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The Patient Centered Microbiology Laboratory:

Improving Quality while Reducing Cost for the Diagnosis of Gastrointestinal Infection


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Intermountain Primary Children's Hospital
The Child First and Always®

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ABSTRACT:

- **BACKGROUND:** Diarrheal diseases are a leading cause of morbidity and mortality in children worldwide and are a significant health burden for children from the United States. In the Intermountain Healthcare system, we follow the process improvement concepts of Edwards Deming and Brent James to improve clinical, service and financial outcomes. In this study we evaluated performance, turn-around time (TAT) and costs for the diagnosis of gastrointestinal infection, comparing traditional methods to a new multiplex molecular diagnostic.
- **METHODS:** The traditional methods used in this study included are found in Table 1. Evaluation of individual stool samples by traditional methods was performed as ordered by the treating physician and often involved a combination of test strategies.
- Traditional methods were compared to the FilmArray (FA) multiplex PCR platform GI panel (BioFire Diagnostics, Inc.). The FA GI panel simultaneously detects 23 of the most common bacterial, viral and protozoan diarrheal pathogens. Traditional testing was performed at Primary Children's Hospital over 2 years (2010-2012). Archived specimens were run the on the FA GI panel. We compared results, TAT and costs for traditional vs. FA testing.
- **RESULTS:** 1281 stool samples were evaluated. Gastrointestinal (GI) pathogens were identified in 51% tested by FA and 22% by standard clinical methods with 88% positive agreement and 98% negative agreement.
- Based on ordered traditional stool culture (STCX), random specimens were selected for evaluation of average cost and TAT. 68% of STCX ordered had 3 or more additional tests ordered. The average cost was $98.08 and the average TAT was 73 hours. Individual cost and TAT for traditional methods are shown in Table 2.
- **CONCLUSIONS:** FA GI panel detected more pathogens than standard clinical methods. With the knowledge that traditionally 2-3 tests were ordered, comparative costs of the two methods were similar. More rapid identification of pathogens causing gastrointestinal infection is expected to help with prompt initiation of targeted therapy and infection control measures. Further studies to evaluate true cost–effectiveness of this method are warranted when it receives FDA approval.

Table 1

Method				Tests			
Bacterial culture	Campylobacter	Aeromonas	Plesiomonas	Salmonella	Shigella	EC 0157	Yersinia
Antigen detection	STEC	Adenovirus 40/41	Rotavirus	Giardia/Crypto			
Microscopic	Ova and Parasite						
Viral culture	Enterovirus						

Table 2

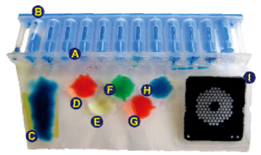
Standard Clinical Test	Cost	TAT
Stool Culture	$ 25.24	48-72 hours
EHEC	$ 37.40	24 hours
Adenovirus 40/41	$ 31.84	24 hours
Clostridium difficile	$ 29.67	4 hours
Rotavirus	$ 28.38	0.25 hours
Giardia/Cryptosporidium	$ 23.54	24 hours
Ova and Parasite	$ 72.94	24 hours
Yersinia	$ 4.34	48 hours
Enterovirus culture	$226.62	120 hours

INTRODUCTION:

The FilmArray (FA) multiplex PCR platform (BioFire Diagnostics, Inc.) utilizes a pouch system that tests for multiple pathogens simultaneously. Figures 1 and 2 show the instrument and the pouch.

Figure 1

Figure 2



A. Fitment with freeze-dried reagents
B. Plungers – deliver reagents to blisters
C. Sample lysis and bead collection
D. Wash station
E. Magnetic bead collection blister
F. Elution station
G. Multiplex outer PCR blister
H. Dilution blister
I. Inner nested PCR array

PERFORMANCE EVALUATION:

- The Film Array GI Panel detected more pathogens than were found in the same samples run by standard laboratory methods.
- Multiple pathogens per specimen were found more often in Film Array testing than in standard laboratory testing as well.
- Table 3 and Figure 3 show pathogen testing methods for standard laboratory procedure as well as well as the pathogens detected by the FA GI panel, respectively.

