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Bacterial co-infections in COVID-19:

Why molecular diagnostics are more important than ever for early diagnosis, informed antibiotic therapy, infection control and antibiotic resistance surveillance

(1) Early diagnosis of secondary bacterial infections limits adverse COVID-19 outcomes by timely informing appropriate antibiotic treatment

Early evidence shows that secondary bacterial infections are a major risk factor for adverse COVID-19 outcomes. A recent retrospective study from China published in the Lancet found that 27 out of 28 patients with secondary bacterial infections died (96%). Half of non-survivors experienced a secondary infection (27 out of 54); ventilator-associated pneumonia occurred in 10 of 32 patients (31%) requiring invasive mechanical ventilation (Zhou et al., 2020). Almost all hospitalized patients receive empirical antibiotic treatment which is known for its potential to inhibit pathogen growth in culture-based testing required for conventional in-vitro diagnostics. In this context, molecular diagnostic solutions that detect the pathogen's DNA (no growth required) are crucial to inform early adjustment of the antibiotic treatment regime for secondary bacterial infections to prevent fatal outcomes.

(2) Rapid detection of bacterial infections protects high-risk patients and limits super-spreading in healthcare facilities

Patients hospitalized with bacterial infections at the time of the 2003 SARS-CoV outbreak were found to be at high risk of being co-infected with SARS-CoV and acting as super-spreaders (defined by one patient infecting more than 10 additional persons). In Singapore, for example, 157 out of 206 (76%) SARS-CoV infections were acquired in a healthcare facility and hospitalized patients with bacterial infections were identified as potential sources of super-spreading (Wilder-Smith, Green, & Paton, 2004). To contain the current SARS-CoV-2 pandemic, it is therefore of utmost importance to effectively triage and isolate patients with bacterial infections by rapid molecular diagnostics to (a) limit adverse outcomes in high risk patients carrying bacterial infections and (b) limit further spreading of SARS-CoV-2 infections in healthcare facilities. This is especially relevant as hospital-related infections have also been widely reported for the current SARS-CoV-2 outbreak.

(3) Implementation and monitoring of appropriate infection control measures limit spreading of SARS-CoV-2 and help flattening the curve

A recent study from Hong Kong reports that nosocomial transmission of SARS-CoV-2 may be largely preventable by appropriate infection control measures based on a combined approach of active and enhanced laboratory surveillance, early airborne infection isolation, rapid molecular diagnostic testing and contact tracing for healthcare workers with unprotected exposure (Cheng et al., 2020). Similarly, effective infection control measures to contain and limit bacterial outbreaks and hospital-acquired infections (HAI) need to be maintained to reduce the risk of bacterial co-infections to an absolute minimum. Gram-negative bacteria are responsible for more than 30% of HAIs and predominate in hospital-acquired pneumonia (Peleg et al., 2010). These pathogens are highly efficient at up-regulating or acquiring mechanisms of antibiotic drug resistance, especially in the presence of antibiotic selection pressure which further aggravates the need for infection control measures, not only for controlling spreading of SARS-CoV-2 but also multi-drug resistant bacteria.

(4) Surveillance of pathogens and antibiotic resistance of secondary bacterial infections from COVID-19 patients is needed to guide therapy

It is known from influenza that patients with secondary bacterial infections are very likely to need hospital treatment. The mortality rate of these hospitalized patients is particularly high in elderly patients or patients with cardiovascular or respiratory illness, in whom pneumonia is much more frequent than in other adults (Low, 2008). *Staphylococcus aureus* is the main cause of secondary infections in influenza but *Streptococcus pneumoniae* and *Haemophilus influenzae* are also commonly found, although it is not yet known which pathogens are associated with secondary infections in COVID-19. Systematic monitoring of antibiotic prescription and treatment response in COVID-19 patients with secondary infections is expected to provide insights to better guide empiric therapy decisions mid-term, while enabling and accelerating the development of novel diagnostics that allow for rapid molecular treatment response prediction in a potential subsequent infection wave.

We at Ares Genetics, a Vienna-based digital diagnostics start-up, are fully committed to fight the COVID-19 crisis by developing the next-generation of infectious disease diagnostics by combining molecular diagnostics with artificial intelligence. Contact us if we can support you with data-driven and next-generation sequencing based solutions as well as our partners' solutions including the CE-IVD marked / FDA approved molecular diagnostic tests for ventilator associated pneumonia or detection of SARS-CoV2.

Let's take infectious disease testing to the next level. Let's fight COVID-19 together!

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