

# Improving the Diagnosis of Diarrhea

Introduction of a new testing algorithm combining a molecular multiplex panel (GPMP) with selective culture (SC)

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## BACKGROUND

- Infectious diarrhea affects millions of people each year and causes significant morbidity and mortality
- Rapid and accurate detection of gastrointestinal (GI) pathogens is vital so that appropriate therapy can be started and infection control measures taken to prevent spread of the disease

## PROBLEMS

Method	Tests for	Turn-around time
Stool culture	Single bacterial pathogen per testing	2-3 days
Ova and parasite (O&P) exam	Parasitic pathogens	Several days-sample must be collected over multiple days
Rapid Tests (Rapid Immunoassays -lateral-flow, immunochromatography, dot blot)	Single pathogen per test	20-30 minutes
Real-time PCR	1-3 pathogens per test	Under 5 hours
ELISA	Single antigen/antibody per test	6-24 hours

*“Can a multiplex molecular test solve these problems?”*

- Improve the diagnosis of diarrhea by having more accurate and timely results (and do it at a reduced cost)

**xTAG® GPP**      **14 bacterial, viral, and parasitic pathogens in a single test**

## METHODOLOGY

1. Validation of multiplex RT-PCR test panel (using **Luminex xTAG GPP**)
2. Application to BC's new Agency for Pathology and Laboratory Medicine **Test Review Committee (TRC)** and subsequent approval by the **Ministry of Health (MOH)** to perform GPMP and SC for a period of 24 months
3. Implementation of new testing algorithm in Island Health with education of laboratory staff and care providers.
4. Measurement of system performance

## Gastrointestinal Pathogen Multiplex Panel (GPMP)

**Pre-PCR**

Sample Pre-treatment  
45-60 minutes

Nucleic Acid Extraction and Purification  
45 minutes

Multiplex Application  
2.5 hours

**Post-PCR**

Bead Hybridization and Detection  
1 hour

Data Acquisition and Analysis by MAGPIX®  
or Luminex® 100/200™  
10 minutes

### GPMP Targets:

Viruses	Parasites	Bacteria & Bacterial Toxins
<ul style="list-style-type: none"><li>• Adenovirus</li><li>• Rotavirus A</li><li>• Norovirus</li></ul>	<ul style="list-style-type: none"><li>• Giardia lamblia</li><li>• Cryptosporidium</li><li>• Entamoeba histolytica</li></ul>	<ul style="list-style-type: none"><li>• Clostridium difficile toxin A/B</li><li>• Salmonella</li><li>• Shigella</li><li>• Campylobacter</li><li>• E coli O157</li><li>• STEC</li><li>• ETEC</li><li>• Yersinia enterocolitica</li><li>• Vibrio cholerae</li></ul>

### Selective culture

<b>Negative</b>	<ul style="list-style-type: none"><li>• <i>Aeromonas</i></li><li>• <i>Plesiomonas</i></li><li>• <i>Yersina</i></li><li>• <i>Vibrio</i></li><li>• <i>Edwardsiella</i></li></ul>
<b>Positive</b> <ul style="list-style-type: none"><li>• <i>Campylobacter</i></li><li>• <i>Yersinia enterocolitica</i></li><li>• <i>Salmonella</i></li><li>• <i>Shigella</i></li><li>• <i>Vibrio cholerae</i></li><li>• <i>E. coli O157</i></li><li>• <i>STEC stx1/stx2</i></li></ul>	<ul style="list-style-type: none"><li>• Susceptibility testing</li><li>• Strain typing</li></ul>

