ORIGINAL ARTICLE

Surveillance for Healthcare-Acquired Febrile Respiratory Infection in Pediatric Hospitals Participating in the Canadian Nosocomial Infection Surveillance Program

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OBJECTIVE. To determine the rates of healthcare-acquired febrile respiratory infection (HA-FRI) in Canadian pediatric hospitals and to determine the vaccination status of patients with healthcare-acquired respiratory syncytial virus (RSV) infection, influenza, or pneumococcal infection who were also eligible for immunoprophylaxis.

METHODS. Prospective surveillance was conducted in 8 hospitals from January 1 to April 30, 2005. All hospitalized patients less than 18 years of age were eligible, except for patients housed in standard newborn nurseries or psychiatric units. Infection control professionals reviewed laboratory reports, conducted ward rounds, and reviewed medical records to identify case patients. Descriptive analyses were completed, as well.

RESULTS. A total of 96 case patients were identified; 52 (54%) were male, and 48 (50%) were aged 1 year or less. Seventy-two patients (75%) had chronic medical conditions. Respiratory viruses accounted for 72 (71%) of 101 pathogens identified, and RSV was the virus most frequently identified. Of these 96 patients, 9 (9%) died, and 3 (3%) of the deaths were related to the patient's HA-FRI. The mean incidence rate was 0.97 infections/1,000 patient-days (range, 0.29–1.50 infections/1,000 patient-days). Only 2 (15%) of 13 influenza vaccine–eligible children who acquired influenza while hospitalized were reported to have been vaccinated, but influenza vaccination status was unknown for most children. However, 4 (80%) of 5 RSV prophylaxis–eligible children who had healthcare-acquired RSV infection had received immunoprophylaxis with anti-RSV monoclonal antibody.

CONCLUSIONS. HA-FRI is mainly caused by viruses such as RSV, and it primarily affects children under 1 year of age and those with chronic medical conditions.

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Healthcare-acquired respiratory tract infection is an important cause of morbidity and mortality in pediatric settings, and these infections reflect viral activity in the community.[1] Respiratory infection may account for approximately half of all admissions to pediatric medical wards in the late fall, winter, and early spring, as outbreaks of different respiratory viruses occur in the community.[2,3] Transmission of viral pathogens on pediatric wards is facilitated by the proximity of large numbers of susceptible and infectious children, as well as the behavioral characteristics of young children, such as inadequate hygiene, frequent oral contact with their hands and other objects, drooling, direct contact between children during play, and the need for frequent hands-on interaction with parents and healthcare personnel.

National recommendations exist for the use of immunoprophylaxis against respiratory syncytial virus (RSV) infection, influenza, and pneumococcal infection.[4-7] For specific, high-risk patient groups, immunoprophylaxis is recommended to prevent illness and hospitalization as a result of infection with these respiratory pathogens, and such prophylaxis may influence the risk of healthcare-acquired infection. Similar recommendations have been published by the American Academy of Pediatrics.[8-10] Although the majority of children who develop febrile respiratory infection (FRI) in the hospital have viral illnesses, bacterial infection also occurs. The specific origins of bacterial FRI are difficult to determine in children unless there is an accompanying bloodstream infection, because invasive procedures to obtain lower airway or pleural specimens are not often performed. In contrast, most viral respiratory infections are readily diagnosed

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by use of tests performed on upper airway secretions, and most children who acquire FRI in the hospital will undergo testing for viruses.

The outbreak of severe acute respiratory syndrome in 2003 prompted the development of national recommendations for surveillance of FRI in acute care settings. We describe surveillance in pediatric hospitals and wards in acute care institutions that participate in the Canadian Nosocomial Infection Surveillance Program. This program is a collaborative effort on the part of the Canadian Hospital Epidemiology Committee, a subcommittee of the Association of Medical Microbiology and Infectious Diseases–Canada, and the Centre for Communicable Diseases and Infection Control of the Public Health Agency of Canada. The objectives of this surveillance were to determine the rates of healthcare-acquired FRI (HA-FRI), describe the clinical and epidemiologic features associated with HA-FRI, and determine whether patients who developed healthcare-acquired RSV infection, influenza, or pneumococcal infection were candidates for immunoprophylaxis.

