Surveillance of severe acute respiratory syndrome (SARS) in the post-outbreak period

I H G Escudero, M I Chen, Y S Leo

ABSTRACT

Introduction: This retrospective one-month survey evaluated the practicality of post-severe acute respiratory syndrome (SARS) surveillance recommendations in previously SARS-affected countries, namely Singapore. These included staff medical sick leave for febrile illness, inpatient fevers, inpatient pneumonia, atypical pneumonia, febrile illnesses with significant travel history and sudden unexplained deaths from pneumonia/ adult respiratory distress syndrome (ARDS).

Methods: Surveillance data on medical sick leave of staff, all inpatient fevers, all febrile (temperature greater than or equal to 38 degrees Celsius) inpatient pneumonia, including atypical pneumonia, and deaths from pneumonia were collected from sick leave reports, ward reports, isolation room rounds and mortuary reports from 1 to 28 September 2003.

Results: Baseline results show 167 (1.4/1000 staff-days) observed in staff sick leave for febrile illnesses, and 1798 (71.3/1000 bed-days) observed for inpatient fever. There were 40, 31 and 12 instances, respectively, of staff having temperatures of high fever (greater than or equal to 38 degrees Celsius), prolonged sick leave (3 days or more), and repeated sick leave (within 7 days) for febrile illnesses. An average of 4.6 wards a day potentially fulfilled the World Health Organisation SARS alert criteria. Of 27 cases with fever, pneumonia and a total white count of less than 10,000 cells per cubic mm as per Ministry of Health, Singapore criteria for the diagnosis of atypical pneumonia, only five were identified by clinicians.

Conclusion: Surveillance is time-consuming and current recommendations are not specific enough to be used practically. Surveillance indicators for inpatients must overcome a high degree of background noise.

Keywords: atypical pneumonia, infectious disease, severe acute respiratory syndrome (SARS), surveillance

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INTRODUCTION

Within the span of a few months, the severe acute respiratory syndrome (SARS) spread rapidly across multiple cities worldwide[1-6]. In Singapore, SARS caused 238 cases and 33 deaths. Economic losses have been estimated at 4.6 billion Singapore dollars for the local tourism industry alone[7]. The disease is now recognised to be due to a new coronavirus that spread through close person-to-person contact via infected droplets[8]. It is uncertain if there will be a future resurgence of SARS. Evidence is mounting that animal reservoirs exist, and that the disease could therefore re-enter the human population leading to future outbreaks[9]. Early detection has been recognised as a critical factor in outbreak management. While the aim would be to detect and isolate cases at diagnosis, it was evident from the previous epidemic that cases with atypical presentation may not be recognised till after their admission to a general ward[10], with potentially devastating consequences[11].

The World Health Organisation (WHO) has issued guidelines on the alert, verification and management of SARS in the post-outbreak period[12]. The Ministry of Health (MOH) in Singapore has also issued internal guidelines on post-epidemic SARS surveillance[13]. Key elements include reporting of "atypical pneumonia" admitted from the community, febrile cases with travel history to other previously SARS affected areas, sudden deaths due to pneumonia and/or adult respiratory distress syndrome (ARDS), and fever clusters among healthcare staff and inpatients.

Tan Tock Seng Hospital (TTSH) is an acute hospital with more than 4,000 staff members, and was the first hospital in Singapore to be affected during the outbreak. Under normal operating conditions, the hospital has over 60 intensive care unit (ICU) beds, about 50 isolation rooms and more than 700 general ward beds. There are close to 30 general wards, with an average general ward numbering about 35 beds. Average length of stay is about six days. Various surveillance measures have been introduced since August 2003. Data from

September 2003 was reviewed in detail to establish the baseline, and evaluate the following surveillance indicators: (1) staff medical sick leave for febrile illness, (2) inpatient fevers, (3) inpatient pneumonia, (4) atypical pneumonia, (5) febrile illnesses with significant travel history, and (6) sudden unexplained deaths from pneumonia / ARDS.

METHODS

Surveillance data were collected for four weeks from the period 1 September to 28 September 2003 (dates inclusive). Data for medical certificates (MC) of staff on sick leave was obtained from a computerised system that have been functional since 1 July 2003. The system collected date of consultation, duration of MC, diagnosis, and principal symptoms of fever, cough, diarrhoea, rash, sore eyes, limb weakness and myalgia. All MCs with fever as a symptom were selected. Prolonged MCs were defined as MCs with duration of three or more days, and repeat MCs were defined as an MC within seven days of the previous MC. A cluster of staff was defined as two or more staff from the same department or work area (e.g. ward, specialist clinic, emergency department) with fever on overlapping MCs.

