

ANALYSIS OF THE 1991-2000 INFLUENZA EPIDEMIC IN GUANGDONG PROVINCE, CHINA

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Abstract. Influenza surveillance networks in Guangdong were established to investigate the epidemiological characteristics of influenza and influenza epidemics. Influenza activity peaked annually from March to July in Guangdong in 1991-2000; influenza H₃N₂ predominated in the epidemic (7 years of 10); the outbreak of influenza in 1996 was the remarkable result of antigenic drift of H₃N₂ strain. Ten isolates of H₉N₂ strains were discovered from human subjects in 1998 and 1999: chicken strains isolated after the Hong Kong fowl influenza outbreak. It was found that there was just one influenza activity season per annum in Guangdong and that the influenza H₃N₂ subtype still predominates in Guangdong. Further research into the pathogenicity of influenza H₉N₂ in humans warranted.

INTRODUCTION

Since the outbreaks of Asian influenza in 1957 and Hong Kong influenza in 1968, the influenza epidemic has been focused in South-east Asia and especially in Southern China, which was considered to be both the Asian and the global influenza epicenter (Webster, 1997). Influenza Surveillance Networks were established in 1988 with the assistance of the World Health Organization (WHO) Influenza Project following the fowl influenza outbreak in Hong Kong in 1997, intensive influenza surveillance began in Guangdong during that same year in order to identify promptly human cases of H₃N₁ influenza. This paper gives an analysis and discussion of the influenza epidemic and surveillance in Guangdong during 1991-2000, enabling lessons about the influenza in Southern China to be learnt and bolstering global influenza prevention strategy.

MATERIALS AND METHODS

Influenza-like cases

Established by the Infectious Diseases

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Management Act, Infectious Diseases Registration Cards contain details of influenza-like illness and other infections for each patient. Physicians in all hospitals and clinics are obliged to complete these cards and deliver them to local Disease Control Agents who collect all local infectious disease data and report them to the respective superior Disease Control Center. Data regarding influenza-like cases in each municipality is sent to the Center for Disease Control and Prevention, Guangdong Province.

Influenza surveillance

Influenza Surveillance Networks were established in Guangdong in keeping with the WHO Influenza Project (Huang, 1990). To ensure effective regional distribution, 4-5 Municipal Influenza Surveillance Spots were chosen; one (1-2 since 1998) municipal surveillance hospital serves as the surveillance sentry hospital for each municipal spot. Surveillance includes: (i) collection of the weekly outpatient numbers of medical, pediatric and respiratory disease cases; these are summarized and reported monthly; (ii) 5-10 throat swabs per week are sent to the Municipal Center of Virology to isolate strains; all isolate data is subsequently reported to the Provincial Centers for Disease Control and Prevention. Isolation methods include chicken-egg inoculation and

MDCK cell-lines; (iii) hemagglutination-positive samples are collected and characterized by the Provincial Center. Any Influenza Surveillance Spots reporting an influenza epidemic was required to begin a program of management. The reference strains (or diagnostic antigens) and anti-serum come from the National Influenza Center. Centers for Disease Control and Prevention, USA (CDC) and the National Institute of Health, Japan (NIH, Japan).

Fowl influenza

Since the emergence of Hong Kong H₅N₁ cases in 1997, fowl influenza surveillance in Guangdong has been ongoing. Fowl influenza virus (H₅N₁) surveillance was launched in Guangzhou, Shenzhen, Zhuhai, Zhanjiang, Shantou, Foshan and Yunfu with the surveillance subjects including patients with influenza-like illness and fowl farmer; surveillance criteria included epidemic surveillance and pathogenicity surveillance. The detection antisera, Anti-H₃, H₅, H₇ and H₉ come from the Harbin Institute of Veterinary Medicine; H₅N₁ antigen come from the CDC and the NIH. All the influenza-epidemic and isolated cases were investigated and dealt with by staff of the Influenza Surveillance Networks.