METHODS

Prospective surveillance for HA-FRI was conducted between January 1 and April 30, 2005. Eight pediatric acute care hospitals participated. Surveillance included all hospitalized patients less than 18 years old, other than those housed in standard newborn nurseries and psychiatric units. The total numbers of patient-days and admissions, excluding those for standard newborn nurseries and psychiatric units, as well as the numbers of patient-days and admissions for the pediatric intensive care unit (PICU) and neonatal ICU (NICU) in each hospital, were used as denominators. The incidence rates of HA-FRI were calculated for each hospital. We included both FRIs that were laboratory confirmed and those that were identified on the basis of clinical assessment alone.

A clinical case was defined as a case occurring in a patient with onset of infection and fever (oral or tympanic temperature greater than 38°C or rectal temperature greater than 38.5°C) at least 72 hours after hospital admission and at least 1 respiratory abnormality for which there was no other evident cause (the relevant abnormalities were as follows: rhinitis, nasal congestion, pharyngitis, sneezing, cough, wheeze, stridor, apnea, dyspnea, labored breathing, increased respiratory secretions, change in the characteristics of chronic secretions, decreased air entry on auscultation, rales, rhonchi, decreased oxygen saturation, need for an increased concentration of inspired oxygen, increased need for ventilator support, increased need for suctioning, and new abnormality on chest radiograph). Laboratory-confirmed cases were those that occurred in patients who satisfied the clinical case definition and had a positive laboratory test result (ie, culture, rapid antigen test or nucleic acid amplification test) that confirmed the presence of a viral or bacterial pathogen in a relevant specimen. The samples tested included nasopharyngeal aspirates, nasopharyngeal and throat swab samples, sputum, tracheal aspirates, bronchoalveolar lavage fluid, pleural fluid, and blood.

Case patients were identified both by review of laboratory reports at least twice weekly and by ward rounds. The medical records of patients who met the case definition were examined by experienced infection control professionals or research personnel associated with each hospital. Basic demographic characteristics, laboratory and clinical data related to the FRI, and details of management and outcome were collected. Case patients were grouped into 4 categories (ie, upper respiratory tract infection, pneumonia with radiological evidence, other lower respiratory tract infection [bronchiolitis, tracheitis, or laryngotracheobronchitis], and respiratory tract infection not specified) on the basis of the specific site of infection and whether there was radiological evidence of pneumonia.

For patients with healthcare-acquired influenza, RSV infection, or pneumococcal infection, information about whether the patient was a candidate for immunoprophylaxis and whether the patient had received immunoprophylaxis prior to infection onset was also collected. Eligibility for prophylaxis was determined on the basis of the National Advisory Committee on Immunizations recommendations for 2004–2005.[4-7]

All deaths that occurred within 30 days after diagnosis of FRI were assessed by the hospital epidemiologist or a designated physician to determine whether the death was attributable to the FRI. The relationship between the cause of death and the FRI was classified as follows: (1) death directly related to FRI, that is, the patient had no other condition that would have caused death at that time; (2) death indirectly related to FRI, that is, the FRI contributed to the patient's death but was not the primary cause; or (3) death unrelated to the FRI.

Data were collected and entered manually on patient data extraction forms and forwarded to the Public Health Agency of Canada for electronic data entry and data analysis. A unique identifier linked to the patient's name was used only to identify patients at each participating hospital and was not transmitted to the Public Health Agency of Canada. All identifying data were kept strictly confidential at the local hospital. Although this surveillance project was observational and did not involve any alteration in patient care, institutional review or ethics board approval was obtained at participating hospitals as required.

Data were entered into Microsoft Access 2002 (Microsoft) and analyzed using Microsoft Excel (Microsoft) and SPSS, version 15.0 for Windows (SPSS). We calculated the frequencies for variables of interest along with measures of central tendency for continuous variables. Descriptive and univariate analyses were performed. The χ^2 test was used to compare proportions. Medians were compared using the Kruskal-Wallis test or Mann-Whitney test, as appropriate.

