

Luminex VERIGENE[®] EP: A Pediatric Experience

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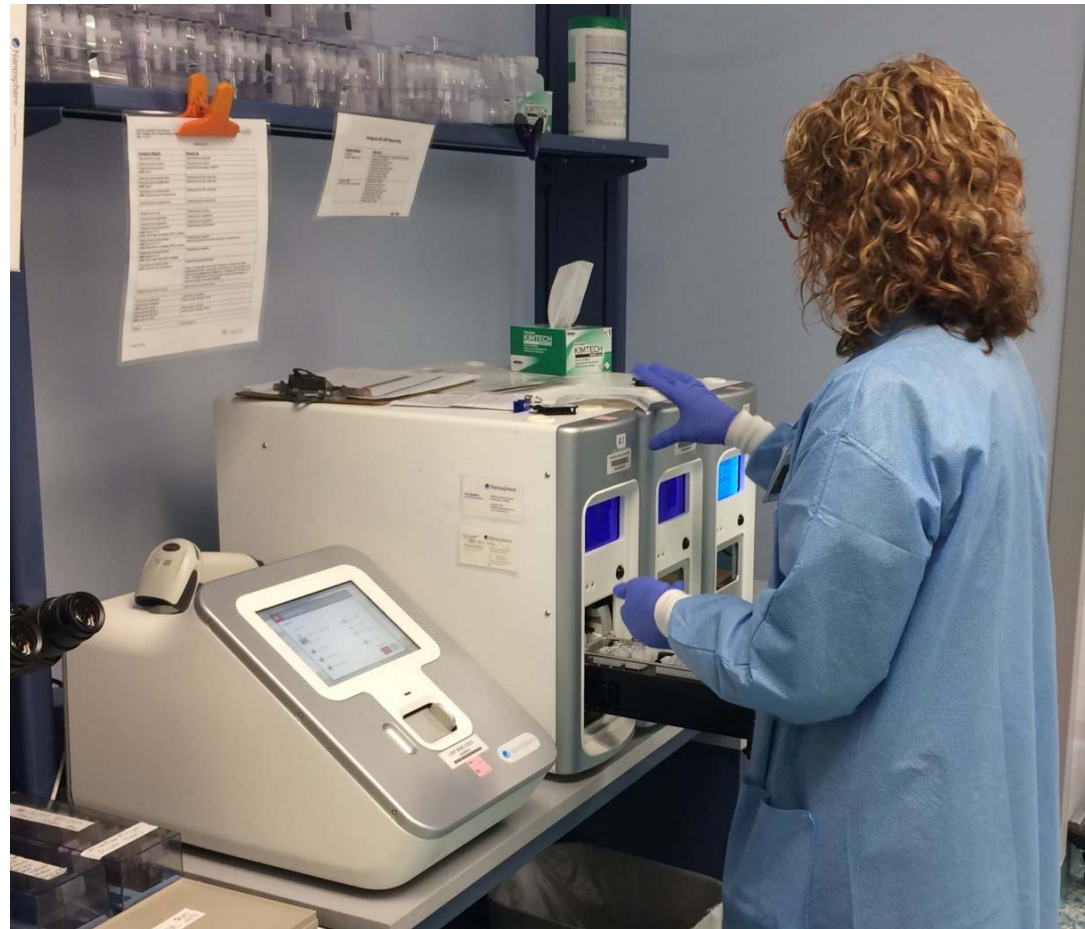
Cook Children's Medical Center



400 bed pediatric hospital in Fort Worth, TX

VERIGENE[®] Assays at CCMC

- Gram-Positive Blood Culture Test (BC-GP)
- Gram-Negative Blood Culture Test (BC-GN)
- Enteric Pathogens Test (EP)