Data on inpatient surveillance was obtained from ward nurses, who would fax the surveillance team a list of patients with any temperature of 38 degrees Celsius or more in the last 24 hours. Information included the patient's working diagnosis, and whether the patient had pneumonia. Pneumonias referred to here are hence only those with fever of ≥38ºC at some point and chest radiograph (CXR) changes as perceived by the treating physician. A cluster of cases was defined as a group of febrile cases within the same ward, which were not in single rooms or isolation facilities. Cases with prolonged fever were those reported to have fever for three or more days; the days of fever did not have to be contiguous.

Cases having fever of three or more days with travel to China, Hong Kong, Taiwan, Toronto and Hanoi within 10 days of onset, or who were suspected of having atypical pneumonia based on their clinical picture, were identified by the emergency department (ED) and admitted to isolation rooms. Subsequently, ward teams would present the cases to a surveillance team led by a senior clinician during the "isolation room rounds". Cases with atypical pneumonia were classified at the round according to guidelines stated in the previously mentioned MOH directive[13], which were: (1) CXR findings suggestive of pneumonia, (2) fever of 38 degrees Celsius or more, (3) total white count ≤10,000 cells/mm^3 on admission, and (4) dry cough.

Of note, ED guidelines were more inclusive, using total white count of ≤12,000 cells/mm^3, and omitting "dry cough" as a criteria. In addition, a group that fulfilled criteria 1 to 3 within two days of admission were identified and analysed separately, to assess the impact of a simplified case definition of atypical pneumonia. The list of deaths was obtained from the mortuary. Death certificates were reviewed for any diagnosis of pneumonia or ARDS. Sudden and unexplained deaths were taken operationally to mean those referred to the coroner. In these, death summaries were used to indicate if the case had pneumonia or ARDS.

Conditions for a SARS alert as defined by WHO were[12]:

1. Two or more healthcare workers from the same healthcare unit fulfilling the clinical case definition for SARS with onset of illness in a 10-day period
2. Hospital acquired illness in three or more persons from the same healthcare unit, including health staff and/or patients fulfilling the clinical case definition of SARS and with onset of illness in the same 10-day period.

A clinical case definition of SARS consisted of fever (≥38°C), cough or shortness of breath, and radiographical or post-mortem evidence of lung infiltrates consistent with pneumonia or ARDS, without any concrete alternative diagnosis. As no staff contracted pneumonia-like illness during the study period, the potential number of SARS alerts was assessed on inpatients alone. The cumulative number of febrile pneumonias in each ward over a 10-day period was assessed after populating a database for the first 10 days of September, and observed for a two-week period from 11 September to 24 September inclusive. There was no attempt to further distinguish if the pneumonias were fully explained by other causes.

RESULTS

Table I gives an overview of the rates for each surveillance indicator. In the four weeks, the absolute number of positive observations for staff fevers, inpatient fevers and inpatients with pneumonia was fairly large, with an average of 65 per day for inpatient fevers, and an average of six to eight observations per day for other inpatient and staff surveillance indicators. Fig. 1 elaborates on the staff MC figures. 40 staff on MC for fever (24%) had a documented temperature ≥38ºC at consultation; 19 of these were ward-based staff, and on 11 occasions there were febrile patients in the ward they serviced.

Table I. Definition and characteristics of surveillance indicators.

	Episodes of staff MC for febrile illness	Inpatient fever days	[1]Prolonged inpatient fever	Inpatient pneumonia	[2]Atypical pneumonia	Febrile illness with travel	[3]Sudden unexplained deaths
Size of surveillance population	4,261 staff as of mid-Sept 2003	[4]25, 228 total bed-days	884 admissions observed to have fever ≥38°C between 1st Sept and 28th Sept		3,901 admissions to TTSH from 1st Sept to 28th Sep inclusive		
Number observed	167 fever MCs	1798 fever days	207 patients	180 patients	16 patients	6 patients	7 cases
Rate / unit	1.40 per 1,000 staff-days observed	71.3 per 1,000 bed-days observed	23.4% of all admissions with fever	20.4% of all admissions with fever	4.10 per 1,000 admissions	1.54 per 1,000 admissions	1.79 per 1,000 admissions