TABLE 1. Incidence of Healthcare-Acquired Febrile Respiratory Infection in Patients Less Than 18 Years Old, Canadian Nosocomial Infection Surveillance Program Surveillance, 2005

Surveillance site	No. of cases	Surveillance period, days	No. of patient-days	Infections per 1,000 patient-days	No. of admissions	Infections per 1,000 admissions
A	7	81	7,699	0.91	1,306	5.36
B	35	111	32,413	1.08	4,338	8.07
C	13	111	11,691	1.11	2,301	5.65
D	3	90	4,906	0.61	747	4.02
E	20	119	13,311	1.50	811	24.66
F	11	113	11,461	0.96	1,938	5.68
G	5	119	11,013	0.45	1,750	2.86
H	2	119	6,802	0.29	491	4.07
Total	96	…	99,296	0.97	13,682	7.02

RESULTS

A total of 96 case patients with HA-FRI were identified in 8 hospitals. The mean incidence of HA-FRI was 0.97 infections/1,000 patient-days (range, 0.29–1.50 infections/1,000 patient-days) or 7.02 infections/1,000 admissions (range, 2.86–24.66 infections/1,000 admissions). The number of days of surveillance ranged from 81 to 119 days, because not all sites were able to start and end surveillance on the specified dates. The number of cases at each site and incidence data are summarized in Table 1. The incidence of HA-FRI in the PICU setting was 2.87 infections/1,000 patient-days (range, 0–4.33 infections), and in the NICU setting it was 0.25 infections/1,000 patient-days (range, 0–1.00 infections). Incidence data for intensive care units are summarized in Table 2.

The 96 case patients' infections included 28 upper respiratory tract infections (29%), 38 cases of pneumonia (40%), 12 other lower respiratory tract infections (13%), and 18 respiratory infections that were not specifically identified (19%). The patients' characteristics are summarized in Table 3. The number of HA-FRIs identified at each site ranged from 2 to 35. No outbreaks were reported. Of the 96 case patients, 48 (50%) were 1 year of age or less, and the median age was 13 months. The median length of stay prior to symptom onset was 24 days (range, 3–1,105 days) for the 89 case patients for whom this information was available. There was no statistically significant difference noted in length of stay prior to symptom onset according to patient age ($P = .26$). Fifty-two (54%) of the 96 patients were male. Fifty-nine (62%) of the patients were hospitalized in a pediatric medicine ward or in a PICU at the time of symptom onset. Eight patients (8%) required transfer to the PICU, and 2 of these patients required mechanical ventilation after transfer. The viral pathogens most commonly recovered from patients transferred to the PICU were RSV and parainfluenza, each of which was recovered from 3 case patients. Coinfection with a bacterial pathogen was also noted in 2 of the case patients transferred to the PICU.

Underlying chronic conditions were noted in 72 (75%) of the patients; the 2 most common were congenital heart disease, which affected 17 patients (24%), and chronic lung disease, which affected 13 (18%). For 2 case patients, it could not be determined whether a chronic condition was present, because the data forms were incomplete. When the patients who had length of stay data available were compared, the

TABLE 2. Incidence of Healthcare-Acquired Febrile Respiratory Infection in the Pediatric Intensive Care Unit (PICU) and Neonatal ICU (NICU), Canadian Nosocomial Infection Surveillance Program Surveillance, 2005

	No. of case patients			PICU		NICU	
Surveillance site	PICU ($n = 28$)	NICU ($n = 4$)	Surveillance period, days	No. of patient-days	Infections per 1,000 patient-days	No. of patient-days	Infections per 1,000 patient-days
A	1	1	81	475	2.11	1,182	0.85
B	21	0	111	4,850	4.33	3,817	0
C	2	1	111	880	2.27	1,634	0.61
D	0	2	90	184	0	2,016	1.00
E	3	0	119	1,565	1.92	1,473	0
F	0	0	113	775	0	1,594	0
G	0	0	119	388	0	4,130	0
H	1	0	119	630	1.59	NA	NA
Total	28	4	…	9,747	2.87	15,846	0.25

NOTE. NA, not available (ie, this site was unable to provide patient-days for the NICU).