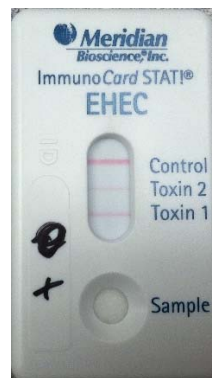
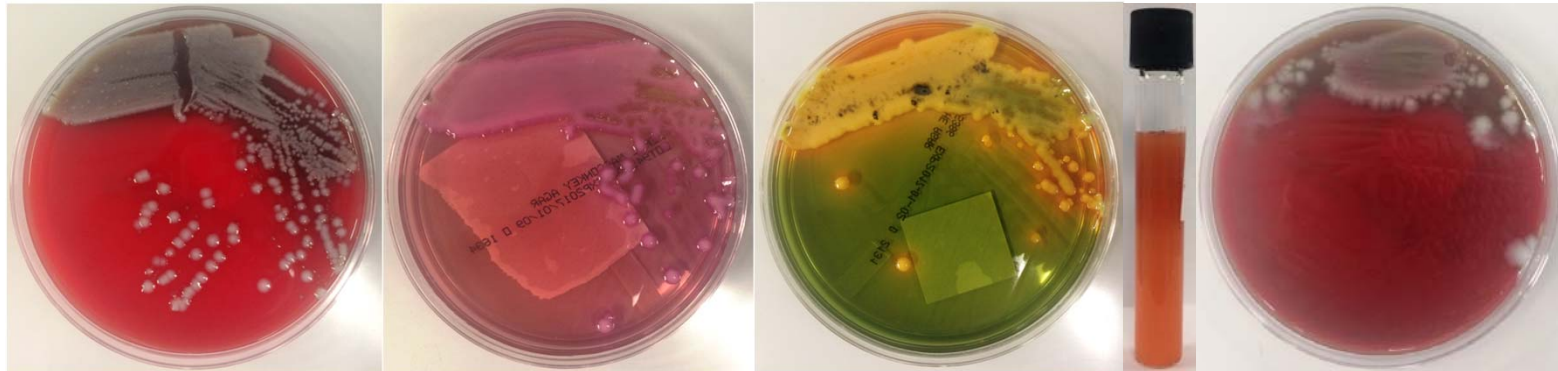


**Why multiplex molecular
stool testing?**

Why VERIGENE[®] EP?

Stool Culture

Cook Children's Microbiology Lab performed ~3,000 stool cultures annually



- Separate orders:
 - Rotavirus antigen
 - O157 antigen
 - *Yersinia* culture
 - Adenovirus 40/41 Ag (sendout)
 - *Vibrio* culture (sendout)
 - Norovirus PCR (sendout)

Advantages of Multiplex Molecular Testing

- Multiplex testing:
 - No need to perform multiple tests/assays
 - IDSA guidelines [CID 2017;66(7):e1-48] recommend testing for:
 - *Yersinia enterocolitica* in people with persistent abdominal pain, especially school-aged children
 - *Vibrio* spp. in people with large volume rice water stools, exposure to salty or brackish water, consumption of raw or undercooked shellfish, or travel to a cholera-endemic country
 - But many providers aren't familiar with the guidelines or don't ask the specific questions!
- Increased sensitivity compared to culture:
 - e.g., *Shigella* and *Campylobacter* die quickly upon passage
 - Molecular methods can detect organisms that may die in transit



Advantages of Multiplex Molecular Testing

- Faster turnaround time:
 - May prevent spread of infectious diarrhea
 - Prevents unnecessary antibiotic treatment
 - Prevents unnecessary imaging studies
 - Prevents unnecessary ordering of other tests
 - e.g., In-house *Clostridium difficile* PCR has a 45 min turnaround time
 - Physicians ordered more often than necessary because it gave a faster result
 - 2014-2015 – average of 16 tests/week → education
 - 2015-2016 – average of 12 tests/week → EP implementation
 - 2017 – average of 8 tests/week
 - 2018 – average of 9 tests/week
 - Facilitates public health surveillance efforts
 - Promotes patient/family satisfaction

But I was hesitant...

