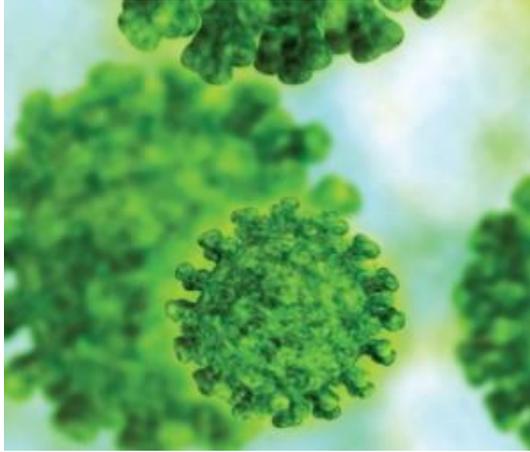


## Unmasking infectious diseases: The role of multiplex assays for the detection of co-infections



*By: Dr Martin Crockard, Randox Laboratories Ltd, Crumlin, Co. Antrim, UK*

As Public Health authorities around the world strive to contain the 2014 Ebola epidemic; the largest of its kind in history; concern over the spread of infectious diseases is at the forefront of the public psyche. The re-emergence of Ebola, a highly contagious disease, has triggered public alarm on a global scale, despite the limited geographical spread of infection. As such, there is a renewed call from health experts around the world for vigilance against the more common infectious diseases that continually circulate within communities.

Within Middle Eastern populations, emerging respiratory tract infections (RTIs) are of particular concern, largely due to the annual Hajj pilgrimage where RTIs, such as community-acquired pneumonia (CAP), increase in incidence each year and not only continue to be the leading cause of hospital- and Intensive Care Unit (ICU) admissions, but are a major cause of severe sepsis and septic shock in ICUs each year.

Sexually transmitted infections (STIs) are also of increasing concern in the Middle East, with the World Health Organization estimating that there were 26 million new cases of curable sexually transmitted infections in the Eastern Mediterranean region in 2008.

Detection of any infectious disease and prompt therapeutic intervention is vital to ensure optimal patient outcomes and to assist in controlling the spread of infection in the community. However, often a clinical diagnosis of infection using single pathogen test methods, particularly where syndromic symptoms are indicated, is insufficient evidence for diagnosis, and subsequent administration of therapeutic treatment regimes.

Infectious diseases by their very nature are complex and are often multifaceted. Primary infections can lead to further development of infections, and the presence of secondary and asymptomatic co-infections can remain undetected as they are masked behind the symptoms of the dominant primary infection. These 'silent' infections prolong a patient's exposure to the pathogens and impede the efficacy of the treatment regime, affecting their recovery; therefore diagnosis of all pathogens present is paramount for optimal treatment outcomes.

## WHAT LIES BENEATH – UNCOVERING CO-INFECTIONS

A June 2014 paper by Memish et al studied the aetiology of severe community-acquired pneumonia (CAP) during the 2013 Hajj, and highlighted the considerable presence of co-infections in pilgrims diagnosed with severe CAP and admitted to a healthcare facility; 68.4% of patients had confirmed co-infections, and 80.7% of patients were found to harbour more than one respiratory pathogen.

The most common respiratory virus was human rhinovirus, detected in 57.7% of the positive samples, followed by influenza A virus (23.1%) and human coronaviruses (19.2%). *Haemophilus influenzae* and *Streptococcus pneumoniae* were the predominant bacteria, detected in 57.7% and 53.8%, respectively, of the positive samples, followed by *Moraxella catarrhalis* (36.4%).

Both bacterial and viral infections were present in 65.3% of patients, demonstrating the complexity of respiratory infections and emphasising the need for broader investigation to accurately detect all pathogens present to better measure and manage infection.

Within respiratory tract infections particularly, detection of the infective causal agent, as well as associated secondary or asymptomatic co-infections, is crucial for ensuring correct diagnosis and, subsequently, appropriate therapeutic intervention. Therapeutic treatment administered to patients will be dictated by the presence of either, or both, bacterial and viral infections, therefore accurate detection of pathogens is paramount in ensuring the correct administration of antibiotics or, conversely, the exclusion of such treatment, which are often the 'go-to' option for cases diagnosed clinically. Molecular testing permits the detection of bacterial and viral infections in a timely manner, providing a comprehensive insight into the workings of the disease acquired to assist in predicting and managing the course of the disease.