RESULTS

Influenza-like cases

The monthly distribution of influenza-like cases in Guangdong in 1991-2000 is shown in Table 1. In comparison with the average number of monthly cases, influenza-like cases peaked during March-June 1992, May-June 1993, June-August 1994, July-October 1995, March-July 1996, April-July 1997, March-August 1998 and March-July 1999; only sporadic influenza was seen in 1991 and 2000. The most remarkable influenza epidemic of the 1990s was in 1996. The data show that the annual influenza season occurred during March-July.

Influenza surveillance

Influenza strain isolates: The influenza strains isolated in 1991-2000 are shown in Table 2. There were 7 years (1992, 1993, 1995, 1996, 1998, 1999 and 2000) in which H₃N₂ strains were overwhelming; H₁N₁ strains were predominant in 1991; influenza B was predominant in 1994 and 1997. H₃N₂ strains and B strains were isolated every year; H₁N₁ strains were not isolated during 1993-1995. H₃N₂ subtype as a percentage of the total number of isolated strains were 60.7% (626/1,031); H₁N₁

Table 1
Influenza-like illness in Guangdong in 1991-2000.

Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
1991	813	264	564	473	609	862	700	185	303	147	24	141	5,085
1992	44	160	577	979	1,247	688	367	253	613	317	322	350	6,004
1993	165	182	136	286	849	508	216	101	218	721	880	102	4,371
1994	334	31	39	397	70	3,387	5,276	1,522	126	37	24	17	11,811
1995	18	59	80	213	303	346	783	730	622	425	201	268	4,048
1996	225	241	1,596	16,188	3,099	2,978	1,954	506	467	450	340	357	28,401
1997	304	181	665	3,208	1,450	1,507	2,719	789	516	550	689	835	13,413
1998	597	418	2,615	3,116	2,729	1,722	1,408	949	348	228	116	567	14,813
1999	271	247	695	595	379	724	497	236	110	206	229	178	4,367
2000	100	124	146	95	132	188	151	122	117	76	51	61	1,363
Total	2,871	1,907	7,113	25,550	10,867	12,910	14,071	5,393	3,440	3,157	2,876	2,876	930,331

Table 2
Influenza isolates in Guangdong in 1991-2000.

Year	Strain					Predominant Strain	Epidemic
	H ₁ N ₁	H ₃ N ₂	H ₉ N ₂	B	Total		
1991	16	2	0	9	27	H ₁ N ₁	
1992	1	28	0	17	46	H ₃ N ₂	+
1993	0	23	0	13	36	H ₃ N ₂	
1994	0	3	0	29	32	B	+
1995	0	11	0	3	14	H ₃ N ₂	
1996	2	34	0	10	54	H ₃ N ₂	+
1997	12	6	0	57	75	B	+
1998	6	114	9	15	135	H ₃ N ₂	+
1999	1	268	1	57	327	H ₃ N ₂	+
2000	65	137	0	82	284	H ₃ N ₂	+
Total	103	626	10	292	1,031	H ₃ N ₂	

Table 3
Relation of influenza strains to influenza-like cases (1998).

Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
ILC	597	418	2,515	3,116	2,729	1,722	1,408	949	348	228	116	567	14,813
Strain H ₁ N ₁	0	0	0	1	0	2	0	2	0	1	0	0	6
Strain H ₃ N ₁	0	2	6	29	27	18	16	7	9	0	0	0	114
Strain B	0	0	0	0	0	7	4	3	0	1	0	0	15
Total	0	2	6	30	27	27	20	12	9	2	0	0	135

ILC: Influenza-like cases

subtypes and B types were 9.99% (103/1,031) and 28.3% (292/1,031) respectively.

Relation on influenza strains to influenza-like cases

The influenza strains isolated and influenza-like cases in Guangdong in 1998 are shown in Table 3. As a percentage of the strains isolated, H₃N₂ subtype was 84.4% (114/135); H₁N₁ subtype was 4.4% (6/135); and B type was 11.1% (15/135). The influenza activity seasonal peak occurred during March-August when in influenza-like cases were 84.7% (12,539/14,813) of the total number of cases and 90.4% (122/135) of the isolated strains. A positive statistical correlation was found between the influenza isolates and the influ-

enza-like cases (r=0.786).

