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Interim report on the A/H1N1 influenza virus pandemic in Marseille, France, April-November 2009

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Abstract

We report here the results of a 7-month survey of the influenza A/H1N1 pandemic in the Virology laboratory of the public hospitals of Marseille (April–November 2009). In total, 8 587 samples were analysed during this period, of which 1 974 (23%) were positive for the novel influenza variant. The analysis of results obtained using rapid influenza diagnostic tests (RIDTs) revealed a global sensitivity of 49.4% (vs. molecular qRT-PCR detection), strongly correlated with age groups (varying from 30% to 58% for patients >40 age and <10, respectively), indicating that RIDTs can be helpful in accelerating the management of suspected cases. Epidemiological analysis showed that the winter influenza wave began in October in Marseille (i.e. 2 to 3 months earlier than usual seasonal influenza outbreaks) and that the majority of autochthonous cases were observed in patients younger than 20 years old, with a low number of cases in patients over 60 years old. In November 2009, 22.2% (167/754) of patients with a laboratory diagnosis of influenza A/H1N1 infection were hospitalized, of which 9% (15/167) were admitted to an intensive care unit (ICU). Patients in the extreme age groups (>40 years old and <1) were significantly more often hospitalized than others, and 2.4% of hospitalized patients died. During the last 3 weeks of the period, the average number of bed-days attributable to H1N1sw-positive patients was 31.4, of which 5.9 were in ICUs.

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Introduction

In late April 2009, a novel A/H1N1 influenza virus (H1N1sw) was isolated in North America [1]. Rapidly, the World Health Organization increased the alert level from phase 5 to phase 6, defining the first influenza pandemic of the 21st century [2]. The first wave affected Mexico, the USA and Canada with severe cases and deaths [3–5]. The following wave affected the southern hemisphere during the southern winter season [6,7], and once again severe cases were observed; over 3 months, 722 patients were admitted to an Intensive Care Unit (ICU) in Australia or New Zealand, representing 28.7 cases per million inhabitants, with a 14.3% mortality [8].

The first cases in metropolitan France were detected in April 2009 in patients returning from Mexico. Until early July 2009, a systematic surveillance based on laboratory confirmation of suspected cases was implemented in the 'Level A' laboratories of the seven French Defence Zones [9]. During the following months, laboratory confirmation was mainly performed in groups at risk and in hospitalized patients.

We report here data collected by the 'Level A' Virology laboratory of the public hospitals of Marseille (Southern Defence Zone) from 25 April to 29 November 2009; the evolution of the outbreak, the distribution among age groups, the results of rapid influenza diagnostic tests (RIDTs) and the characteristics of hospitalized patients are described and discussed.

Materials and Methods

Clinical samples

All clinical nasal samples were obtained using Virocult swabs (Virocult MW950; Medical Wire and Equipment Co.). Laboratory investigations for diagnostic purposes and epidemiological assessment, warranted by patients' signatures at the hospital entrance office, were performed in accordance with French national regulations (Huriet-Sérusclat law, #881138) and did not require ethical committee approval.

Rapid influenza diagnostic testing (RIDT)

RIDT was performed using the Directigen EZ influenza A+B test (BD EZ Flu A+B, Becton, Dickinson and Company) according to the manufacturer's instructions.

RNA extraction

Samples were spiked with in-house MS2 phage internal control [10] and RNA was extracted using the EZ1 Virus Mini Kit v2 on the EZ1 Biorobot (both from Qiagen).

Quantitative real time PCR assays

Samples were analysed by two qRT-PCR assays: (i) a qRT-PCR assay using SYBR Green technology detecting all influenza A viruses [10], and (ii) a qRT-PCR assay specific for H1N1sw, recommended by the French Influenza Reference National Centre [9] as previously described.

Database of patients infected by H1N1sw

During the last 4 weeks of the study (November 2009) data regarding in-patients and patients presenting at the hospital emergency department with a subsequent laboratory confirmation of H1N1sw infection were collected from the database of the public hospitals of Marseille. The age, sex, arrival and discharge from hospital dates, category of hospitalization unit (paediatric medical unit, adult medical unit, paediatric ICU and adult ICU) and number of deaths were analysed using an anonymized database.

Results

From 25 April to 29 November 2009, we analysed 8 587 specimens for detection of the novel A/H1N1 virus. A total of 5 848 (68.1%) originated from public hospitals in Marseille, the remaining samples being sent by other hospitals from the French South Defence Zone. Until late June the numbers of samples tested remained low but they increased progressively until early September (Fig. 1). During this period, the

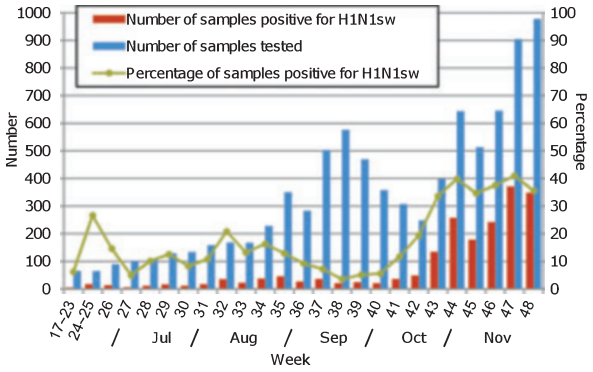

FIG. 1. Time distribution of samples tested and samples positive for H1N1sw during 7 months in the Virology laboratory of the public hospitals of Marseille.

percentage of H1N1sw-positive samples remained stable at *c.* 10%. In September, the number of samples increased suddenly but the percentage of H1N1sw-positive samples decreased (Fig. 1). This episode was associated with the circulation of other respiratory viruses such as rhinoviruses and coronaviruses. The influenza winter wave began effectively in October (weeks 41–42) with a marked increase of both tested and positive samples. From late October, the percentage of H1N1sw-positive samples remained stable (30–40%) but the number of positive samples continued to increase (Fig. 1).

We analysed the distribution among age groups of tested samples (N) and H1N1sw-positive samples (N′) during the study period. Until late August, patients over 20 years old represented 60% of all tested patients and more than 50% of H1N1sw-positive patients. During this period, patients in the 10–19 years age group represented 30% of H1N1sw-positive patients (Fig. 2a,b) but this proportion increased in September (weeks 36–38), to reach more than 40% of infected patients. From mid-September, the proportion of patients younger than 10 years who were tested or infected by H1N1sw increased, representing approximately 40% of both groups and the distribution among age groups remained globally stable afterwards (Fig. 2a,b). The N′/N ratio (allowing standardization of the number of samples in the age groups) showed that the highest proportion of positive patients was observed in the 10–19 years age group (30–60%) and that this proportion fluctuated *c.* 20% for patients over 40 years old (Fig. 2c). During the complete study period the majority of patients infected by H1N1sw were younger than 20 years old.

Among the 8 587 samples tested for influenza virus using qRT-PCR, a total of 7 459 (including 1615 qRT-PCR positive with both systems) were also tested using RIDT. Of the 7 459 samples, 798 (10.7%) gave positive results in the RIDT, all of these being positive for molecular detection of the