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Seroepidemiological Survey of Influenza C Virus in Hiroshima Prefecture, Japan

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Influenza C virus, which was first isolated from a patient with a mild influenza-like illness in 1947 (1), has been considered an etiological agent for respiratory infections in human beings (2). However, the epidemiological information regarding this virus, such as the mechanisms of its transmission and maintenance in nature, have been limited, as compared with those of influenza A and B viruses. We investigated the antibody prevalence of this virus in the residents of Hiroshima Prefecture to elucidate the extent of influenza C virus infection, and in this paper we report the results of the age distribution of antibody against influenza C virus in comparison with those against influenza A and B viruses.

A total of 186 sera, which were collected from residents living in Hiroshima Prefecture in the age range of 0-84 years in 1997, were measured for hemagglutinin-inhibition (HI) antibody titer against influenza A, B, and C viruses. The age-related distribution of HI antibody and the positive rate in age groups against influenza C, A, and B viruses are shown in Figures 1 and 2. Significant levels of HI antibody-positive rate (134/186: 73.6%) against influenza C virus were found in the sera tested, with the titers ranging from 1:10 to 1:80. The pattern of the HI antibody-positive rate in age groups against influenza C virus was markedly different from those of influenza A and B viruses; a high percentage of antibody-positive rate (more than 50%) was shown only in the age groups of 0-14 years against A/Sydney/5/97(H3N2), or in that of 5-24 and 30-39 years against B/Harbin/7/94, while the positive rate against A/Beijing/262/95(H1N1) was generally low in all age groups. In contrast, the antibody-positive rate against C/Hiroshima/290/99 was high in all age groups except for that of 0-4 years. Similar antibody-prevalence patterns in age groups against influenza C virus have also been reported

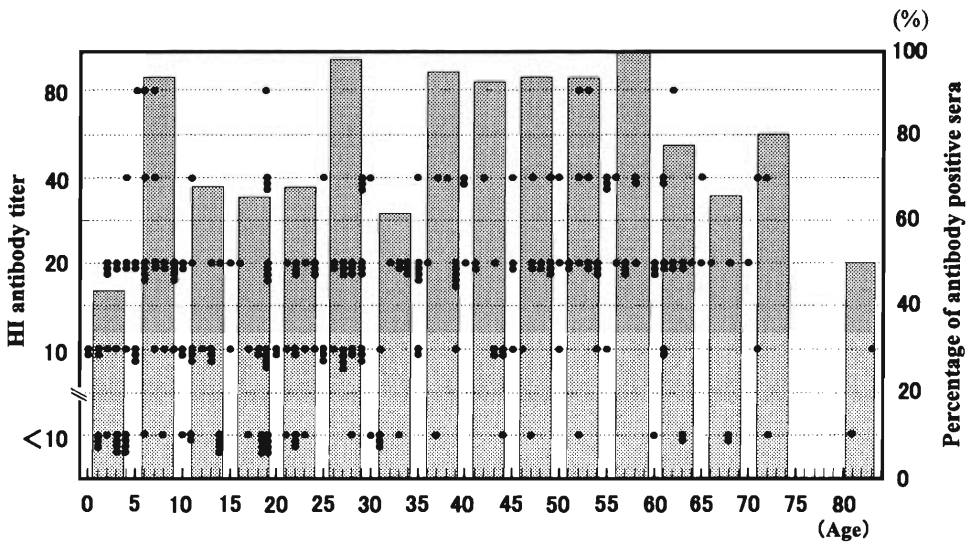

Fig. 1. Age-related distribution of antibody and antibody-positive rate in age groups against influenza C virus. Hemagglutination-inhibition (HI) titers of 186 sera collected from residents of Hiroshima Prefecture in 1997 were determined using the microplate technique described by Homma (3). The antigen for HI test was the isolate of influenza C virus (C/Hiroshima/290/99) (5). HI titers were expressed as the reciprocal of highest serum dilution that inhibited hemagglutination, and were plotted against age. The percentages of antibody-positive sera (HI titer of 1:10 or more) were determined every 5 years of age, and are shown as bars on the graph.

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been declining markedly in the era of HAART, which includes the use of two nucleoside reverse-transcriptase inhibitors (NRTIs) and an HIV-specific protease inhibitor (PI). However, adherence to these regimens is often difficult because of the large number of pills, side effects, and drug-drug interactions related to PIs. Furthermore, reports of unexpected serious side effects in patients exposed to PIs over a long period are increasing in number. In particular, metabolic disturbances such as increased levels of cholesterol or triglycerides and insulin-resistant diabetes in association with abnormal fat redistribution, which is referred to as lipodystrophy syndrome (1), have been observed. Non-nucleoside reverse-transcriptase inhibitors (NNRTIs) are advantageous due to the lower burden of pills and fewer drug-drug interactions compared with PI. Therefore, HAART consisting of 2 NRTIs and 1 NNRTI is being prescribed as initial therapy in treatment-naive patients, and 'switch therapy' with NVP in place of PIs is being prescribed for patients with long-term sustained viral suppression (2). Leukocytopenia caused by ZDV was reported soon after its approval (3). However, there has been little information regarding myelotoxicity caused by antiretroviral regimens containing NVP in adults. At our hospital, 44 patients have been treated with NVP-containing regimens since 1997. Seventeen underwent regimens containing NVP and ZDV. As described above, 3 out of 17 patients (17.6%) developed leukocytopenia 3-5 weeks after the commencement of antiretroviral therapy. In cases 1 and 2, regimens including ZDV and NVP were introduced as the first antiretroviral therapy, resulting in leukocytopenia. In case 1, ZDV was replaced by d4T, while 3TC and NVP were not changed in the second regimen, this patient had no further episodes of leukocytopenia. Although case 3 had been treated with ZDV/ddI since 1996, he had never developed leukocytopenia until dual-PIs were changed to NVP. These observations appear to indicate that luekocytopenia by ZDV might be intensified by NVP.

Toxic hepatitis and Stevens-Johnson's syndrome have been reported as serious adverse events associated with NVP. However, in previous studies of NVP in combination with ZDV, serious leukocytopenia has not been reported among the more than 400 participants studied (4). In our cases, the patients were relatively older. If advanced age is a predisposing factor for leukocytopenia, this will have clinical relevance. Lipodystrophy syndrome can cause cardiovascular complications (5). Therefore, older patients should likely be given PI-sparing regimens to avoid complications. Our observations appear to suggest that the myelotoxicity of ZDV can be exacerbated by NVP. It may therefore be important to be aware of this potential side effect, especially during the first 5 weeks of therapy in elderly patients.

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