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"SYNDROMIC SURVEILLANCE" AND THE REEMERGENCE OF YELLOW FEVER IN SÃO PAULO STATE, BRAZIL, 2009

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Dear Editor:

Urban cases of yellow fever (YF) have not occured in Brazil since 1942. However, an annually variable number of sylvatic YF cases are reported to the health surveillance system (1). Traditionally, there was an extensive area in Brazil that was termed "endemic" for sylvatic YF. It included all the states in the north (Amazonia) and middle-west regions. Since the late 1990s, that area has been continuously expanding to the south and east, reaching more populated states. This is a matter of concern, since YF vaccine is currently not included in the immunization schedule for children living outside the "endemic" area.

The last two years have witnessed a substantial increase in the sensitivity of YF surveillance (2). This was partly due to active surveillance of epizootic events among non-human primates, a phenomenon that usually precedes the occurrence of human YF (3). However, the registration of human cases still relies mostly on traditional forms and strict case definition. A suspected case is defined as "an acute febrile disease accompanied by jaundice and hemorrhagic manifestations in a person who lives in or has traveled to an affected area and who was not vaccinated against YF in the last ten years". Clearly, this definition does not work for the initial cases in a recently affected area. Also, it does not detect non-icteric and/or non-hemorrhagic patients, a situation that probably accounts for the great majority of cases.

"Syndromic surveillance" is a method, proposed by the US Centers for Disease Control and Prevention (CDC, Atlanta) for early and enhanced detection of emerging infectious diseases (4). It relies on the identification of a set of signs and symptoms (a syndrome) from many sources (e.g., medical charts) and the application of a broad diagnosis approach. We aim to demonstrate how a hospital-based syndromic approach allowed early identification of YF cases in São Paulo state and the implementation of control measures (a vaccination campaign) in a timely fashion.

In 2005, the Brazilian Ministry of Health instituted a network of epidemiological surveillance offices in tertiary hospitals throughout the country. All participating hospitals were asked to develop alternative approaches to increase the sensitivity of their surveillance systems. Two teaching hospitals of the Botucatu Medical School (in Botucatu and Bauru cities, São Paulo state) chose to implement a surveillance of acute febrile ictero-hemorrhagic syndrome (AFIHS). The rationale of the surveillance was to avoid missing cases of hemorrhagic fevers, like leptospirosis and Brazilian spotted fever (BSF). Both diagnostic and therapeutic measures against AFIHS followed a syndromic approach, which indicates that all patients should be tested serologically for dengue, YF, BSF and leptospirosis. Additionally, blood cultures were performed to exclude sepsis of unknown origin.

On February 28th 2008, a woman from Sarutaiá (a city 70 km away from Botucatu) was admitted to the Bauru State Hospital (one of the teaching hospitals) with fever and jaundice. Laboratory tests revealed elevated liver enzymes and altered coagulation. The initial diagnostic hypothesis was leptospirosis. Still, the AFIHS approach was employed. Despite life-support measures, the woman developed massive hemorrhage of the respiratory tract and died within two days of admission. YF was serologically confirmed *postmortem*. On March 13th, a man from Itatinga (another city near Botucatu) was admitted to the Clinical Hospital of Botucatu Medical School with a hypothesis of fulminant viral hepatitis. He presented signs and symptoms similar to those of the first case, so that the AFIHS approach was also employed. YF was confirmed soon after his death. A summary of all other AFIHS cases, admitted to either of the teaching hospitals, is shown in Table 1.

One should note that the first two cases would have had their diagnosis delayed (or even missed) without AFIHS syndromic surveillance. All subsequent hypotheses of YF were based on the knowledge of those experiences. Moreover, active examination of symptomatic individuals in the cities where the first cases occurred

permitted the finding of new cases. A total of 22 persons from four municipalities, in the Botucatu region, had YF diagnosed. There was a rapid response from the São Paulo State Health Surveillance Office, with an extensive vaccination campaign initiated on March 21st. More than 92% of the 509,000 inhabitants from 29 municipalities in the Botucatu region were vaccinated. No new cases have been registered in the region since the campaign. However, three YF cases were diagnosed in another region of São Paulo state in April 2009 (5).

Our point is that hospital-based syndromic surveillance aided in the timely implementation of control measures and prevented new cases and deaths. Perhaps the surveillance of other syndromes, like encephalitis and acute respiratory illnesses, could further improve our detection of emerging and reemerging diseases.

Table 1. List of patients admitted to the teaching hospitals of Botucatu Medical School with acute febrile ictero-hemorrhagic syndrome (AFIHS), from February to April, 2009. The first two cases identified by syndromic surveillance are printed in boldface

Patient	Hospital	Gender	Age	Initial hypothesis	Final diagnosis	Outcome
1	**Bauru State Hospital**	**Female**	**28**	**Leptospirosis**	**Yellow fever**	**Death**
2	**Clinical Hospital**	**Male**	**39**	**Fulminant viral hepatitis**	**Yellow fever**	**Death**
3	Clinical Hospital	Male	47	Yellow fever	Yellow fever	Death
4	Clinical Hospital	Male	14	Yellow fever	Yellow fever	Death
5	Clinical Hospital	Male	23	Leptospirosis	Undetermined	Cure
6	Clinical Hospital	Male	51	Yellow fever	Yellow fever	Death
7	Clinical Hospital	Female	30	Yellow fever	Yellow fever	Cure
8	Clinical Hospital	Female	Newborn	Yellow fever	Yellow fever	Death
9	Clinical Hospital	Male	33	Yellow fever	Yellow fever	Cure
10	Clinical Hospital	Female	17	Yellow fever	Yellow fever	Cure
11	Clinical Hospital	Male	30	Yellow fever	Yellow fever	Death
12	Clinical Hospital	Female	42	Yellow fever	Yellow fever	Death
13	Clinical Hospital	Male	23	Yellow fever	Yellow fever	Cure
14	Clinical Hospital	Male	15	Yellow fever	Leptospirosis	Cure
15	Clinical Hospital	Male	41	Sepsis	Undetermined	Death
16	Clinical Hospital	Male	30	Yellow fever	Undetermined	Cure
17	Clinical Hospital	Male	38	Yellow fever	Undetermined	Cure
18	Clinical Hospital	Female	20	Brazilian spotted fever	Viscerotropic disease*	Death
19	Clinical Hospital	Female	18	Yellow fever	Undetermined	Cure

Severe adverse reaction after yellow fever vaccination.

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