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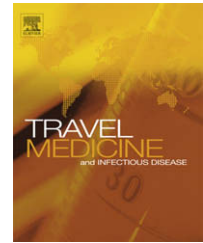
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INVITED SUBMISSION

# Imported infectious diseases and surveillance in Japan

Kiyosu Taniguchi\*, Makiko Yoshida, Tomimasa Sunagawa, Yuki Tada, Nobuhiko Okabe

*Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, Japan*

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## KEYWORDS

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**Summary** Surveillance of imported infectious diseases is important because of the need for early detection of outbreaks of international concern as well as information of risk to the travelers. This paper attempts to review how the Japanese surveillance system deals with imported infectious diseases and reviews the trend of these diseases.

The cases of acquired infection overseas were extracted from the surveillance data in 1999–2008. The incidence and rate of imported cases of a series of infectious diseases with more than one imported case were observed by the year of diagnosis and place of acquired infection.

During the period 10,030 cases that could be considered to be imported infectious diseases were identified. Shigellosis ranked as the most common imported disease, followed by amebiasis, malaria, enterohemorrhagic *Escherichia coli* infection and the acquired immunodeficiency syndrome, typhoid fever, dengue fever, hepatitis A, giardiasis, cholera, and paratyphoid fever. The annual trends of these diseases always fluctuated but not every change was investigated.

The study reveals that the situation of imported infectious diseases can be identified in the current Japanese surveillance system with epidemiologic features of both temporal and geographic distribution of cases of imported infectious diseases. However, further timely investigation for unusual increase in infectious diseases is needed.

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## Introduction

Because of the current global travel and trade, there is no border for infectious diseases. Even in Japan, which belongs to a temperate climate zone many tropical infectious diseases are found in the local hospitals. But there have been several case reports describing difficulty of early

\* Corresponding author. Tel.: +81 3 5285 1111; fax: +81 3 5285 1129.

E-mail address: [tanigk@nih.go.jp](mailto:tanigk@nih.go.jp) (K. Taniguchi).

diagnosis and treatment.<sup>1–3</sup> It is important to provide information to travelers on particular risks and to increase protection, as well as information for local clinicians on the current situation of endemicity of infections in the foreign countries in order to facilitate early diagnosis and to avoid nosocomial infection. From the viewpoint of public health, the introduction of new pathogens may result in their establishment in the country.

Public health surveillance is one of the essential components for infectious disease control and no doubt a starting point for control. Because of current circumstances a surveillance system should be designed not only at the national level but also at the global level of infectious disease control. Current National Epidemiological Surveillance for Infectious Diseases (NESID) in Japan requires that all notifiable diseases should be reported with the presumptive place of infection. This report summarizes the data from the NESID from 1999 to 2008 on the situation of imported infectious diseases in Japan.

## Materials and methods

### Surveillance of infectious diseases in Japan

The National Epidemiological Surveillance for Infectious Diseases (hereafter referred to as NESID) is conducted based on the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections (hereafter referred to as the Infectious Disease Control Law) enacted in April 1999. Infectious disease surveillance system before then is described elsewhere.<sup>4</sup> Infectious diseases included in this law were categorized into I–V with specific means for control based upon the public health impact of each disease as shown in Table 1.

All physicians must report cases of Categories I–IV immediately and Va within 7 days after identification to local public health centers which are the primary level institution for disease control and prevention located strategically throughout the nation. Local public health centers are expected to enter data into the nationwide electronic surveillance system, which enables data to be shared throughout the system including all local public health centers, local and national governments, quarantine stations, local infectious disease surveillance center, local public health laboratory and central infectious disease surveillance center, which is the Infectious Disease Surveillance center of National Institute of Infectious Diseases. Category Vb diseases, which include sentinel reporting diseases, should be reported by designated sentinel medical institutions weekly or monthly with the number of clinical cases aggregated by sex and age groups. All reports should be compatible with the reporting criteria which were documented in detail for each disease including clinical and laboratory case definitions for categories Va and Vb of hospital sentinel reporting disease, and only clinical case definitions for other Vb sentinel reporting diseases.<sup>5</sup>

Cases of category I–Va diseases should be reported with sex, age, method of laboratory confirmation, symptoms on diagnosis (descriptive), date of onset, date of consultation, date of diagnosis, estimated date of infection, date of

death (if patients died), area of permanent residence (in-country or foreign countries), presumptive place of infection (domestic or foreign countries), contact to the vectors or activities on the fields (Yes or No), estimated infection route, another patients in the family members, colleagues, or neighbors (Cluster or NOT). The presumptive place where infection was acquired should be described based on reasonable situation considering travel history and incubation period according to the interview of patients.

### Surveillance data and method of analysis

The cases with the presumptive place of infection in a foreign country (hereafter referred to as imported cases) were extracted from the NESID data from April 1999 to March 2008. Data in 1999 are only available in April–December because of the change of the law in April 1999 and data in 2008 are included until March. Finally nine years data are reviewed. Annual trend of total, imported, and domestic cases of disease containing one or more imported one are recorded and attributable events and causes are investigated with information in the line listing data and relevant epidemiological reports. Incidence rates per 1,000,000 population are calculated using the 2002 census population and imported disease per 1,000,000 outbound travelers are calculated using the 2002 outbound travelers by the Japan National Tourist Organization.