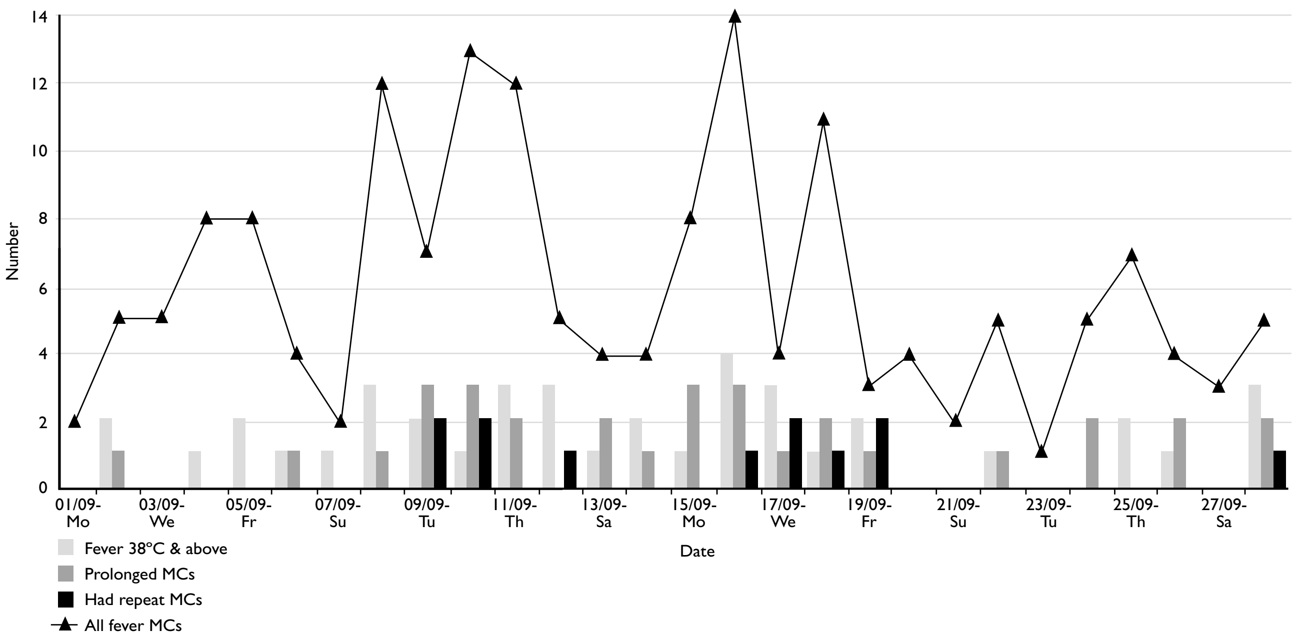
1 Prolonged inpatient fever were those reported to have fever for 3 or more days.

2 Atypical pneumonia as classified in isolation rounds.

3 Sudden unexplained deaths from pneumonia / ARDS based on mortuary records.

4 901 beds occupied (average for midpoint, 14/9 & 15/9).

Fig. 1 Staff MC surveillance for febrile illness.



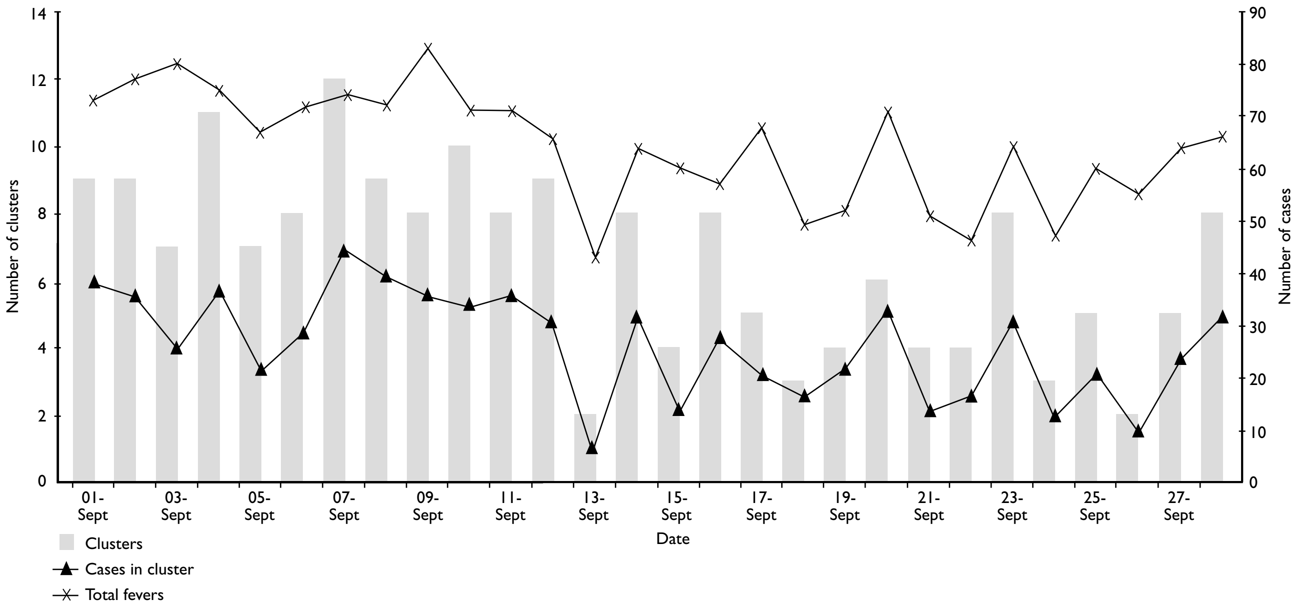
Prolonged MCs and repeated MCs were also uncommon observations (31 and 12 instances accordingly).

