

MIXED INFECTIONS WITH INFLUENZA A AND B VIRUSES

B. TŮMOVÁ, *V. KAŠOVÁ, A. ŠTUMPA

Institute of Hygiene and Epidemiology, Czechoslovak Influenza Centre,
100 42 Prague; and *Virology Dept., Regional Hygiene Station, Ústí nad Labem, Czechoslovakia

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Summary. — In the course of an influenza A and B epidemic, influenza virus was isolated from 46 patients. Seven of these patients showed seroconversion against influenza virus plus another respiratory virus. In 9 patients, simultaneous antibody increase against both influenza A and B viruses was demonstrated, but only a single virus type was isolated. In one case the isolated virus population could be separated into type A and B viruses.

Key words: influenza; mixed infection

In acute respiratory diseases and their complications, simultaneous infections with two or more agents have been demonstrated mostly by serological methods (Plachtová *et al.*, 1967; Bláhová *et al.*, 1973; Strnad *et al.*, 1975; Syruček *et al.*, pers. comm. 1980). Isolations of two agents from the same patients have been less frequent, those of influenza virus + another respiratory virus being more common than of two influenza virus types (A + B).

The pathogenesis of these so-called mixed infections has been studied only little. In some cases even seroconversion cannot be definitely evaluated as offering evidence of demonstration of the aetiological agent + an accidental agent or evidence of an actual mixed infection accompanied by replication of two viruses.

We repeatedly demonstrated such mixed infections in the period from January to April, 1980, in the course of an influenza A and B epidemic in the North Bohemia region. Most patients, i.e. 30 (65%) of 46 from whom influenza virus was isolated, showed in haemagglutination inhibition (HI) and complement-fixation tests seroconversion against the isolated strain. In 34% of patients, seroconversion suggested a mixed infection: in 7 patients against influenza virus + another respiratory agent and in 9 patients we observed a simultaneous significant increase in antibody titres against both influenza A and B viruses. But only one virus type was isolated from these 9 (A + B)-positive cases, namely 8 times influenza B and once influenza A(H3N2) virus. Identification of antigens and subsequent cloning confirmed that pure virus lines were involved. Examination of the patients' sera in gel immunodiffusion tests (Palmer *et al.*, 1975) revealed antibodies only against NP antigen of the isolated strains, suggesting infection with and replication

Table 1. Two influenza virus types in a human isolate. Identification of antigens and inhibitor marker in HI tests

Immune rat sera	Orig. isolate	Virus lines after neutralization with serum against					
		influenza A(H3N2)			influenza B		
		E1*	E2	E3	E1	E2	E3
A(H3N2)	<10	0	0	0	160	160	320
B/Singapore/222/79	40	80	160	160	0	0	0
Inhibitors							
Rat serum	0	0	0	0	0	0	0
Guinea pig serum	<10	0	0	0	80	80	80

Initial serum dilution was 1 : 10.

* E1, E2, E3 = egg passages of the cloned virus lines.

of only one virus type, probably with simultaneous, may be abortive, replication cycle of the second virus.

In addition to the isolates just mentioned, among a further 34 isolates we found a virus population, recovered from a 12 years old child, which was inhibited in the HI test with specific anti-influenza B serum. It also was partially inhibited with the starting dilution of the antiserum to (A(H3N2)), which is considered insignificant in routine practice (Table 1). The same phenomenon was demonstrated with normal guinea pig serum the inhibitors in which are a specific marker of the A(H3N2) subtype. By cloning in the presence of specific antibody with subsequent selection by the limiting dilution method we obtained from this virus population lines of influenza B and A(H3N2) viruses. Only convalescent serum from the patient was available; it contained antibody only against one type of virus, like in the cases mentioned above.

Our findings indicate that the so-called mixed infections represent a more complex problem than suggested by certain laboratory results. Detection of a single mixed isolate among 80 isolated strains of influenza virus is indicative of an accidental and exceptional character of such cases. Nevertheless we would like to stress that, before used in further work, all influenza virus strains isolated in the course of mixed epidemics should be examined not only for their antigenic properties but also for other markers.

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