Fowl influenza surveillance

Fowl influenza strain isolate: The fowl influenza strains isolated during 1997-1998 showed a concentration of strains during May, June, July and August; a total of 23 influenza strains were isolated; H₉N₂ subtype strains were identified without H₅N₁ strains.

Human fowl influenza strain: Five and 4 influenza strains were isolated from throat swabs taken from respiratory disease patients in Shaoguan (August, 1998) and in Shantou (November, 1998) respectively: a total of 9 strains. Only one strain was isolated in Guangzhou (November, 1999). The strains were serologically characterized as H₉N₂ influenza.

DISCUSSION

The data from Guangdong influenza-like cases suggest that influenza activity decreased at the end of the 1980s and the beginning of the 1990s. An influenza epidemic in 1996 was reported (Huang *et al*, 1997). Using serological antigen analysis to compare the antigenicity of A/GD/1/96 (H₃N₂ subtype) in 1996 with that of three strains in 1995, it was shown that remarkable antigen drifts occurred and that antigenic domains were modified (Huang *et al*, 2001). On the other hand, influenza H₁N₁ subtype strains were predominant in 1991 and influenza B strains were predominant in 1994 and 1997, although occasionally less evident than the H₃N₂ subtype. As clinical influenza-like cases lack typical physical symptoms and reliable laboratory diagnosis, a reluctance to diagnose influenza cases in clinics may have resulted in under-reporting of infectious diseases. Although they cannot accurately reflect an influenza epidemic, influenza-like case numbers show the annual trend and duration of the influenza activity season.

The notion of two seasons per annum of influenza activity in Southeast Asia has been advanced (Brown *et al*, 1996): one from November to February (winter) and another from April to June (summer). It has been suggested that this two-season behavior could be seen in Guangdong, although our findings indicate only one peak season per annum, usually from March to July.

The predominant strains were the H₃N₂ subtype (7 years during 1991-2000) and H₁N₁ and B type (three years). It was found that H₃N₂ subtype influenza was predominant in the epidemic strains in 1991-2000. A positive correlation between the number of monthly-isolated influenza strains and influenza-like cases was shown. Influenza strains found since 1995 showed 'O Phage' variation, *ie* the strains adapted to the medium of MDCK cell-lines but had difficulty growing during the chicken-egg culture (Huang *et al*, 2001). It is suggested that

the influenza surveillance at Municipal Spots establishes tissue culture with a MDCK cell-lines technique as soon as possible, in order to increase the positive rate of the isolated strains.

No H₂N₁ strains were isolated during the fowl influenza surveillance in Guangdong; 10 human throat swabs produced H₉N₂ strains. We believe that this is further evidence of H₉N₂ strains infecting human beings; moreover, H₉N₂ strains were isolated from human subjects in Hong Kong (Peiris *et al*, 1999) when analysis of 8 RNA fragments of these Hong Kong strains showed that the subtype strain gene fragments came from the whole genome of chicken H₉N₂ influenza. Influenza H₉N₂ strains have been isolated previously only in birds or fowl without any pathogenicity in fowl and further study of the impact of the H₉N₂ strain on human beings is warranted.

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REFERENCES

- Brown EL, Hampson WA, Webster GR. Options for the control of influenza III. Amsterdam: Elsevier Science BV, 1996: 85-9.
- Huang P, Shen G, Ni HZ, *et al*. Molecular evolution of Guangdong influenza isolates in influenza outbreak in 1996. *Virologica Sinica* 2001; 16: 1-5.
- Huang P, Zhou HQ, Ni HZ, *et al*. An influenza outbreak in Guangdong in 1996. *Dis Surveill*, 1997; 12: 205-7.
- Huang ZX, Hong T, Liu CB, Medical Virology Foundation and Laboratory Technique, 1st ed. Beijing: Scientific Press, 1990: 661-96.
- Peiris M, Yuen KY, Leung CW, *et al*. Human infection with influenza H₉N₂. *Lancet* 1999; 354: 916-7.
- Webster GR, Predictions for future human influenza pandemics. *J Infect Dis* 1997; 176 (suppl): S14-9.