There were 27 occasions with clusters of two or more febrile staff from the same department, but only five clusters of three or more. When restricted to staff with temperatures ≥38ºC, there were only two clusters of two staff, and no clusters with three or more staff. About 81.4% of fever MCs was reported on the date of issue, and 15.6% on the day after, leaving only five instances with a delay of two or more days.

Fig. 2 examines inpatient fevers over the period of observation, with "fever clusters" of size three and above. 185 clusters were observed; on the average 6.6 wards per day had "fever clusters". The effect of altering the definition of a "fever cluster" is explored in Fig. 3. If cluster cut-off size were defined as 3 and above, more than 25 cases per day would qualify. For cluster sizes of 5 and above, an average of 11 cases in 2 clusters can be expected.

Table II shows the number of cases and the proportions assessed in isolation rounds for various target surveillance groups. The majority of pneumonia and prolonged fevers were never assessed in the isolation rounds, as well as more than half the patients meeting the simplified "atypical pneumonia" criteria. There was poor correlation between the "atypical pneumonia" classified during the isolation rounds and those identified with the simplified criteria, with only 5 cases common to both groups. An average of 4.6 wards a day potentially fulfilled the WHO SARS alert criteria of having three or more pneumonias

Fig. 2 Ward clusters and fever cases.



within the last 10 days; there was a turnover of about one ward in two days.

DISCUSSION

This paper is the first to profile the baseline for various surveillance indicators that have been suggested for SARS. In a literature review, several other studies have explored the incidence of sick leave in healthcare workers in relation to infectious disease[14,15]. One study, which used all-cause sickness absence, noted a lack of correlation between sickness absence and the northern hemisphere influenza season[15]. The study recognised that all-cause sickness absence was a crude indicator, and may have obscured its ability to detect genuine increases in respiratory illness. The other study[15] commented on how documented fever was only present in 2.8% of 879 sick visits recorded in a year amongst 2,400 employees.

Our study concurs that documented fever is a rare occurrence in sick leave among staff, and finds that among indicators aiming to detect secondary transmission of a severe infectious disease within the hospital, a system for monitoring of febrile illness in staff is practical and likely to be effective. Other than looking for a "clustering effect", it may also be useful to identify staff with prolonged MCs, repeated MCs, and high fevers. These events occur about once a day or less in a pool of more than four thousand staff, and hence are candidates for early surveillance signals.

The difficulty is in distinguishing staff that are ill with other febrile conditions from SARS within

Fig. 3 Effect of cluster size on number of patients and clusters under observation.

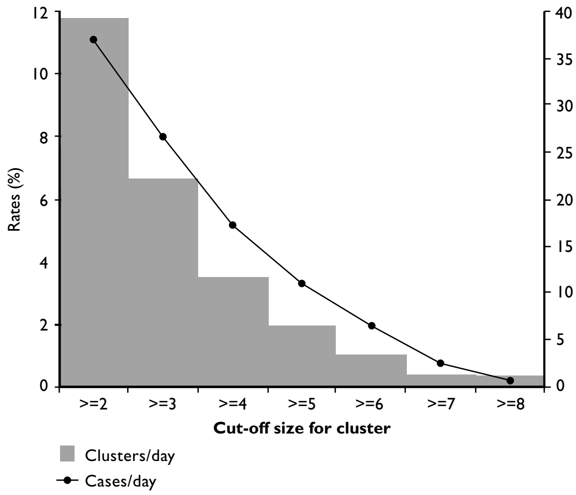


Table II. Proportion of surveillance cases assessed in isolation rounds.

