tr>
<tr>
<td>Upper-middle</td>
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<td>High income</td>
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<tr>
<td>Lower-middle</td>
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Data sources: National surveillance systems in each country, (low income: less than $1.25/day, lower-middle: $1.25-$4.99/day, upper-middle: $5.00-$10.00/day) per capita income

Typhoid risk map

Risk stratification by income level

Who is your patient?
- Children
- VFR
- Medical conditions that might increase the risk of acquiring typhoid?
- What is their perception/understanding of the risk?
- How do they manage risk/make decision? Are they
  - Acceptors?
  - Rellers?
  - Searchers?

Who are you as a practitioner?
- What is your expertise
- Experience as a clinician/person
- How do you manage risk?
- What is your practice setting?
How long is your patient travelling for?

- Majority of cases in reviewed studies occurred after 2 weeks of travel
- Quebec: no cases occurred in persons travelling less than two weeks
- USA: less than 20% of cases occurred in persons travelling for less than two weeks
- GeoSentinel: long term travellers (length of stay more than six months) more likely than short term travellers to be diagnosed with enteric fever (typhoid and paratyphoid)

What will your patient be doing?

- Rural vs urban areas
- Lodging type
- Activities
- Contact with local population

Incorporating patient preferences in practice guidelines

- Requires: expertise and practical wisdom
- Often complex process, context replete with emotional and social influences
- When patient preferences are important, guideline panels should indicate so and produce a conditional or weak recommendation, a suggestion
- Guidelines should present features of the options in ways that support shared decision making

The balancing act: a delicate equilibrium

Conclusion

- Guidelines are not perfect
- Tools that we have to adapt and use for our patients’ best interest
- Need a reflective/thoughtful approach that starts with us as practitioners
- No recipes, no one size fits all approach
- There are no contradictions in life, only paradoxes and different paradigms
- Finding a middle way that can encompass the diversity of our own and of our patients’ values/beliefs systems

Further reading

- Pronovost PJ. Enhancing Physicians’ use of clinical guidelines, JAMA, December 2013, vol 310, no 23.
- Rehfues EA, AMI EA. Current experience with applying the GRADE approach to public health interventions: an empirical study, BMC Public Health 2013.
Thank you!

Questions/comments?