- Do the benefits outweigh the cost?
- Is molecular GI testing too sensitive?
 - Increased positivity based on the literature
 - Increased co-infections
 - Experience sending positive specimens to a colleague for validation of a non-VERIGENE platform

Comparator Assay Results

Sample	Cook Routine Result(s)
1	<i>Salmonella</i>
2	<i>Campylobacter</i>
3	<i>Salmonella</i>
4	<i>Shigella sonnei</i>
5	Rotavirus
6	<i>Aeromonas</i>
7	<i>Shigella sonnei</i>
8	<i>Campylobacter</i>
9	<i>E. coli</i> O157, Stx2
10	<i>Campylobacter</i>
11	<i>Shigella sonnei</i>
12	<i>Shigella sonnei</i>

*Confirmed positive by alternative PCR

Why VERIGENE EP?

- CCMC had VERIGENE platform in-house for blood culture assays
- Wanted an assay without *Clostridium difficile* and parasite targets
- Based on in-house evaluation, VERIGENE EP had excellent performance
 - Wish list: *Campylobacter upsaliensis*, adenovirus 40/41

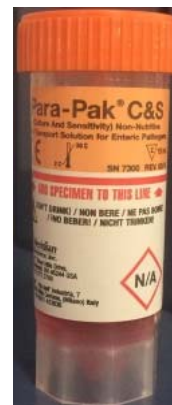
Justification

- Cost analysis:
 - VERIGENE EP costs the CCMC lab ~\$40 more than stool culture
- Justifications for increased cost:
 - Improved sensitivity/specificity
 - Faster turnaround time
 - Decrease unnecessary antibiotic usage
 - Improve antibiotic prescribing when needed (azithromycin for *Campylobacter*, amoxicillin for *Salmonella*)
 - Decrease *C. difficile* testing
 - Infection control had asked about bringing a norovirus PCR in-house
 - Patient charge would actually be less than for a stool culture
 - Patient/family satisfaction
 - Lab work distributed throughout all shifts, rather than only first shift

Implementation

Verification/Validation Results

- 106 specimens:
 - Transport media
 - 71 stools in C&S (FDA cleared)
 - 35 ESwabs (off-label use)
 - Validation samples
 - Clinical specimens
 - Spiked/contrived specimens
 - Commercial specimens
- Discordant results were tested by FilmArray[®] GPP



Verification/Validation Results

- 71 positive samples:
 - 6 – *Campylobacter*
 - 18 – *Salmonella* (11 serotypes)
 - 11 – *Shigella*
 - 6 – *Vibrio*
 - 6 – *Y. enterocolitica*
 - 8 – Shiga Toxin 1
 - 6 – Shiga Toxin 2
 - 6 – Rotavirus
 - 8 – Norovirus
- 35 negative samples



Discordant Results

EP Result	Routine Result	Result After Discordant Testing
<i>Shigella</i>	Normal Flora	<i>Shigella</i>
<i>Shigella</i>	Normal Flora	Tech rechecked culture and found a single buried green colony on HEA → <i>Shigella</i>
None Detected	<i>Shigella</i> (moderate)	<i>Shigella</i>

EP Overall Performance

- Accuracy:
 - 99.1% (105/106)
- Sensitivity:
 - 98.6% (70/71)
 - 91% for *Shigella* (10/11)
 - 100% for all other targets
- Specificity:
 - 100% (35/35)