Surveillance group	Total cases	Ever assessed in isolation rounds (%)
1. Inpatients with prolonged fever	207	46 (22.2%)
2. All inpatients with pneumonia	180	64 (35.6%)
#3. Atypical pneumonia classified during isolation rounds	16	^NA
#4. Inpatients meeting simplified criteria for atypical pneumonia	27	12 (44.4%)
5. Deaths with pneumonia	57	17 (29.8%)
6. Sudden deaths with pneumonia	7	1 (14.3%)
7. Fever with travel history	6	^NA

Only 5 cases appear under both surveillance indicators 3 and 4.

^ Not applicable: by sampling definition, all cases classified in this category are assessed.

as short a period of time as possible. Studies are hence needed to compare retrospective data on early presentations of SARS against other common illnesses in otherwise healthy healthcare workers. While we were limited by time and resources in our ability to investigate the clusters of febrile illness detected among staff in this study, we would recommend that any prospective studies also attempt to identify the aetiological agents involved in such clusters, as knowledge on the identity of such agents may further aid in distinguishing clusters of febrile illness. This was certainly the case during the outbreak of acute respiratory febrile illness at the Institute of Mental Health in Singapore during the SARS period[16], where the diagnosis of influenza B helped to rule out SARS. Moreover, such clusters also have nosocomial transmission potential in their own right, and be amenable to preventative measures, as is the case in influenza.

In contrast, surveillance methods aimed at detecting transmission in inpatient populations require more detailed clinical information in order to improve specificity. At least one episode of fever exceeding 38 degrees Celsius was noted among 36%[17] and 29%[18] of patients in two other studies of inpatients from acute hospitals; this is comparable to the 22.7% found in our study. As a result of the high prevalence, clusters of high fevers in general wards are hence common events. In order to achieve a manageable number of false alarms, the cut-off may need to be raised to 5 or more cases. Should an outbreak of SARS occur at a point when background noise from other febrile illnesses in that ward is at a maximum, a fairly large outbreak will be required to generate a surveillance signal.

Unpublished data from the outbreak of SARS in TTSH show that attack rates in staff were generally higher than for inpatients. Where multiple inpatients were infected, healthcare workers were already infected in numbers that trigger the present staff surveillance system. Combining staff with inpatient surveillance may help in detecting smaller-sized outbreaks, but the improvement in performance is marginal. Of 19 ward-based staff with fevers (≥38ºC), more than one-half were from wards with concurrently febrile inpatients. Unless there are other reasons for monitoring inpatient fever clusters, it would be more expedient to flag all high fevers in ward-based staff, rather than routinely collect daily temperature data on several hundred inpatients.

The study also assessed the possibility of shifting the focus of inpatient surveillance from febrile clusters towards identification of individual cases which could potentially have "atypical SARS" missed on admission. The majority of prolonged inpatient fevers and pneumonia cases had never been assessed in the isolation rounds. Isolation and investigation for SARS in all cases fulfilling these non-specific definitions would strain resources. It was also difficult to further reassess the large number of such cases in detail from a centralised surveillance office. In essence, the objective of tracking such cases and the issue of how to distinguish them from active SARS has not been resolved. Even where such cases are identified, the surveillance team would still have to rely on the clinical judgment of the managing ward team.

The numbers of atypical pneumonias and deaths from pneumonia were more manageable as surveillance indicators. The team encountered difficulties in defining what constituted sudden unexpected deaths. While referral to the coroner's was used as a proxy indicator of "unexpectedness", this definition is likely to miss cases of SARS in patients, as what constitutes "unexpectedness" can be highly subjective. Surveillance for atypical pneumonias also demonstrated problems with consistent application of complex and subjective case definitions. The majority of cases labelled during the isolation rounds did not have documented temperature of ≥38ºC, or had total white counts exceeding 10,000 cells/mm^3, while 22 cases with pneumonia, fever and a low or normal total white were never labelled as "atypical pneumonia".

