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Transcriptional Profiling to Distinguish Bacterial and Viral Respiratory Infection

More accurate tests for microbiologic diagnosis of acute respiratory infections (ARI) are needed. Acute respiratory infections occur commonly throughout life, accounting for substantial morbidity and mortality in adults, and these infections are a leading cause of antibiotic overuse. Unnecessary antibiotic use is a major driver of the increase in antimicrobial resistance, which is considered to be one of the most urgent threats to global public health. In most cases of ARI, the precise microbial etiology is unknown and antibiotics are administered empirically in illness in both inpatient and outpatient settings. Although sensitive molecular diagnostics such as polymerase chain reaction (PCR) allow clinicians to rapidly and accurately diagnose a wide variety of respiratory viruses, their impact on patient management and antibiotic prescription has been modest primarily due to concern about bacterial co-infection. Sensitive and specific diagnostic tests for bacterial lung infection are currently lacking. Clinical parameters such as fever, purulent sputum, white blood cell count and radiographic patterns do not provide sufficient precision to reliably distinguish viral from bacterial infections. Thus, "ruling out" bacterial respiratory infection is extremely difficult, resulting in a default position of prescribing antibiotics to almost all patients hospitalized with respiratory infection and many outpatients as well. This practice results in significant antibiotic overuse, with resultant adverse effects and increased antimicrobial resistance. Recently, serum biomarkers such as procalcitonin have shown some promise as a supplement to clinical judgment in assessing patients with ARI but a need for more accurate tests remains. Gene expression profiling of whole blood represents a powerful new approach for analysis of the host response during infection. Preliminary studies indicate that viruses and bacteria may trigger specific host transcriptional patterns in blood, yielding unique "bio-signatures" that may discriminate viral from bacterial causes of infection. This approach can be used to supplement pathogen detection allowing clinicians to target antibiotic use for those patients that need treatment and thereby reducing unnecessary antibiotic use and resultant antimicrobial resistance. New rapid molecular diagnostics that incorporate detection of common respiratory viruses and bacteria combined with a limited number host genes discriminatory for bacterial and viral infection will be developed. The eventual goal is to simplify testing such that point of care ARI diagnostics can be employed in hospitals, emergency rooms, clinics and physicians' offices for the maximal impact on patient care and antibiotic prescription.