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Abstract

Background: Broad-range amplification and sequencing of conserved housekeeping genes provides a culture-independent method to detect infectious pathogens in clinical specimens. The Emerging Infections Network (EIN) surveyed ID physicians to assess use of this novel technology.

Methods: 1572 EIN members were surveyed in 03/13. Respondents who reported having performed broad-range PCR were asked about frequencies of submitted specimen types, positive results and their clinical usefulness.

Results: Of the 700 (44.5%) respondents to the survey, 297 (42%) had used broad-range PCR. The most common reason for not using these tests was lack of availability (76%), followed by a lack of knowledge about the test (28%). 201 respondents answered questions about their use of broad-range PCR. 60/201 (30%) had used it more than 10 times; the majority (50%) had used it 1-5 times. The most commonly submitted specimens were osteoarticular, CSF, and endovascular samples, including blood, each submitted by more than 50% of respondents. Most specimens were submitted in the setting of inflammation on histopathology with negative pathogen stains and culture. A majority of respondents (65%) could submit specimens with no laboratory utilization review. Most respondents reported only rare (36%) to occasional (38%) positive results. 89% of respondents who had used broad-range PCR more than 10 times and 80% of respondents who used it less than 10 times reported test results to be helpful (not significant). Contaminant results were reported by similar proportions of respondents regardless of how frequently the test was ordered.

Conclusions: Increasing the use of broad-range PCR for diagnosis of suspected infections will depend on increased availability and awareness of the test as well as increased specificity and decreased frequency of contamination. Positive results need to be interpreted with caution due to risk of contamination. Studies that help physicians correlate test results with clinical decision-making and treatment strategies can help develop guidelines for use of this test.

Background

- Molecular diagnosis has an increasing role in the diagnosis of many infectious diseases. Broad-range amplification and sequencing of conserved housekeeping genes provides a culture-independent method to detect infectious pathogens in clinical specimens.
- Increasing reports in the literature regarding use of broad-range PCR suggest that use of this test is increasing; however, there are few prospective studies on the utilization and impact of this test.

Objectives

To assess how infectious disease experts use broad-range PCR including:

- Frequency of utilization
- Frequencies of submitted specimen types
- Positive results and their clinical usefulness

Methods

- Respondents who reported having performed broad-range PCR in a web-based survey were asked to fill out a sub-survey
- The link to both surveys was sent electronically with 2 weekly reminders to non-responders from February 28 to April 4, 2013
- The sub-survey was developed by the University of Iowa in collaboration with the University of Utah and Emerging Infections Network (EIN) staff

Conclusions

- Availability, cost and awareness of broad-range PCR is limited.
- There is no consensus on the appropriate setting in which to use this test.
- Increased specificity and decreased frequency of contamination might lead to more frequent use of broad-range PCR.
- Studies that help physicians correlate test results with clinical decision-making and treatment strategies could help develop guidelines for use of this test.

Results

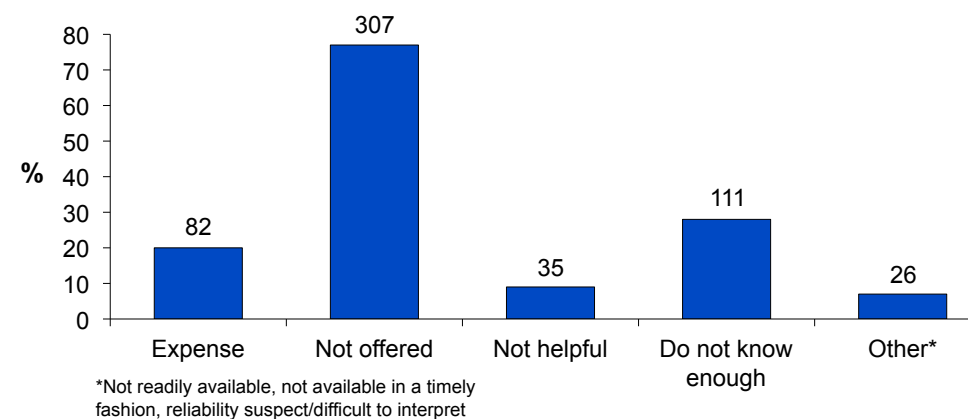
EIN members: 1572

Respondents to survey: 700

Never used broad-range PCR: 306

Respondents to the sub-survey: 201

Figure 1. Reasons for not using broad-range PCR (%)



Respondents more likely to use broad-range PCR varied significantly by:

- Region (p<0.0001)**
West North Central Region vs MidAtlantic Region (72% vs 31%)
- Experience (p=0.0009)**
< 5 years vs > 25 years (62% vs 39%)
- Employment (p<0.0001)**
State/local government or university medical school (67 and 62%, respectively) vs federal government and military (33 and 20%, respectively)
- Type of hospital (p=0.0002)**
University hospital vs city/county hospital, community hospital or VAMC/military hospital (61% vs 62%)
- Hospital size (p=0.0393)**
Institutions > 600 beds vs 200 beds (59% vs 40%)

Settings in which broad-range PCR were used

Setting	Count	Percentage (%)
Stains, cultures, and inflammation on histopathology negative	24	12%
Stains and culture negative, inflammation on histopathology positive	169	87%
Stains or pathology positive for organisms, culture negative	100	51%

Policy of the institution on when to submit specimen

Policy	Count	Percentage (%)
None	65	65%
Only after cultures are finalized	2	2%
Only if stains positive, cultures negative	3	3%
With approval of lab director	25	25%
Other	6	6%

Table 1. Specimen types submitted

Specimen Type	Never	1-10 times	>10 times
Osteoarticular tissue / fluid	88 (44%)	103 (52%)	10 (5%)
Cerebrospinal fluid	85 (42%)	99 (49%)	17 (8%)
Endovascular tissue / fluid	94 (47%)	97 (48%)	10 (5%)
Skin / soft tissue	143 (71%)	53 (26%)	5 (3%)
Other*	137 (74%)	38 (20%)	11 (6%)

*Respiratory/pleural/BAL/lung (by 19), brain abscess/tissue (by 6), cardiac heart valve/vegetation (by 7), deep biopsy/surgical specimen (by 7)

Table 2. Frequency of results

Result Type	Never	1-10 times	>10 times
Any positive result	25 (13%)	144 (74%)	25 (13%)
Possible contaminant	66 (37%)	103 (57%)	10 (6%)

Table 3. Effect of results in clinical application

Application	Never	1-10 times	>10 times
Negative results aid to stop antimicrobials	28 (15%)	131 (69%)	29 (16%)
Helpful in clinical decision making	6 (3%)	121 (65%)	61 (32%)

Most frequently positive and clinically helpful test result