TABLE 3. Demographic and Clinical Characteristics of 96 Patients With Healthcare-Acquired Febrile Respiratory Infection, Canadian Nosocomial Infection Surveillance Program Surveillance, 2005

Characteristic	Value
Age, median (range), months	13 (0–195)
Male sex	52 (54)
Length of stay prior to symptom onset, median (range), days[a]	24 (3–1,105)
Ward housing patient at time of symptom onset	
Pediatric medicine	31 (32)
Pediatric intensive care unit	28 (29)
Hematology or stem cell and organ transplantation	15 (15)
Surgery	12 (13)
Other	10 (10)
Underlying chronic medical condition	
Any	72 (75)
Congenital heart disease	17 (24)
Chronic lung disease	13 (18)
Neurologic and/or genetic disorder	11 (15)
Other or unknown	8 (11)
Outcome at 30 days	
Discharged home	62 (65)
Remained in hospital	22 (23)
Death	9 (9)
Transferred to another hospital	3 (3)

NOTE. Data are no. (%) of patients, unless otherwise indicated.
[a] Length of stay data were unavailable for 7 patients.

median length of stay prior to infection for the 68 patients with underlying chronic medical conditions was 28 days, whereas it was 14 days for the 21 patients without such conditions ($P = .15$). The median age of patients with underlying chronic medical conditions was 17 months, compared with 8 months for patients without such conditions ($P = .22$).

Nine deaths occurred within 30 days after the FRI; 1 was directly related to the FRI, and 2 were indirectly related to the FRI. All deaths occurred in patients with underlying chronic medical conditions, and 7 (78%) of the deaths occurred in patients aged 1 year or less (Table 4).

Treatment with antibiotics was provided to 38 patients, whereas only 5 patients were treated with antiviral medications. All case patients treated with antiviral medication had laboratory-confirmed viral infections (2 patients were infected with RSV, 1 with influenza A, 1 with influenza B, and 1 with adenovirus).

Laboratory confirmation of infection was available for 88 patients (92%), from whom 101 pathogens were recovered. Eight case patients received a clinical diagnosis without laboratory confirmation of their infections. Respiratory viruses accounted for 72 (71%) of the pathogens recovered. The results of the microbiological analysis are summarized in Table 5. There were 65 patients from whom only viral pathogens were recovered, 18 from whom only bacterial pathogens were recovered (a single organism was recovered from 14, and multiple organisms were recovered from 4), and 5 from whom both viruses and bacteria were recovered. Bacterial pathogens were commonly recovered from patients who received mechanical ventilation in the ICU. Overall, 23 (82%) of 28 patients who were already receiving mechanical ventilation developed nosocomial pneumonia, and bacteria were recovered from 20 (87%) of these patients.

Blood cultures yielded pathogens for 2 patients with bacterial infection. The onset of infection occurred in the ICU for 15 (83%) of 18 patients infected with bacterial pathogens alone, compared with 11 (17%) of 65 patients infected with viral pathogens alone ($P < .001$). There were no statistically significant differences noted between patients with bacterial pathogens and patients with viral pathogens with regard to mean age or length of stay.

Influenza vaccination was documented for only 2 of 13 patients with influenza who were also candidates for influenza vaccination; 2 were not vaccinated, and data were not available for the other 9. However, 4 of 5 patients infected with RSV who were also eligible for immunoprophylaxis had received prophylaxis. Of the 3 patients with pneumococcal infection, none were high-risk candidates eligible for the conjugate vaccine on the basis of age or chronic disease criteria.

DISCUSSION

To our knowledge, this is the first report of systematic surveillance across Canada for HA-FRI in the pediatric population. The results reaffirm the importance of viruses, particularly RSV, as the pathogens most frequently observed to cause these infections. Furthermore, the patients most likely

TABLE 4. Characteristics of 9 Patients Who Died Within 30 Days After Onset of Healthcare-Acquired Febrile Respiratory Infection (FRI), Canadian Nosocomial Infection Surveillance Program Surveillance, 2005

Patient number	Age	Sex	Medical condition(s)	Pathogen (preventive treatment status)	Housed in ICU at time of onset	FRI contributed to death
1	1 month	M	Congenital heart disease, receipt of organ transplant	RSV (received RSV mAb)	Yes	No
2	3 months	F	Congenital heart disease	RSV (did not receive RSV mAb)	Yes	No
3	4.8 years	M	Congenital heart disease	Influenza A (received influenza vaccine)	Yes	No
4	4 months	M	Leukemia	RSV[a]	No	Could not be determined
5	6.7 years	F	Neurodegenerative disorder	*Staphylococcus aureus* (NA)	Yes	No
6	7 months	M	Severe combined immunodeficiency, receipt of hematopoietic stem cell transplant	*Stenotrophomonas maltophilia* (NA)	Yes	No
7	Newborn	F	Congenital heart disease	Adenovirus (NA)	Yes	Yes, indirectly
8	1 month	F	Short gut, chronic lung disease	RSV (received RSV mAb)	Yes	Yes, directly
9	1 year	M	Cholestasis, chronic lung disease[b]	*Serratia marcescens* (NA)	Yes	Yes, indirectly

