

1. Past 50 Years of Influenza Virus Research and It's Future

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Fifty years ago influenza A, B, and C viruses had already been discovered and many of the features including hemagglutination, virus neutralization, virus replication in ferrets, mice and eggs, enzyme activity, incomplete virus (Von Magnus phenomenon), P-Q-R variation, genetics and reactivation, antigenic variation and the swine influenza lifecycle had been documented (Hoyle 1968). Fowl plague virus of chickens was soon to be recognized as an influenza virus by Shaffer (1955), and interferon was soon to be described by Issacs and Lindenmann (1957). Vaccines for influenza in humans were still rather crude and were reactogenic in children. Original Antigenic Sin had been described by Francis (1953). Antigenic drift in influenza virus explained the continuous variation in serological reactivity but the occasional major changes that occurred with the emergence of new pandemic strains like Asian/H2N2/1957 or Hong Kong/H3N2/1968 were unexplained.

In the past 50 years, influenza virus has served as a superb model system for the study of the replication, genetics, immunology and structure of segmented RNA viruses. By necessity I will focus only on a limited number of areas including Original Antigenic Sin, the ecology of influenza A viruses and their global distribution in aquatic birds, genetic drift and shift and the emergence and pathogenesis of influenza viruses in animal models. Recent studies using reverse genetics have established that the NS1 gene of

the A/Hong Kong/156/97 (H5N1) influenza virus can counteract host cell cytokine activity and that pigs infected with constructs containing this gene were severely ill.

The future is extremely exciting for influenza viruses can now really be "made to order" and the genomics of both the virus and the host are at hand. Influenza is a truly global problem and there is still a paucity of information on influenza genomics. Through continuing international collaborations this information will be obtained and we will define both the viral and host factors that permit influenza viruses to transmit between species and may then be able to predict pandemic potential. During this process we must be cognizant that influenza has continuing potential to be a man made or natural bioterrorism agent and that new strategies to control influenza are urgently needed including stockpiling of antiviral drugs.

References

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