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Clinical Benefits of Rapid Pathogen Testing with PCR/ESI-MS

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Dr. Mark Wilks, Clinical Scientist, Microbiology at Barts Health NHS Trust in London, UK, talks abouttheir experiences of using PCR/ESI-MS technology over a period of 18 months. During its use for the RADICALstudy, the department also ran clinical samples ofinterest through the technology.

Which patient groups could potentially benefit from the PCR/ESI-MS technology?

There are a number of distinct clinical groups for which this technology promises to be quite rewarding, including patients with severe sepsis, pneumonia and compromised immune systems. Patients can be immunocompromised because they have recently had a transplant, or they could be haematology oncology or HIV patients. All the immunocompromised groups tend to be infected with unusual bacteria and fungi, which you might not normally look for. In addition ordinary bacteria, which do not harm immunocompetent people, can have serious consequences in this group.

How would you summarise your experience with this technology?

In general it's been quite an exciting process and one which has caused a lot of interest in microbiology and in different clinical departments in the hospital. In some cases it has been quite difficult to interpret the results, because there has been no technology like this before, so we have no framework with which to base our understanding of the results. It is a steep learning curve. Occasionally we have been baffled by an unexpected organism, one that is quite hard to culture in the laboratory usually.

How does this technology differ to conventional testing and what are its advantages?

There are a number of ways in which it differs from conventional microbiology testing. First is the speed of testing. We are used to a kind of 'gardening' approach, where nothing much happens for a minimum of 18 hours or perhaps 2 or 3 days, whereas with PCR/ESI-MS technology results are available in 6 hours. Another difference is that a lot of bacteria and especially fungi are very difficult to grow and are very slow growing. So with PCR/ESI-MS technology we are getting a lot more positives coming through. With this technology you do not need to try and think of the name of an organism and try to grow it. You rely on the fact that this technology has a very broad coverage and therefore does the thinking for you. You just look for any infectious agent.

How would you recommend using this technology to rule in or rule out infections?

At the moment it is too early to give clear guidance. Obviously if you put the sample through and you get a positive result then it's up to you to decide whether to act on it or not, as with any other test. That is relatively easy compared to ruling out infections where you are relying on the high negative predictive value of the technology to rule out infections. This requires a lot of confidence and experience for people to act on that result and therefore to stop treating and maybe stop looking for further agents.

Why is the high negative predictive value so important in ruling out infections in patients?

The main hope is that we'll have enough confidence in the results to rule out infection. For example, a lot of patients in ICU, who were thought to be septic, actually don't have any infection at all. They might have SIRS, but that could be nothing to do with infection - it could be due to surgery, trauma or another reason. But obviously the possibility of infection has to be considered and treatment may well be started. And there may be no underlying infection at all. What we hope is that our experience so far with ruling out infection will be maintained, and that we will have increasing confidence to act on the results and not to narrow antibiotic treatment or stop antibiotic treatment. In patient groups such as haematology oncology patients there is a huge amount of prophylactic anti-fungal treatment, despite the fact that clinicians don't really have any evidence of the patient having a fungal infection. However, the consequences of not treating an invasive fungal infection are so serious that they dare not take the risk. This has implications for costs as well, if they can rule out having to treat these patients. Barts and London NHS Trust, for example, spends up to two million pounds per year on antifungal treatment, much of which is almost certainly unnecessary.

Another patient group where this high negative predictive value is important is preterm babies, who are admitted to neonatal intensive care units with possible sepsis. Often they are given five days or more antibiotic treatment. The consequences of unnecessary antibiotic treatment are extremely serious. It is not just the question of unnecessary treatments and encouraging antibiotic resistance. It can double their chances of getting necrotising enterocolitis and late-onset sepsis and death.

Direct detection of *Mycobacterium tuberculosis*

1 year old boy with possible septic arthritis in one elbow, but all testing for bacteria and viruses was negative. We tested a specimen of his synovial fluid with PCR/ESI-MS technology, and to our complete astonishment we detected Mycobacterium tuberculosis. To make matters more confusing, in the same group of three or four specimens Mycobacterium tuberculosis was also detected directly from blood in a 67-year-old male patient in ICU. I was frankly skeptical about the results, thinking that at least one was a contaminant and maybe both were artifacts of some kind! And we repeated the tests several times after cleaning everything with bleach always with the same result. In fact both cases turned out to be genuine. Although the boy had no family history of TB or travel history, he did have an Il12/Tnfα imbalance. There was no question of treating him as the test was not CE marked at the time, but over a month later we grew Mycobacterium tuberculosis from his elbow and typing showed that it was in fact Bacillus Calmette–Guérin (BCG) and treatment was started. The 67-year-old male patient on ICU turned out to be a multi-drug resistant tuberculosis patient, which was not known to the admitting physicians.

36-year-old male builder, PMH of lymphoma. Admitted septic, meningitic (first CT scan brain reported normal), one eye was "bulging" and there were cavities on chest x-ray. Repeat CT Head scan showed possible intracerebral lesions. All conventional microbiology and virology were negative. There was a debate about this being a possible fungal infection or TB meningitis; in fact he was put on quadruple therapy for TB vancomycin, tazocin and ambisome. PCR/ESI-MS of his BAL detected Consiella and several other anaerobic bacteria which are hard to grow. The addition of metronidazole to cover anaerobes led to a rapid improvement and prob-ably saved his life. The patient's poor dentition then fitted in with aspiration pneumonia and anaerobic cerebral abscesses, but without the hint we may never have treated the patient in time.

DISCLOSURE:
"Point-of-View" articles are part of the ICU Management Corporate Engagement Programme.

See Also: Rapid Pathogen Testing With PCR/ESI-MS

See Also: Rapid Pathogen Testing With PCR/ESI-MS In Practice

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