The profound seasonality of infectious disease occurrence has been recognized since ancient times, but mechanisms underlying seasonality remain poorly defined. Although “environmental” factors (i.e., “miasmata”) were thought to cause epidemics until the 19th century, the perceived importance of environment in infectious disease occurrence declined with the identification of microbial pathogens. However, understanding of the seasonality of infectious diseases, and the role of environmental influences in seasonality, has become increasingly important in the context of global environmental change, emerging infectious disease, and new challenges in public health surveillance. Current epidemiological efforts to define the role of environmental exposures in infectious disease occurrence are limited by the sparse nature of public health surveillance data for certain diseases, and confounding of associations by other seasonal occurrences (e.g., population behavior patterns or co-occurrence of other infectious diseases) when aggregated exposure or outcome data are used. The case-crossover study design is a novel epidemiologic technique useful for defining causal relationships between repeated transient exposures and rare outcomes. It has proven useful in the study of environmental influences on non-infectious disease, but has not been widely used in the study of infectious diseases. We present the results of analyses in which both traditional regression methods and case-crossover design were used to study uncommon but important bacterial respiratory diseases of public health importance (legionellosis, meningococcal disease, and invasive group A streptococcal disease). We suggest that the use of a case-crossover approach provides novel, complementary insights into environmental factors in disease occurrence which are not identified using more traditional epidemiologic methods.