YALE JOURNAL OF BIOLOGY AND MEDICINE 90 (2017), pp.163-164.

INTRODUCTION

YJBM

Infectious Diseases

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Before accepting germ theory, scientists and physicians posited that "bad air" must be responsible for the spread of disease. Miasma theory put forth the notion that air could take on an infectious form, and that certain noxious fumes could inoculate those unfortunate enough to breathe it. With the advent of the microscope and the discovery of microorganisms, modern medicine adopted germ theory as a replacement near the end of the 19th century. This switch from miasma to germ theory drastically altered our medical philosophy of infectious disease and marked the beginning of a public health revelation. During the century that followed, we went from simply knowing the symptoms of infectious diseases to understanding the processes of infection to precise molecular detail. In this issue of the *Yale Journal of Biology and Medicine* (*YJBM*), we turn our attention towards a variety of infectious diseases—few of which are described here—and our progress towards understanding these germs.

Zika virus, among the infectious agents discussed here, rose as a major epidemic over the past two years. In their concise and informative mini-review, Hastings and Fikrig emphasize that Zika's ability to be transmitted through sexual intercourse differentiates it among similar flaviviruses like West Nile Virus and Dengue. This characteristic opposes the previously accepted dogma that flaviviruses are solely vector-borne. The virus's additional mode of transmission combined with high persistence in the genital tract and its ability to cause severe birth defects greatly adds to the threat of Zika, which currently has no FDA approved vaccine. Hastings and Fikrig describe the current laboratory methods of studying transmission of Zika and offer the field's perspective on how sexual transmission effects virulence of the disease.

Like Zika, the blindness-inducing protozoa *Acanthamoebae* possess a number of unique pathogenic features. Upon infection, which is often facilitated by contact lens use, these amoeba trigger *Acanthamoeba keratitis* on the corneal surface. In their review, Neelam and Niederkorn explain that the pathogenicity is caused by a proteolytic enzyme released from the parasite and that the bacterial flora on the ocular surface provides a niche for exacerbating this effect. Studies from Niederkorn and colleagues suggest that neutrophils and other components of the innate immune system are equipped to tackle the disease in most individuals, and this hypothesis offers an explanation to the relatively low incidence of infection.

Symbiosis between *Acanthamoebae* and cornea-residing bacteria harkens back to our September 2016 issue focusing on the microbiome. As biology will have it, the microbial environment is a crucial factor in the pathogenesis of many diseases. Although pulmonary fibrosis is not an infectious disease itself, its symptoms are intensified by infectious pathogens in the lungs. Here, Chioma and Drake present a review of the many microbial contributions to pulmonary fibrosis. They cite examples of viral, bacterial, and fungal pathogens and suggest that the use of antimicrobials may halt or slow the progression of disease. Overall, Chioma and Drake provide a conceptual demonstration of how infectious agents modify existing human diseases.

Reminiscent of our December 2016 issue on epigenetics, Turner and Margolis describe how the cell's epigenetic mechanisms can control latency of the Human

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†Abbreviations: FDA, Food and Drug Administration; HIV, Human Immunodeficiency Virus.

Keywords: Infectious diseases, Zika, *Acanthamoeba keratitis*, HIV, typhoid, Vancomycin

Immunodeficiency Virus (HIV). The latent reservoir of this pathogen in infected individuals remains as one of the greatest challenges to eradicating the disease. New therapies are focused on latency reversal methods followed by antiretroviral therapy, often referred to as the "shock-and-kill" approach. Turner and Margolis argue that the host's epigenetic landscape is a promising target for therapeutic inducing viral transcription. In addition, they review a number of important transcriptional control mechanisms that are thought to effect HIV latency, and they describe the latency reversal agents currently available.

Two additional articles presented here focus the innate ability of certain individuals to combat HIV. Gonzalo-Gil describe the characteristics of patients known as HIV+ elite controllers—patients with undetectable virus loads without antiretroviral therapy—and the molecular mechanisms behind this phenomenon. Along with this review, we present a brief communication by Pohlmyer et al. assessing the molecular features of elite controlling patients. HIV-1 mRNA levels in CD4+ T-cells, they report, were significantly lower in elite controllers compared to chronic progressors. The authors further demonstrated that upregulation of HIV-1 mRNA levels are comparable between the two groups upon T-cell activation. These results implicate ongoing viral replication as a persistent threat to well-being, even in elite controllers.

In contrast to HIV, a pathogen discovered only a few decades ago, disease outbreaks due to *Salmonella typhi* have been described for centuries. In this issue, Chong et al. offer an in-depth review of typhoid toxin, the gene responsible for life-threatening typhoid fever in humans. They describe the cellular and molecular features of the typhoid inducing components, down to crystallographic structure-level resolution. This overview draws attention to the importance of typhoid toxin for *S. typhi* biology, and encourages one to consider putative targets for antibiotics.

Finally, we highlight an insightful review on resistance to the antibiotic Vancomycin. McGuinness et al. emphasize the molecular mechanisms by which *Staphylococcus aureus* may become resistant to the widely used antibiotic Vancomycin, resulting in a highly infectious bacterial form associated with poor clinical outcomes. This resistant strain of *Staphylococcus* poses a significant threat in hospital settings, and the authors acknowledge the importance of new technologies for identifying it as a cause of infection in the clinic.

The fifteen articles in this issue cover just a few well-studied pathogens, but the implications for understanding human infection and disease are much broader. While the medical division of infectious disease comprises a range of pathogens much too extensive to be covered in one issue of *YJBM*, we have chosen a representative collection of infectious agents currently relevant in the United States. Each article, and the wealth of knowledge contained therein, reminds us of the progress made by physicians and researchers in the past century since germ theory was generally accepted. We hope this issue provides a sense of the many mechanisms pathogens use to thrive within their hosts and of the disease or molecular characteristics to be exploited for treatment.