There could be various explanations for the discrepancy. Clinicians may have had strong suspicion of SARS or "atypical pneumonia" in cases that did not strictly fulfill the surveillance case definitions. Conversely, there could have been a lack of "dry cough" or the presence of alternative diagnoses in cases that fulfilled the simplified definition but were not reported. Some cases may also have developed pneumonic changes only after admission. As cases of "atypical SARS" presenting with a normal chest radiograph were responsible for some of the super-spreader events in the outbreak, such underreporting is of concern[11]. Moreover, the inconsistent application of case-definitions is a problem in itself, as it can lead to inaccurate baselines and artificial surges in notifications should an alert be raised. These factors degrade the utility of an atypical pneumonia notification system in detecting outbreaks of SARS in the community.

The study also assessed how frequently a WHO SARS alert may occur from clusters of inpatient pneumonias. While the overall number of such instances identified was manageable, the retrospective detection of the clusters limited our ability to investigate these cases and rule out SARS through definitive laboratory investigations, as well as document the presence or absence of laboratory-confirmed alternative diagnoses. We are only able to surmise, in retrospect, that these were not SARS due to the lack of onward transmission by the cases involved. We would like here to comment that the danger of applying the WHO SARS alert is that it specifies in its case-definition that the cases involved should lack an alternative diagnosis.

We note that the presence of "alternative diagnoses" can lead to a failure to diagnose SARS, particularly among inpatients with multiple co-morbidities. Notably, internal retrospective investigations detected four cases that were infected as inpatients which were not classified as probable SARS during the height of the outbreak, in spite of having significant contact histories; two of these also had definite radiographical evidence of pneumonia. These cases were only detected upon the review of serological test results for SARS, in a post-outbreak reclassification exercise concluded on 16 July 2003[19]. However, due to the high index of suspicion at the time, all four were managed with adequate contact and respiratory precautions during their admission to TTSH.

There were several limitations to this study. First, the period of surveillance is short, and it is uncertain whether and how seasonal trends may affect surveillance indicators. In particular, there is concern that an outbreak of influenza may lead to multiple clusters of febrile illness in staff leading to an untenable number of false alarms. Other than difficulties in extrapolating across time periods, inpatient surveillance indicators from TTSH may also not be applicable to other hospitals of different sizes and ward structures. Secondly, visitor surveillance was excluded from the study due to the complexity of data collection from this group.

Thirdly, the period of surveillance coincided with the admission of an isolated case of SARS contracted from a laboratory accident. This may have generated a heightened sense of alertness – indeed, during the incident; thorough contact tracing was performed for lists of patients exposed to the index at another health care institution. No evidence of transmission to hospital staff and inpatients was ever uncovered. However, we did retrospectively detect one exposed patient who had presented and was admitted to a general ward within our institution for prolonged fever, and was subsequently confirmed to have dengue virus infection. The incident highlights how such a surveillance system fails in its ability to detect and differentiate the large volume of febrile cases presenting to our acute hospitals, and its ultimate reliance on frontline clinicians to diagnose, differentiate, and then report unusual cases of febrile illnesses.

Moreover, there are limits of accuracy and detail in the present methods of notification. Since surveillance is a routine function, the need for accuracy and detail must be balanced against the burden of data collection. As it is, the present system of inpatient fever surveillance is resource intensive and untested in its effectiveness. Ultimately, the critical question is whether such surveillance measures are able to detect future outbreaks of SARS. There is no data on the sensitivity and time-sensitivity of any of the above methods, and in the absence of a new outbreak, modeling approaches will be required to answer such questions.

While awaiting the answers, there is a pressure to sacrifice specificity with the hope of increasing sensitivity. However, an unreasonable number of false alarms can lead to surveillance fatigue, leading to a failure to respond appropriately in the event of a real outbreak. The efficient nosocomial transmission of SARS, its significant mortality, and its wider impact of disruption to society and economies, has led to an interest in workable surveillance systems, particularly those aimed at detecting intra-hospital transmission.

To this end, practical indicators have to be found in staff surveillance. Inpatient surveillance will only be useful when universal respiratory precautions are deployed, where widespread transmission may then occur without affecting staff.

However, it must be noted that surveillance systems for intra-hospital transmission are targeted at the first generation of secondary cases resulting from an infectious patient being admitted to the general ward. The hospital's best defence is thus sound clinical judgment at the level of the admitting services, guided by accurate surveillance information from international and national sources. For this purpose, it is also imperative to simplify case definitions used for atypical pneumonia, and improve the consistency of reporting. SARS may or may never recur, but the need to constantly evaluate and re-evaluate our present surveillance systems goes on.

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