ANTIBIOTICS IN INFANCY AND SUBSEQUENT CHILDHOOD DISEASES

The growing specter of antimicrobial resistance threatens to vitiate the remarkable innovation and progress made in the field of antibiotic discovery and development. Such resistance reflects the versatility of bacteria in developing strategies that surmount the bacteriocidal and bacteriostatic effects of antibiotics. A major underpinning of this phenomenon is the widespread prescription of antibiotics, especially in the absence of a justified indication. In the present issue of Mayo Clinic Proceedings, Aversa et al point to another concern with antibiotic usage: the occurrence of unexpected diseases in childhood following exposure to antibiotics in infancy. Using the Rochester Epidemiology Project (REP) medical records-linkage system to identify children born between January 1, 2003, and December 31, 2011, these authors extracted data pertaining to demographic features, disease diagnostic codes, and antibiotic prescriptions in the following years until June 30, 2017. The study population comprised almost 15,000 children, with girls and boys each numbering more than 7000. In the first two years of life, 70% of children received at least one antibiotic. Girls and boys who received at least one course of antibiotics exhibited a higher incidence of asthma, rhinitis, being overweight, and attention deficit hyperactivity disorder; atopic dermatitis and celiac disease were significantly increased in girls, and obesity increased in boys. The risk for the increased occurrence of certain diseases depended on the number of prescriptions received. For example, for children receiving 1 or 2 prescriptions, girls but not boys were at an increased risk for celiac disease and asthma. With 3 or 4 prescriptions both girls and boys were at an increased risk for asthma, atopic dermatitis, and being overweight. With 5 or more prescriptions, either sex exhibited a higher risk for asthma, allergic rhinitis, obesity, and attention deficit hyperactivity disorder. The risk for subsequent disease depended not just on the number of prescriptions but also the antibiotic prescribed, with cephalosporins associated with the widest range of conditions and a relatively specific susceptibility to autism and food allergies. Children who received antibiotics, especially multiple prescriptions, were more likely to exhibit dyads or triads of diseases. The strengths of this study are multiple, including, in particular, its interrogation of a unique data base (REP) that enables long duration of follow-up, accurate determination of antibiotic prescriptions, and the accurate documentation of a range of childhood diseases (not just a single disease as is commonly available in published studies). The authors point out that these findings are associative and not causal and that limitations in interpreting their findings may stem from confounding by indication or reverse causality. Nonetheless,
these findings are not only important and timely, but they are also concerning as they point to the risk of childhood diseases that attend prior antibiotic use; these studies thus underscore the need for judicious prescribing of antibiotics in infancy. Additionally, the findings of Aversa et al set the stage for preclinical and clinical studies that can test causality. Finally, as perceptively discussed by the authors, these findings draw attention to the role of the microbiome in determining homeostasis and health. From birth onwards, the microbiome that progressively gathers in the growing infant and child exerts abundant salutary effects including those that promote immunity and the healthy development of major organs and metabolic systems. Impairing the microbiome by antibiotics, especially during such nascency, may predispose, conceivably, to subsequent childhood diseases.


