·小评论·

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关于流感病毒毒性评估

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[关键词] 甲型 H1N1 流感病毒；病毒毒性；毒性评估

[摘 要] 病毒在人群中的流行速度或病毒在人群传播过程中所显示的毒力主要反应出人群的遗传异质性。当一个病毒性疾病在不同亚群之间的发病率和死亡率不表现出明显差异时，该病毒的毒力可能十分强大。相反，当这些差异存在时，则其毒力较低；差异种类越多，差异程度越大，则毒力越小。

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Virulence Assessment on Novel A/H1N1 Influenza Virus

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[**KEY WORDS**] Novel A/H1N1 Influenza Virus; Virulence of a Virus; Virulence Assessment

[**ABSTRACT**] The virulence of a virus, perceived by the speading speed of the virus within a population, reflects the population's genetic heterogeneity. When the difference of morbidity and mortality of a virus-caused disease within various ethnic groups is trivial, the virulence of the virus may be very powerful. In contrast, when the difference is significant, the virulence is quite low. The greater the difference between the ethnic groups, the lower the virulence.

2009 年 6 月 18 日，我校客座教授、苏州大学特聘教授李凯就当前流行的甲型 H1N1 流感为我校师生做了一场学术报告。该学术报告题为“猪流感病毒毒性评估和早期检测方法的开发”，除重点论述论题所涉及的问题之外，报告还详细分析了 1908 年西班牙流感大流行时造成其第二波冲击的可能原因并非病毒的新突变所致的理由，并提出了中国人不是本次甲型 H1N1 流感病毒的易感人群的观点。

对一次新爆发的流行病如流感大流行，如何在其爆发早期对该新出现的新亚型或新型病毒的毒力进行评估，具有十分重大的社会和医学价值，能直接影响相关防治措施的科学决策。缺乏对新的病毒毒力的早期评估手段，是导致世界卫生组织(WHO)和部分成员国对此次毒力和致死率远小于普通季节性流感采取最高级别预防政策的主要原因[1]。与季节性流感导致每年 25 万至 50 万人死亡相比较，此次甲型 H1N1 对人类的整体健康水平而言并无任何影响。

尽管该学术报告的许多观点应属一家之言，其中有关在流行病流行之初对新病毒毒力进行早期评估的方法，无论对流行病学研究还是对实验医学研究，都有一定的参考价值。诚然，在造成此次甲型 H1N1 全球大流行的流感爆发的 4 个多月后的今天，我们可以利用感染率和死亡率等指标对该病毒的毒力进行比较准确的定性，即该病毒毒力很低，但在疾病流行早期的病毒毒力评估，意义更大。

基于基因突变理论和个体化医学模式，李凯教授在报告中解释了可用于早期评估病毒毒力的指标，如疾病爆发初期的不同年龄、不同性别和不同族裔之间的发病率与死亡率是否存在差异。当一个病毒性疾病在不同亚群之间的发病率和死亡率不表现出明显差异时，该病毒的毒力可能十分强大。相反，当这些差异存在时，则其毒力较低；差异种类越多，差异程度越大，则毒力越小。当一个新的流行性疾病从首发地传播到其他城市或国家时，从输入病例到局部二代病人产生的时间长短，以及二代病人的病例倍增时间，应当被用于病毒毒力早中期评估的重要指标[2]。

根据上述有关早期评估新病毒毒力的方法，报告者介绍了其早在 5 月 8 日时提出的中国人不是本次甲型 H1N1 易感人群和可能原因[3]，主要为族群基因异质性和 1975 年曾在中国流行过的猪流感的长期免疫作用。与 WHO 的早期预警认为此次甲型 H1N1 流感可能造成全球数以万计患者死亡不同，通过对新的病毒流行性疾病阶段病毒毒力的早期评估，本报告者在早至 4 月时即提出了中国人不是本次甲型 H1N1 流感的易感人群的观点，并认为此次流感造成的全球死亡人数可能不及季节性流感所致一天死亡人数(1 000 人/天)[4]。

报告中强调的几个常识性观点同样具有一定的学术价值。首先对新的病毒性疾病的早期诊断，应该以 PCR 或 rt-PCR 为主要方法；其次对呼吸道传染病，当病毒毒力较弱和无症状携带者在社区大量存在时，强制性隔离措施的医学意义和社会意义甚微；第三，在病毒本身没有突变或突变不大时，临床上观察到的随着流行时程延长，

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后发病例较先发病例轻微,后流行区域的发病率和死亡率均较先发区域低的现象,不是因为流行过程中病毒毒力下降的原因,而是由于病毒从高危人群流行向中、低危人群流行的扩散过程。

从 2003 年的 SARS 到 2009 年的甲型 H1N1 流感,新的病毒性疾病随时都有可能发生,如何早期诊断和科学决策防治过程,是医学界也是包括 WHO 在内的决策部门所面对的挑战。

本报告所阐述的早期病毒毒力的评估,有望对未来防治其它新的病毒性流行病具有参考意义。

[参考文献]

[1] http://www.who.int/csr/resources/publications/swineflu/interim_guidance/en/index.html.

[2] Genetic heterogeneity prevents novel A/H1N1 from catastrophic pandemic spread. Whether the novel A/H1N1 virus or future new virus can cause a catastrophe similar to the 1918 flu is a serious public concern. The consecutive raising alert level about this new flu by WHO from three to five within days partially reflects the potential risk we are facing. High alert level urges international collaborations and prompt governmental responses, which may help to slow down and minimize the spreading of a new viral disease. However, genetic heterogeneity is a crucial factor of whether a person having contact history becomes to an infected patient and whether an infected individual is severely sick.

Genetic heterogeneity affects susceptibility to viral infection is well documented in AIDS. For example, individuals with CCR5 mutations or anti-CCR5 antibody positive are relatively HIV-resistant. Another example is SARS. Most of the more than eight thousand infected cases and nearly eight hundred deaths are Chinese nationality (WHO). Guangdong province, Hong Kong and Beijing are the three regions from where most of the SARS cases were reported. When SARS spread to Vietnam, Singapore, and Canada (Toronto), this spread route itself implicated ethnic differences in their susceptibility to SARS. Different genetic background within Chinese subpopulations and different ethnic genetic heterogeneities between Chinese nationality and other ethnic groups are the major factor determined why the majority of infected cases and dead cases are Chinese nationality at specific locations. Years later, retrospective study demonstrated that IL-12 and IFN-gamma variants are highly associated with the susceptibility to SARS as well as the severity of the disease of the infected individuals.

Three facts demonstrated that the transmission dynamics of the new A/H1N1 virus is similar to SARS. Firstly, the doubling time of the epidemic is different in different cities within Mexico. Secondly, the doubling time of the epidemic is different between Mexico/USA/Canada/Spain and the rest of the world. Thirdly, no confirmed case report of the new flu in several minorities within Mexico indicates the ethnic differences in susceptible to A/H1N1. These three features are good news to healthcare society in the panic time in facing the new A/H1N1 flu virus. Albeit genetic mutations are harmful sometime as they are associated with genetic disease and cancers; what we are sure now is that ethnic heterogeneity is powerful for human being combating viral infections. It is our genetic heterogeneity that is preventing the novel A/H1N1 from a catastrophic pandemic spread. This letter to editor was submitted to NEJM on May 6th 2009 and was not accepted.

[3] http://blog.sina.com.cn/s/blog_4e5eb50f0100djp6.html.

[4] http://blog.sina.com.cn/s/blog_4e5eb50f0100deyl.html.

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