

# Preface

From the first detailed clinical description of the disease in the Midwestern United States in 1918, to the isolation of the causative agent, the first of any influenza virus, in 1930 (Shope 1931) to its role in the genesis of the 2009 human pandemic (Garten et al. 2009), swine have played a central role in the ecology of influenza. Although not considered the major natural reservoir for influenza A viruses, that distinction belongs to aquatic waterfowl, swine are host to a limited but dynamic assortment of viruses (Webster et al. 1992). A number of subtypes of influenza A viruses of human and avian origin, including H1, H2, H3, H4, H5, H7, and H9, have been isolated from global swine populations (reviewed in Brockwell-Staats et al. 2009). Most of these isolations have, however, been limited in number and it is only H1 and H3 influenza viruses that are known to have formed stable lineages in swine. In this respect, swine influenza viruses (SIV) are similar to their counterparts in humans where H1 and H3 viruses have also been maintained. The nature of these H1 and H3 viruses differs between the two host populations, however, and, as discussed throughout this book, are even different in swine populations in different geographic regions of the world due to multiple introductions of avian and human influenza viruses.

The dynamic nature of SIV poses difficulties for the swine industry as a recurring respiratory disease, and also for public health as a source of zoonotic infection. Human infections with SIV have been recorded regularly since the introduction of more routine testing in humans. Many of these zoonotic events have occurred in instances where humans and swine are in close contact and have typically been dead-end events with little to no further spread in humans. The virologic features of SIV that limit their spread in humans are largely unknown, but the host range barrier between human and swine highlights the fact that adaptation of a virus in one mammalian host does not necessarily mean that it is well adapted to replication in another (Landolt et al. 2003). This observation is somewhat in conflict with earlier dogmas in influenza where it was suggested that mammalian passage of avian influenza viruses was a prerequisite for the emergence of human pandemics. Swine were often identified as this mammalian host due to a number of factors including the limited number of other described natural mammalian hosts and the

fact that swine appeared unique in having the receptors preferred by both human and avian influenza viruses (Ito et al. 1998). The observation that swine appeared uniquely susceptible to avian and human viruses and that avian viruses grew poorly in humans led to the postulation that these animals were the mixing vessel for human pandemic viruses; and for a number of years popular thinking, without much definitive proof, was that the 1957 and 1968 human pandemics likely arose in pigs (Scholtissek et al. 1978). Subsequent human infections with H5N1, H7, and H9N2 viruses with domestic poultry as the likely source and realizations that swine were not unique in their ability to harbor avian and human viruses shifted thinking toward poultry being as important as swine as reservoirs of viruses with pandemic potential. Indeed, the global spread of highly pathogenic H5N1 viruses focused a lot of research effort and funding toward avian hosts at the expense of solidifying activities in swine. Although surveillance and research activities of influenza in swine continued, and to some degree increased, during the first decade of the twenty-first century, these activities were dwarfed by the efforts going on in wild and domestic poultry species. The isolation of a novel influenza virus (i.e., pandemic H1N1) from a 10-year-old boy in California in April 2009 indicated that more of the influx of resources should have been funneled into further understanding the global SIV situation. The virus from the 10-year-old was obviously of SIV ancestry, but it was different enough from any other virus characterized that its direct precursors still remain a mystery. In addition, in 2012 zoonotic transmission of SIV (both H3N2 and H1N2 subtypes) containing the matrix gene from the pandemic H1N1 virus was reported. These strains appeared to be able to spread more easily from pigs to people than other influenza viruses of swine. More than 300 people from 10 states were reported to have been infected with these new strains resulting in hospitalizations and 1 death; limited human-to-human transmission was detected (Lindstrom et al. 2012). Importantly, the main risk factor for infection was exposure to pigs, mostly in the context of agricultural fair settings.

With these events firmly at center stage, it is a good opportunity to review what we know about SIV as a disease of swine and also as a continued zoonotic threat. The 15 chapters presented in this book provide contemporary reviews of research on SIV. The book begins with a general overview of influenza viruses by Stephan Pleschka discussing the virus and its replication in detail. The history of SIV in North America, Europe, and Asia is discussed by Stacey Schultz-Cherry, Christopher Olsen, and Bernard Easterday, by Roland Zell, Christoph Scholtissek, and Stephan Ludwig, and by Huachen Zhu, Richard Webby, Tommy Lam, David Smith, Malik Peiris, and Yi Guan, respectively. As indicated in these reviews, the European, North American, and Asian SIV evolution follows different pathways. Whereas descendants of classical SIV and the novel triple reassortant viruses are found in North America, avian-like swine H1N1 viruses emerged in Europe in 1979 after an avian to swine transmission and spread to all major European pig-producing countries where they circulate with H3N2 and H1N2 reassortants. Classical swine H1N1, human-origin H3N2, avian-like H1N1 and the triple reassortant viruses all co-circulate in Asian pigs. The clinicopathological features of SIV infections in pigs are described by Bruce Janke. Macroscopic and

microscopic lesions of SIV infection, after natural and experimental infection, are described. The use of accurate diagnostics assays for diagnosis and surveillance for SIV are summarized by Susan Detmer, Marie Gramer, Sagar Goyal, Montserrat Torremorell, and Jerry Torrison. Since our collective knowledge regarding the worldwide occurrence of influenza among swine is incomplete, this review focuses on basic laboratory assays needed for the detection of the virus and viral nucleic acids within clinical samples and for antiviral antibodies in serum samples.

The epidemiology of swine influenza worldwide is of exceptional importance with the potential of the pig acting as a “mixing vessel” where both avian and human influenza viruses can undergo genetic reassortment resulting in the creation of novel viruses. The reviews by Alessio Lorusso, Amy Vincent, Marie Gramer, Kelly Lager, and Janice Ciacchi-Zanella on North American, by Ian Brown on European, and by Young-Ki Choi, Philippe Noriel Pascua, and Min-Suk Song on Asian swine influenza epidemiology shed light on how this unique ability of pigs results in ever expanding new genotypes and subtypes in pigs. Vaccination is still one of the most important and effective strategies to prevent and control influenza for both the animal and human population. The review by Kristien van Reeth and Wenjun Ma discusses the current and future options to control this economically important swine disease.

The zoonotic aspects of SIV infections are reviewed by Whitney Baker and Gregory Gray. Most of these infections have been sporadic cases with a recent increase of case reports in concert with modern pig farming and the emergence of triple reassortant SIV. The advent of pandemic H1N1 and its impact on human health is discussed by Ian York and Ruben Donis, while Julia Keenlside discusses its impact on animal populations. Hadi Yassine, Chang-Won Lee, and Yehia Saif describe another important interspecies transmission event of influenza A viruses, namely the one between swine and poultry. Swine viruses are continuously isolated from poultry species, especially turkeys, and they are causing economic losses. Finally, Elena Govorkova and Jonathan McCullers cover the critical area of approved and investigational antiviral drugs.

We would like to thank the contributors for their patience during the assembly of this volume. We hope that all readers will gain insight from these contributions that will enhance their individual research and teaching activities.

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