AN OUNCE OF PREVENTION AND VIRAL SPREAD

In the present issue of Mayo Clinic Proceedings two articles demonstrate that adherence to recommended practices to prevent viral transmission are associated with salutary outcomes regarding the circulation of respiratory viral pathogens in a general community and the transmission of SARS-CoV-2 in a specific community. Freeman et al used the Biofire, FilmArray respiratory panel, performed on nasopharyngeal swabs, to evaluate the seasonal profile for respiratory viral pathogens detected during the months from April and July, before (2017 to 2019) and after (2020) the start of the COVID-19 pandemic. From April 2020 onwards such Centers for Disease Control and Prevention (CDC) recommendations as physical distancing, masking, and frequent handwashing were commonly followed. Freeman et al showed that during these months in 2020, as compared with the same months in the three prior years, there was a steep decline in the percentage of positive tests, with monthly test positivity decreasing from 25% to 2%. The test results in 2020 were notable from two additional perspectives: First, the decline in 2020 was observed, in particular, for rhinovirus/enterovirus, the most prevalent respiratory virus circulating in the community; and, second, there was a stark absence of double positive tests detected during these months in 2020, whereas double positive tests occurred in more than 3% of reports in prior years. These findings are complemented by those of Parkulo et al which are derived from examining SARS-CoV-2 transmission in a specific environment, that is, health care workers in a surgical environment; these health care workers were exposed to 2 coworkers who tested positive for SARS-CoV-2 towards the end of March 2020. In this surgical environment, as is true for surgical units in general, standard precautions were in place and the use of surgical masks quite prevalent. Surveillance testing was conducted of all health care workers who may have had workplace contact with these index cases. Notably, of the exposed 394 health care workers tested, only one case was positive, and on repeat testing one week later in 387 of these health care workers, no additional cases were detected. Parkulo et al conclude that the risk of spread of SARS-CoV-2 in health care environments in which personnel comply with masking and hand hygiene procedures is relatively low. In discussing how to restrain a different phenomenon from spreading — fires in the city of Philadelphia — Benjamin Franklin wrote in 1735 that “an ounce of prevention is worth a pound of cure.” This now long embraced cornerstone concept in medical practice underpins the findings of Freeman et al and Parkulo et al and emphasizes relatively simple practices and behaviors in preventing viral spread, including those pertaining to SARS-CoV-2 in the current pandemic.


COVID-19 AND SOCIAL DETERMINANTS OF DISEASE

Susceptibility to COVID-19 may be increased and outcomes from COVID-19 worsened by personal characteristics (for example, age, male sex, decreased cardiopulmonary fitness, obesity) and co-morbidities (for example, pulmonary diseases, cardiovascular diseases, diabetes, hypertension, cancer, immunosuppressed state). In the present issue of Mayo Clinic Proceedings, Ossimetha et al address whether an association exists among socioeconomic disadvantage, community mobility reduction, and outcomes from infection with SARS-CoV-2. Mobility reduction reflects social distancing, a central strategy in confronting the COVID-19 pandemic. In this study, mobility levels were obtained from Google COVID-19 Mobility Reports which provide data on the change in frequency of visits to specific places as referenced to a baseline time-frame before the onset of the COVID-19 pandemic. Places assessed in the current analysis included workplace, grocery and pharmacy, and retail and recreation, as for these places relatively complete data were obtainable by the authors. Cases of SARS-CoV-2 were determined from the database maintained by the Johns Hopkins University Center of Systems Science and Engineering. The Social Deprivation Index (SDI) was used to assess socioeconomic disadvantage. SDI is an integrated county-level index that incorporates 7 socioeconomic elements including, for example, living in overcrowded housing, unemployment rate, and poverty rate. The findings in the study by Ossimetha et al demonstrate that counties with higher SDI had increased percentages of Black and Hispanic populations; counties with greater SDI as compared with counties with lower SDI exhibited lower mobility reductions for workplace, grocery and pharmacy, and retail and recreation; and counties with a greater SDI exhibited a higher number of SARS-CoV-2 infections and deaths. Thus economically and socially disadvantaged communities are more vulnerable to SARS-CoV-2 and have worse outcomes. As underscored by Ossimetha et al, testing for SARS-CoV-2 and the tracing of contacts are especially required in these communities. Social distancing is universally recommended as another strategy, but achieving this in communities with a high SDI (and a lower mobility reduction) may be challenging for a number of reasons speculated upon by Ossimetha et al. Long before the start of the COVID-19 pandemic, abundant literature attested to the fact that the risks for assorted diseases are markedly influenced by social determinants. The current study of Ossimetha et al persuasively adds to the mounting evidence that the same is true for infection with SARS-CoV-2 and outcomes from such infection.


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