Table 3

Pathogen	Primary Methods
Adenovirus F40/41	Enzyme Immunoassay
C. difficile	illumigene
STEC	Enzyme Immunoassay
E.coli 0157	MACS, SBA, Latex Agglutination
G. lamblia	Direct Fluorescent Antibody
Cryptosporidium	Direct Fluorescent Antibody
Entamoeba	Ova and Parasite, microscopic evaluation
Rotavirus A	Immunoassay, antigen
Aeromonas	SBA, Gram stain, TSA slant, oxidase, APIE, Vitek2
Campylobacter	CVA, Gram stain, oxidase, catalase
Salmonella	Hektoin, MAC, Selinite F, TSI, Urea, SIM, Colour latex, Vitek2
Shigella	Hektoin, MAC, Selinite F, TSI, Urea, SIM, Colour latex, Vitek2
Yersinia	CIN agar, Gram stain, SBA, oxidase, Vitek2

Figure 3

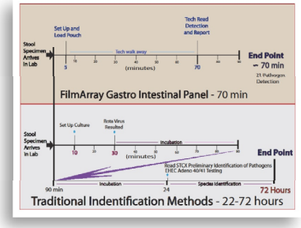
EVALUATED TAT:

Table 4 shows the average TAT for stool cultures performed by standard laboratory methods and Figure 4 is a comparative timeline showing the difference in TAT between the two methods from setup to result.

Table 4

Pathogen Test	# of specimens tested in study	Tech Time per identification in minutes	Turn-around Time	Comments
Adenovirus F40/41	164	30 minutes	24 hours	Batched once a day
C. difficile	969	15 minutes	4 hours	Run on the even hours 24/7
STEC	543	35 minutes	24 hours	Batched once a day
E. coli 0157	556	10 minutes	24-48 hours	Stool cultures are read once a day
G.lamblia/ Cryptosporidium	304	25 minutes	24 hours	Batched once a day
Entamoeba	63	1 hour	24 hours	Batched once a day
Rotavirus A	235	15 minutes	35 minutes	as the come into the lab
Aeromonas	556	30 minutes	48 hours	Vitek2
Campylobacter	556	45 minutes	up to 72 hours	
Salmonella	556	90 minutes	up to 96 hours	biochemical, latex, Vitek2
Shigella	556	90 minutes	up to 96 hours	biochemical, latex, Vitek2
Yersinia	49	25 minutes	up to 72 hours	sub, Vitek2

Figure 4



EVALUATED COSTS:

- The average cost for identification per isolate by standard laboratory methods can be reviewed in Table 5.
- The cost of the FA GI Panel (cost of pouch is based on cost of FDA approved respiratory and blood culture pouches) per sample was estimated to be $115.00 with only 10 minutes of hands-on technologist time for setup and reporting results.

Table 5

Pathogen	Cost of reagents Consumed (Cost per reagent)	Cost per Isolate	Tech Time per identification in minutes	Tech test time X national wage*	Total cost of test per Isolate
Adenovirus F40/41	$31.84 EIA	$31.84	30 minutes	$23.00	$54.84
C. difficile	$29.67 illumigene	$29.67	15 minutes	$11.50	$41.17
STEC	$37.40 EIA	$37.40	35 minutes	$26.83	$64.23
E. coli 0157	$25.24 Stool culture $ 1.54 Latex	$26.78	10 minutes	$7.67	$34.45
G.lamblia/ Cryptosporidium	$23.54 DFA	$23.54	25 minutes	$19.17	$42.71
Entamoeba	$72.94 O & P	$72.94	1 hour	$46.00	$118.94
Rotavirus A	$28.38 ImmunoAntigen	$28.38	15 minutes	$11.50	$39.88
Aeromonas	$25.24 Stool culture $ 4.80 Vitek2	$30.04	30 minutes	$23.00	$53.04
Campylobacter	$25.24 Stool culture	$25.24	45 minutes	$34.50	$59.74
Salmonella	$25.24 Stool culture, $5.93 Latex, $4.80 Vitek2	$35.97	90 minutes	$69.00	$104.97
Shigella	$25.24 Stool culture, $5.93 Latex, $ 4.80 Vitek2	$35.97	90 minutes	$69.00	$104.97
Yersinia	$ 4.34 Yersinia, $ 4.80 Vitek2	$9.14	25 minutes	$19.17	$28.31

* U.S. Bureau of Labor Statistics and MLO annual salary survey

CONCLUSION

- More pathogens and more multiple pathogens per specimen were detected by the FA GI panel than by standard laboratory methods.
- 70 minute TAT for testing of 21 common stool pathogens.
- Cost of the average of three tests ordered by standard laboratory methods per specimen was comparable to running the FA GI Panel that can detect 21 pathogens.
- Further studies to evaluate the true cost-effectiveness of the FA GI method are warranted when it receives FDA approval.

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