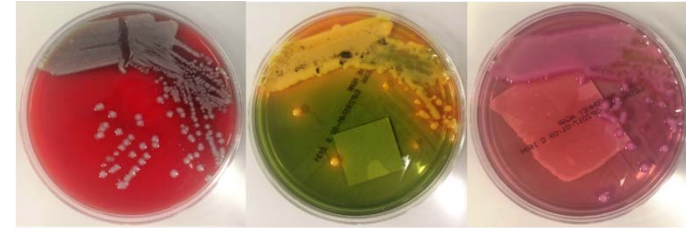


Implementation

- Go-live date: December 16th, 2016
- Positive feedback from clinicians:
 - Infection Control – excited to have norovirus PCR in-house
 - “This looks great!! I know I’m a nerd, but this gets me excited!!”
 - “This looks great!!!!!!”
 - “Wow! This is awesome!”
 - “Thanks! This is exciting.”
 - “THAT IS WAY COOL, THANKS”
 - “Great!”
- 1st shift techs like having additional time to tend to other cultures/tasks



Implementation



- Reflex “mini” stool culture if *Salmonella* or *Shigella* is detected by EP:
 - Isolate organism for susceptibility testing
- “Mini” stool culture is still available, but is not orderable in the EMR:
 - In case provider is concerned about *Aeromonas* or *Plesiomonas*
- *E. coli* O157 culture is still available:
 - Working on O157/shiga toxin education with clinicians
- Discontinued:
 - Rotavirus and O157 EIAs
 - *Yersinia* culture and *Vibrio* culture (sendout)
 - Norovirus PCR (sendout)

Clinical Impact

Cook Children's Results

- Specimens tested (through May 12, 2018): 5,558
 - Detected: 1,683 (30.3%)
 - Not Detected: 3,875 (69.7%)

Target	# Positive
<i>Campylobacter</i> Group	128
<i>Salmonella</i> species	190
<i>Shigella</i> species	61
<i>Vibrio</i> Group	1
<i>Yersinia enterocolitica</i>	8
Shiga Toxin 1	56
Shiga Toxin 2	46
Norovirus	895
Rotavirus	371

Case

- 11 year old female with a history of elevated A1C and insulin, otherwise healthy
- Presented in winter to PCP with 4 days of headache and 3 days of fever:
 - 2 days 37.9°C/100.3°F
 - 1 day 39.4°C/103°F
- Flu and strep testing were negative:
 - Diagnosed with viral illness

Case

- 3 days later, presented to Emergency Department with complaints of:
 - Headache, fever
 - Cough, congestion, and sore throat
- Denied nausea/vomiting/diarrhea
- Returned from Pakistan 1 week prior to onset of symptoms

Case – Lab Results

Test	Result
AST	85 (15-40)
ALT	69 (27-42)
CRP	4.8 (0-1)
Rapid flu A/B	Negative
<i>Brucella</i> Ab	Negative
<i>Rickettsia</i> and Typhus Ab	Negative
Malaria smear	Negative
Urine culture	Mixed flora
Blood culture	Pending

Case

- Infectious Diseases physician was concerned for typhoid fever and ordered an Enteric Panel:
 - Positive for *Salmonella*
- 3 days later, blood culture was positive for *Salmonella*:
 - Sent to TX State Lab for serotyping → *Salmonella* Paratyphi

Case

- Feedback from ED physician:
 - “I was totally confounded by what was causing her prolonged fever until the *Salmonella* showed up.”
- 8.5% of Gram-negative bacteremias at Cook Children’s are *Salmonella*:
 - EP allows earlier diagnosis

Why do we care about faster, more sensitive testing if most stool pathogens aren't treated?

Benefits of EP

- Allows for faster treatment when indicated:
 - *Campylobacter* – all pediatric patients
 - *Salmonella* – patients ≤ 3 months of age
 - Immunocompromised patients
 - Ill-appearing patients
- Even if not treating, provides a diagnosis:
 - Some children return with bacteremia or sepsis → already have diagnosis
 - Prevents unnecessary antibiotic treatment
 - Improved awareness of hand hygiene

Benefits of EP

- “We use the viral data to educate/allay fears of something more serious. We try to minimize antibiotic treatment in general, but having good info makes it much easier not to do so and I think limits families pursuing other providers that have a lower threshold to treat with antibiotics. It is a great test and it is changing the way we practice for the better.”

– Medical Director, Emergency Department

Questions?

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