NOTE. ICU, intensive care unit; NA, not applicable; RSV, respiratory syncytial virus; RSV mAb, anti-RSV monoclonal antibody.
[a] Patient was not eligible for RSV prophylaxis.
[b] Patient also received total parenteral nutrition.

to be affected are those with underlying chronic medical conditions and those aged 1 year or less. In particular, children with a high risk of FRI-related mortality include those with underlying congenital disease and/or immune deficiency and those admitted to the ICU.

There are few publications that document the rate of healthcare-acquired respiratory infection among pediatric patients in Canada. In 1989, rates of 2.5–16.9 infections/1,000 admissions were reported for healthcare-acquired respiratory infection in different age groups at a major Canadian pediatric hospital.[11] Most studies of healthcare-acquired respiratory infection in pediatric patients have focused on RSV infection alone. The role of other respiratory viruses in healthcare-acquired infection has not been studied as frequently. In 1997, Langley et al.[12] reported that 91 (6%) of 1,516 patients with RSV infection in 9 Canadian university-affiliated hospitals had healthcare-acquired infection; 4 of these patients died. In another report, 19 cases of healthcare-acquired influenza that occurred over a 5-year period from 1994 to 1999 were identified by retrospective medical record review.[13] These cases represented 7.6% of all influenza diagnoses at the institution during that period. Rates of infection were not reported in these studies.

Similarly, there are sparse published data on the rates of HA-FRI in pediatric hospitals outside of Canada. A prospective study performed in Germany reported a healthcare-acquired lower respiratory tract infection rate for children less than 3 years of age of 0.79 infections/1,000 hospital-days.[14] As 50 (52%) of the 96 HA-FRIs we observed involved the lower respiratory tract, this rate is similar that observed in our study. The rates of healthcare-acquired RSV infection in a hospital in the United States were found to be 0.98 and 0.73 infections/1,000 patient-days, respectively, before and after intensive multidisciplinary infection control interventions.[15]

There were some limitations to the surveillance for this study. The results may not be representative of pediatric wards across Canada; the sites that took part in this project were all tertiary care pediatric centers, and these hospitals treat the most complex pediatric cases. The wide variation in infection rates among the sites may be related to differences in the complexity of cases and volume of patients treated at these institutions. Comparisons among hospitals may be of limited value. The intensity of exposure to respiratory infection likely varies from one hospital to another. It was also assumed that the viral respiratory infection season was identical for the populations under surveillance, although there may be some variation from one region to another. In addition, total hospital rates do not consider the differences between hospitals with respect to case mix. Certain populations, such as those housed in surgery wards, contribute to the denominator data but may be at lower risk of exposure to respiratory infection.

Furthermore, there was no assessment of the differences between sites with regard to infection control practices or policies that may have contributed to the variation in rates. One issue that we did not address in this surveillance is the incubation periods of different pathogens. Some cases of FRI may have been misclassified as healthcare acquired if symptoms of infection were not evident at admission as a result of the prolonged incubation period of some pathogens (eg, RSV has an incubation period of 2–8 days[16]). However, this is unlikely to have affected our results significantly, because the median length of stay prior to symptom onset was 24 days.

In addition, the sites may have varied regarding their in-

TABLE 5. Distribution of 101 Pathogens Recovered From 88 Case Patients With Healthcare-Acquired Febrile Respiratory Infection, Canadian Nosocomial Infection Surveillance Program Surveillance, 2005

Pathogen	No. (%) of isolates
Respiratory syncytial virus	38 (38)
Influenza A	9 (9)
Influenza B	8 (8)
Parainfluenza	11 (11)
Adenovirus	6 (6)
Staphylococcus aureus[a]	7 (7)
Haemophilus influenzae	4 (4)
Moraxella catarrhalis	4 (4)
Streptococcus pneumoniae	3 (3)
Pseudomonas aeruginosa	3 (3)
Enterobacter cloacae[b]	2 (2)
Other bacteria	6 (6)

[a] Includes 2 patients with bacteremia due to 2 organisms, *S. aureus* and *E. cloacae*.

