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**Evolution of EBV seroprevalence and of age at EBV primary infection in France in the 2001-2015 period: analysis of 81,000 serologies**

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**Background:** Few studies reported a change in the age of acquisition of EBV in developed countries, leading to an increase of late primary infections (PI), and of the number of infectious mononucleosis (IM) as well as severe IM. We aimed to determine whether PI age had evolved in the population of the Isère department, France, and to which extent age and EBV PI intensity were correlated.

**Material/methods:** We retrospectively studied 2 large French EBV serology databases (IgG and IgG VCA, IgG EBNA, heterophile antibodies):

- From Grenoble university hospital (2001 to 2015, n=53,553)
- From a city private laboratory network including 25 collecting centers in Isère department (2008 to 2015, n=27,485).

Using state-of-the-art interpretation of serological profiles, we determined for each year i) the seroprevalence of EBV for patients aged over 19, and ii) the age at EBV PI. We also collected the

clinical and biological data of each patient with a serologically proven EBV PI from the hospital database.

**Results:** In the hospital database, we observed a significant decline of EBV seroprevalence over years ( $R^2=0.63$ ,  $p<0.01$ ) in the subjects older than 19: 2.1%, 2.5% and 3.1% were EBV seronegative in the 2001-2005, 2006-2010 and 2011-2015 periods, respectively. In the city laboratory database, the same trend was observed, but did not reach statistical significance ( $p=0.06$ ).

In the hospital database, age at PI was significantly higher between 2008 and 2015 than between 2001 and 2007 ( $13.7\pm 11$  vs  $15.6\pm 12$ ,  $p=0.03$ ), and there was a significant increase of PI age over the 2001-2015 years ( $p=0.05$ ). This was not observed in the city laboratory database (18.0 and 17.9 years between 2008 and 2011, and between 2012 and 2015, respectively).

In the hospital database, we observed a significant correlation ( $p<0.01$ ) between age and hepatic abnormalities (ASAT, ALAT,  $\gamma$ GT, bilirubin) and thrombocytopenia, but not between age and neutropenia, activated lymphocyte count, or hospitalization duration.

**Conclusions:** In the population explored in Grenoble university hospital, the age of EBV PI increased in the last 15 years, as observed recently in UK and Japan. Consistently, seroprevalence decreased in the population aged over 19 years. We also confirmed a correlation between age and biologic abnormalities during PI.

Our data suggest a shift in the age of acquisition of EBV, probably associated with an increased risk of severe IM.