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Abortive Pandemics of Influenza Viruses

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Introduction

The last century witnessed three pandemics of influenza worldwide, each of which was at variance from the others in etiology, epidemiology, and severity of the disease [Kumar et al., 2010a, Kumar et al., 2010b]. The HA antigens of the 1957 and 1968 pandemic influenza A viruses showed major changes from the corresponding antigens of the immediate predecessor pandemic strains of the viruses [1,2,3]. However, if we look back into the past, a number of influenza outbreaks occurred, which although posed considerable threat to the world, but did not progress to the level of a pandemic. A whole lot of attention has been gained by the massive flu outbreaks in the past, but only little has been talked about such abortive, or the so-called, pseudo-pandemics in the history of influenza. Thus, the present chapter aims to enlighten the readers over the true impact of the influenza pandemics.

1947: Extreme Intra-subtypic Antigenic Variation: (H1N1)

In late 1946, an influenza outbreak occurred among the American troops in Japan and Korea and spread to the other military bases in the United States in 1947. Initially, it was difficult to ascertain the cause of the epidemic, mainly because of the causative strain was different from the previous strains of influenza A viruses. Nevertheless, the 1947 influenza A (H1N1) virus resulted in only mild pandemic owing to the low mortality caused in spite of its global spread. However, the signs and symptoms that were presented by the 1947 influenza A virus infected young recruits strongly matched with those of the experienced patients who were earlier infected with the previous influenza virus strains [4,5].

A vaccine containing the H1N1 strain of influenza A virus was effective from 1943-1945, but failed to protect the large number of vaccinated US military personnel. Antigenic mutations were noted previously also, but they had not compromised the vaccine induced immunity to such a degree [6]. In the later years, after extensive characterization of HA and NA antigens of the 1943 and 1947 viruses, conspicuous variations were found in the amino acid sequences. Murine model investigations also suggested that the 1943 vaccine provided no protection against the 1947 influenza virus [6]. Successive bacterial cultures during the Fort Monmouth epidemic, documented the long suspected association of influenza virus infection to group A streptococcal carriage and disease [5].

1957: Asian Influenza: (H2N2)

Post the 1918 influenza pandemic, the virus went back to its typical pattern of mild regional epidemics in the 1930s,

1940s, and early 1950s. The first isolation of a virus from humans in 1933 [Smith et al., 1933] led to speculation about the probable role of a similar virus in the 1918 outbreak. However, it was difficult to believe this hypothesis until the 1957 pandemic occurred. It was for the first time that the laboratory investigations could be carried out immediately while the virus was actively spreading the disease across the globe. Except the individuals aged 70 years or more, the human population encountered the virus strain, with which it had had no prior infection. It was also observed that the virus alone (without any bacterial co-infection) was sufficient to cause mortality in the infected population [Rogers et al., 1958].

1976: Potentially Pandemic, Swine Influenza Virus Epidemic: (H1N1)

Another abortive pandemic in the history of influenza outbreaks was in Fort Dix, New Jersey in 1976, provisionally suspected due to swine influenza viruses [Kilbourne, 1976]. A high-yield, genetic reassortant virus (X-53) was generated, which was subsequently tested as a vaccine in a clinical trial in 3,000 people. An even higher yielding HA mutant virus, X-53a, selected from X-53 was later used in the mass vaccination of 43,000,000 people. In the consequent months, the National Immunization Program for the control of influenza was abandoned, due to the lack of cases outside Fort Dix and the occurrence of neurologic complications of Guillain-Barré syndrome in association with administration of swine influenza vaccine. Thus, the whole attempt of vaccination was considered as a failure.

1977: Russian Flu, the Return of Human H1N1 Virus

The Russian flu (also known as red influenza or red flu) initially came to attention in November 1977, in the Soviet Union, but later reported to be originated in north-eastern China in May 1977 [Beveridge, 1978]. The epidemic spread rapidly among the population and was almost completely restricted to persons <25 years of age. The causative influenza virus strain rendered typical symptoms of influenza, but caused a mild disease. The reason for exclusive young age infectivity was credited to the absence of H1N1 viruses in humans after 1957 and the subsequent successive dominance of the H2N2 and then the H3N2 influenza subtypes. The antigenic and molecular characterization and comparison of both HA and NA antigens of the 1977 to the 1950s virus strains showed notable resemblance among them. This discovery raised interesting queries regarding the relatively conserved genome of the 1977 virus. How come the virus remained relatively unchanged even after 20 years, as the successive transmission in humans, must have led to the antigenic drift causing various mutations in the virus during the 2 decades. The fact that influenza viruses, previously, never underwent latency, dismissed the idea of reactivation of a dormant infection. Speculations arose that if the virus had been in a deep freeze. But, since this thought suggested hidden experimentation with live virus, it was disturbing. Delayed mutations and consequential evolutionary stasis in an animal host seemed logical, but again the question remained, in what host? Thus, the concluding answer to the 1977 outbreak is still not known.

Conclusion

The emergence and re-emergence of the influenza virus-led outbreaks [Kumar et al., 2011] has posed and continues to pose a huge threat on the socio-economic front for the pathogen's various host species. The history gives the account of many such threats providing profound implications for better preparedness [Khanna et al., 2006d; Khanna et al., 2013] for future outbreaks by development of unique diagnostic and therapeutic strategies [Khanna et al., 2011; Rajput et al., 2012; Kumar et al., 2013; Rajput et al., 2014; Rajput et al., 2015]. While assessing the pandemic risk, we tend to forget the fact that influenza virus contains 2 immunogenic protective antigens. Thus, consideration of both the antigenic determinants [Khanna et al., 2006c; Kumar et al., 2014] and the other antigens [Rajput et al., 2012; Khanna et al., 2011] is necessary for efficient preventive measures to deal with the subsequent influenza pandemics or epidemics.

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