[b] Pathogen recovered from 2 case patients who had bacteremia due to 2 organisms, *S. aureus* and *E. cloacae*.

dications for performing diagnostic tests, and they may not have had the same diagnostic tests available, both of which would have affected the number of laboratory-confirmed cases. For example, our surveillance did not identify any cases of human coronavirus infection, because testing for such infection is not usually part of routine laboratory analysis of respiratory specimens in Canada. In contrast, targeted surveillance in France has produced reports of human coronavirus causing healthcare-acquired infections in patients in PICUs and NICUs.[17,18] With regard to the 18 case patients in the present study who had infections of presumed bacterial origin—except for the 2 case patients who simultaneously had bacteremia—it is uncertain whether the organisms recovered were those that caused the infection. These organisms were identified in tracheal aspirate samples and bronchoalveolar lavage fluid specimens. However, the vast majority of patients (20 [87%] of 23) identified by this surveillance who were already receiving mechanical ventilation and went on to develop nosocomial pneumonia also had bacterial pathogens recovered from respiratory samples, which suggests true bacterial infection. Overall, the laboratory methods used and the period of surveillance selected (fall and winter) favored the identification of viruses. We chose this approach to assess the nosocomial infection rates during the period of highest risk.

Clinical cases (ie, cases that were not laboratory confirmed) accounted for only 8 (8%) of 96 cases of HA-FRI identified by this surveillance and may thus have been underreported. Clinical surveillance requires more time and effort than laboratory surveillance, and the effort expended to identify these cases may not have been consistent across sites. Nevertheless, clinical surveillance has the advantage of detecting patients with HA-FRI who may be infected with viruses for which there are currently no readily available or standardized tests, and this approach ensures that results will not be affected by variations in how frequently laboratory testing is performed at different sites. The frequency of testing could be addressed in a future study by sampling a cohort of all medical records for review.

Despite these limitations, the results of the present study provide Canadian pediatric centers with baseline data that can be used for comparison in the future. Rates for individual hospitals will be useful for comparison over time and for monitoring the results of new infection control measures.

Another issue that is not routinely addressed in most hospital surveillance is the contribution of staff and visitors to the overall burden of HA-FRI in pediatric hospitals. Our surveillance was not designed to monitor FRI in the relevant adult population, a factor that complicates the assessment of HA-FRI in pediatric centers. It is important to note that our surveillance was also not designed to detect HA-FRI in patients who were discharged early. No postdischarge surveillance was conducted to identify patients who may have later developed symptoms at home. Because FRI acquisition is affected by length of stay, this surveillance was more likely to detect infection in specific patient populations with a prolonged length of stay.

Information on influenza vaccination was missing for many patients with influenza. In contrast, most patients eligible for RSV immunoprophylaxis were known to have received it, which suggests that awareness regarding RSV immunoprophylaxis is quite high. This prophylaxis is usually provided by specialized, hospital-based clinics, and information on vaccination status may be more easily accessible for this select group of patients than for the very broad group of children eligible for influenza vaccination. Furthermore, some of these patients may never have left the hospital.

In conclusion, these data will help clarify the burden of HA-FRI in Canadian pediatric hospitals. Accurate identification of high-risk patients will help infection control programs improve current practices, with the ultimate goal of eliminating HA-FRI from pediatric wards. For the first time, incidence rates are available that can be used for comparison in the future. Further work needs to be done to raise awareness regarding influenza vaccination among medical personnel so that vaccination status becomes a routine question when a patient is admitted during the influenza season, and patients eligible for vaccination are offered vaccine in the hospital where possible.

MEMBERS OF THE CANADIAN NOSOCOMIAL INFECTION SURVEILLANCE PROGRAM WHO PARTICIPATED IN SURVEILLANCE FOR HEALTHCARE-ACQUIRED FEBRILE RESPIRATORY INFECTION IN 2005

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