## Testing restrictions

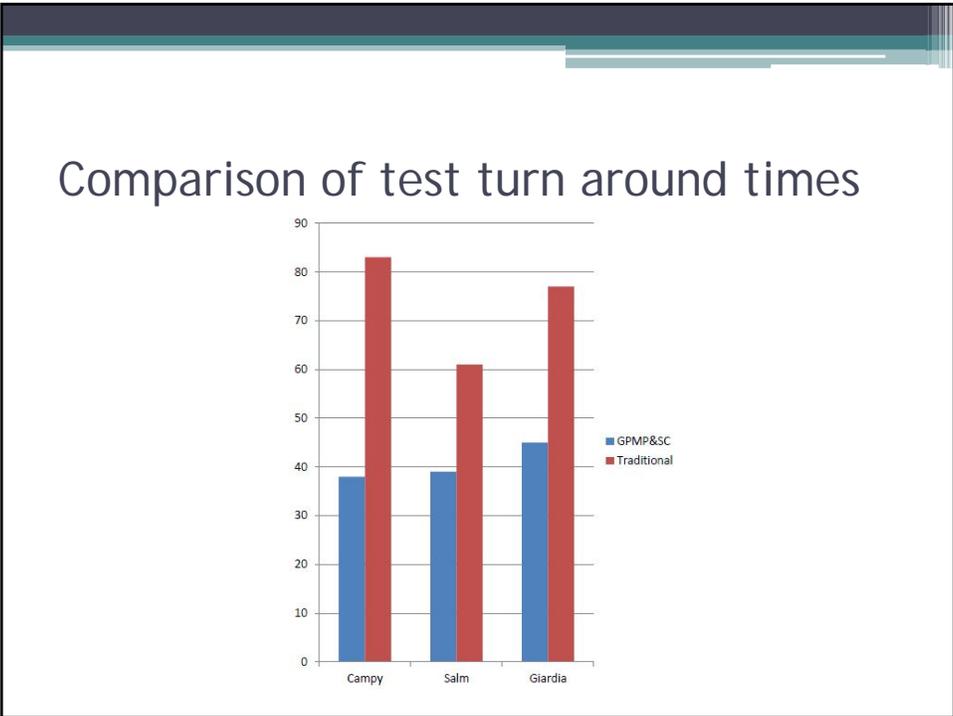
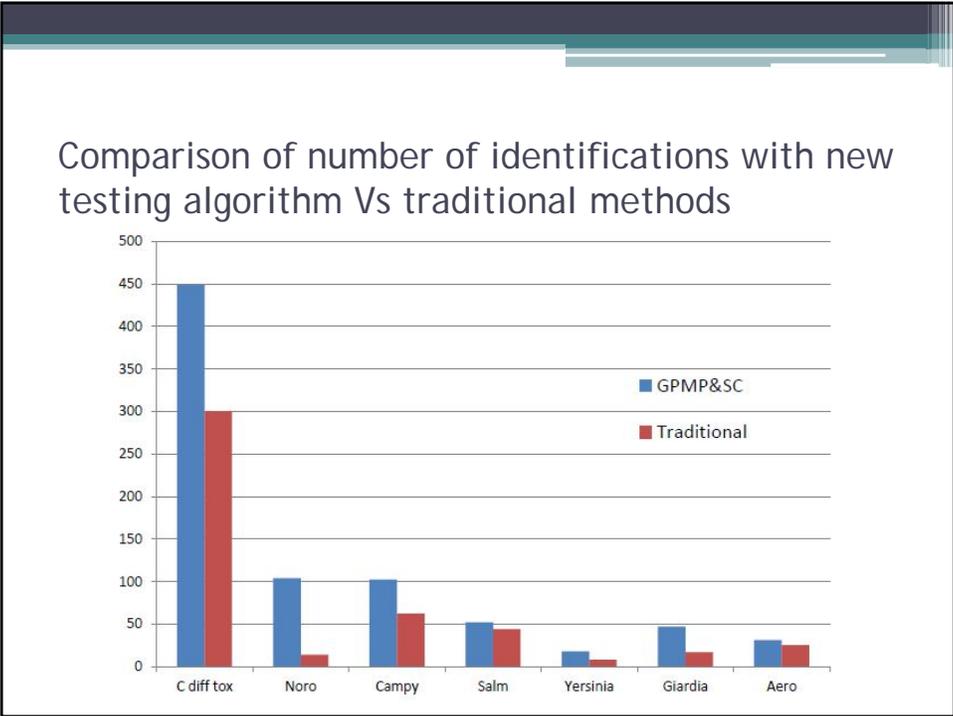
- **GPMP testing limited to once every 7 days**
- **If inpatient >72 Hr C. diff only**
- **Restriction of microscopic O&P to high risk patients**
  - Children < 13 years old
  - Travelers
  - New Immigrants to Canada
  - Immunocompromised

## DATA ANALYSIS

- **After testing 3776 specimens in 6 months:**

At least one pathogen detected by GPMP in 22.2%

- **Most common pathogens:**
  - C diff toxin 11.9% Noro 2.75%
  - Campy 2.7% Salm 1.37% Giardia 1.25%
  - Microscopic O&P testing reduced > 70% ←



## SUMMARY

- **Easier for patients**
- **Easier for lab staff**
- **Better for care givers**

Syndromic testing using a panel of targets significantly improved the turn around time and sensitivity for the specific etiologic agents of infectious diarrhea.

## FUTURE CONSIDERATIONS

- Report to TRC & MOH
- Applicability to other BC Laboratories
- Investigation of associated clinical outcomes
- Further research into “mixed” infections



## PROJECT TEAM

- Dr John Galbraith - Lead
- **Project Participants:**
- Dr Pamela Kibsey, Pan Sivananthan
- Lorraine Holfeld, Brian Isberg
- Molecular Diagnostics Laboratories Staff
- Luminex



# Questions ?