Similarly, a recent study investigating the prevalence of STIs amongst patients with confirmed herpes simplex virus (HSV) at the King Abdulaziz University Hospital in Jeddah, Saudi Arabia, found that of the 343 HSV-positive patients enrolled in the study, co-infection with HIV was present in 45 patients (13.1%). Gonorrhoea and chlamydia were the next most prevalent infections, with 44 cases (12.8%) and 43 cases (12.5%) respectively. From this small cohort, a wealth of sexually transmitted infections was found to co-exist with primary HSV infection and the authors concluded that full screening of larger populations is likely to yield much higher results again.

The prevalence of co-infections remains underestimated, particularly amongst certain population groups. Cultural nuances, such as low awareness of STIs particularly amongst young females, the lack of comprehensive STI screening and reporting of infection, as well as the reluctance of patients to report symptoms and the unwillingness of healthcare practitioners to take a full sexual history, contribute to the growing spread of STIs in the Middle Eastern region. Ideally, when a patient presents with a potential STI, a comprehensive screen of a range of pathogens using molecular approaches should be conducted to ensure all infections are detected rapidly at first presentation and treated accordingly to help eliminate this escalating problem.

## MEASURE IT, MANAGE IT – MULTIPLEX ASSAYS FOR COMPLETE DIAGNOSES

Molecular laboratory testing is the key to identifying both causal infection and co-infections. Highly sensitive and specific molecular assays provide substantial benefits not only to the molecular laboratory performing the test, but also to health authorities conducting surveillance, and of course to the patient and wider public.

Utilising multiplex molecular assays to detect current and emerging infectious diseases will not only provide substantial time and cost savings to the laboratories and ease the burden on the payer, but in

a surveillance setting, furthers understanding of how pathogens are adapting, spreading and reacting to current treatment.

Through molecular testing, accurate diagnoses and recording of all infections present will assist in surveillance of infection, thus enabling Public Health authorities to accurately monitor what viruses are circulating in the community and adjust Public Health policy accordingly. Improved infection control measures based on response to circulating pathogens can also be relied upon to identify agents and track outbreaks. As seen with the current Ebola epidemic, the identification of existing infectious diseases, as well as new pathogens, through molecular testing and tracking of the development of resistant infections is paramount to protect Public Health.

Patients are diagnosed more accurately and rapidly, with appropriate therapeutics administered in a timely manner for optimal treatment of infection. For both the patient and the wider public, the appropriate use of antibiotics will help curb the current problem of antimicrobial resistance that is particularly prevalent in cases of RTIs and STIs.

#### FIRING BLANKS – THE DEATH OF THE MAGIC BULLET

Appropriate prescribing of antibiotic treatment is a topic that has received much attention in recent years, and continues to permeate the mind-set of both patient and prescriber alike. Historically, antibiotics have been hailed as the panacea to curing many infectious diseases, however our overuse of these 'magic bullets' has brought us to the current situation we now face, where many common and treatable infectious diseases, such as *Neisseria gonorrhoea*, *Staphylococcus aureus* and *Streptococcus pneumoniae* have acquired resistance to treatment.

Antimicrobial resistance is caused by the unrestricted access to antimicrobials, overuse and poor quality of antibiotics, as well as natural genetic mutations within disease organisms. It has been speculated that in the Middle East region, resistance rates are partially above 50% and the burden in the community is high, approximately 10% in the region.

Overuse of antibiotics is of both clinical and economic importance. In a nationwide study in Kuwait in 2010, 50% of patients with upper respiratory tract infections were prescribed antibiotics, despite the use of antibiotics being indicated in only eight patients. Additionally, in many Middle Eastern countries, antibiotics can easily be obtained over the counter as a study in Riyadh, Saudi Arabia, found; in 78% of pharmacies antibiotics could readily be obtained without a prescription.

Responsible prescribing of antibiotics and a concerted effort to reduce unnecessary use is a crucial step in combating antimicrobial resistance from the front line.

#### CONCLUSION

Adopting routine use of molecular assays to test for infectious pathogens at first presentation is a protective strategy to ensure appropriate treatment and control of infection in the community. In particular, multiplex diagnostic assays that simultaneously test for a wide range of infections are widely being considered the optimal method for diagnosis and management of disease. Not only will the test results improve patient outcomes, but it will contribute to our understanding of the epidemiology of infection and empower us with a wealth of new information on resistance, geographical distribution, and risk groups to help better arm us against the threat of infectious diseases, both old and new.

#### REFERENCES

References available on request ([magazine@informa.com](mailto:magazine@informa.com))