## Results

In the period observed 10,030 cases that could be considered to be imported infectious diseases were identified. These include various infectious diseases as listed in Table 2 with reported number of cases (imported, domestic, unknown and total), imported case rate among imported and domestic cases, incidence rate of domestic cases per year per 1,000,000 population and the incidence rate of imported cases per year per 1,000,000 outbound travelers.

Shigellosis ranked as the most common imported infection, followed by amebiasis, malaria, enterohemorrhagic *Escherichia coli* (EHEC) infection and the acquired immunodeficiency syndromes (AIDS), typhoid fever, dengue fever, hepatitis A, giardiasis, cholera, and paratyphoid fever. The rate of imported diseases of malaria, dengue fever and rabies is complete as they are not endemic in Japan and over 50% in coccidioidomycosis, paratyphoid fever, typhoid fever, cholera, shigellosis and Echinococcosis (*Echinococcus granulosus*). Although coccidioides is not considered to be indigenous, a domestic case is identified with no history of overseas travel. However, this case was a dealer of imported cotton and he may have acquired the infection from fungi attached to the imported cotton.<sup>6</sup>

The annual trends of imported diseases always fluctuate because of the local situation and sometimes there is sudden increase because of cluster among the same tour groups. The Figure shows the annual trend of selected diseases with a large number of imported diseases every year (Fig. 1 for diarrheal disease and Fig. 2 for febrile diseases). Cholera and giardiasis did not show much change. However, case reports of cholera increased in 2004 with 67 cases, among which many were returning travelers from the Philippines in June

**Table 1** Target diseases of the Infectious Diseases Control Law (Reportable infectious diseases under the National Epidemiological Surveillance of Infectious Diseases)*Target diseases to be notified all cases by all physicians*

## Category I (to be notified promptly after diagnosis)

Crimean-Congo hemorrhagic fever,<sup>a</sup> Ebola hemorrhagic fever,<sup>a</sup> Lassa fever,<sup>a</sup> Marburg disease,<sup>a</sup> Plague,<sup>a</sup> Smallpox,<sup>a</sup> South American hemorrhagic fever<sup>a</sup>

## Category II (to be notified promptly after diagnosis)

Acute poliomyelitis,<sup>a</sup> Diphtheria,<sup>a</sup> Severe acute respiratory syndrome (due to SARS coronavirus),<sup>a</sup> Tuberculosis,<sup>a</sup> Avian influenza virus infection (H5N1 subtype)<sup>a</sup>

## Category III (to be notified promptly after diagnosis)

Cholera,<sup>a</sup> Enterohemorrhagic *Escherichia coli* infection,<sup>a</sup> Paratyphoid fever,<sup>a</sup> Shigellosis,<sup>a</sup> Typhoid fever<sup>a</sup>

## Category IV (to be notified promptly after diagnosis)

Anthrax,<sup>a</sup> Avian influenza virus infection (excluding H5N1 subtype),<sup>a</sup> Botulism,<sup>a</sup> Brucellosis,<sup>a</sup> Coccidioidomycosis,<sup>a</sup> Dengue fever,<sup>a</sup> Eastern equine encephalitis,<sup>a</sup> Echinococcosis,<sup>a</sup> Epidemic typhus,<sup>a</sup> Glanders,<sup>a</sup> Hantavirus pulmonary syndrome,<sup>a</sup> Hemorrhagic fever with renal syndrome,<sup>a</sup> Hendra virus infection,<sup>a</sup> Hepatitis A, Hepatitis E,<sup>a</sup> Herpes B virus infection,<sup>a</sup> Japanese encephalitis,<sup>a</sup> Japanese spotted fever,<sup>a</sup> Kyasanur Forest disease,<sup>a</sup> Legionellosis,<sup>a</sup> Leptospirosis,<sup>a</sup> Lyme disease,<sup>a</sup> Lyssavirus infection (excluding rabies),<sup>a</sup> Malaria,<sup>a</sup> Melioidosis,<sup>a</sup> Monkeypox,<sup>a</sup> Nipah virus infection,<sup>a</sup> Omsk hemorrhagic fever,<sup>a</sup> Psittacosis,<sup>a</sup> Q fever,<sup>a</sup> Rabies,<sup>a</sup> Relapsing fever,<sup>a</sup> Rift Valley fever,<sup>a</sup> Rocky Mountain spotted fever,<sup>a</sup> Scrub typhus (Tsutsugamushi disease),<sup>a</sup> Tick-borne encephalitis,<sup>a</sup> Tularemia,<sup>a</sup> Venezuelan equine encephalitis,<sup>a</sup> West Nile fever (including West Nile encephalitis),<sup>a</sup> Western equine encephalitis,<sup>a</sup> Yellow fever<sup>a</sup>

## Category Va (to be notified within 7 days after diagnosis)

Acquired immunodeficiency syndrome,<sup>a</sup> Amebiasis,<sup>a</sup> Acute encephalitis (excluding Eastern equine encephalitis, Japanese encephalitis, Rift Valley fever, Tick-borne encephalitis, Venezuelan equine encephalitis, West Nile encephalitis and Western equine encephalitis),<sup>a</sup> Congenital rubella syndrome,<sup>a</sup> Creutzfeldt–Jakob disease,<sup>a</sup> Cryptosporidiosis, Giardiasis, Measles,<sup>a</sup> Meningococcal meningitis,<sup>a</sup> Rubella,<sup>a</sup> Severe invasive streptococcal infections (Streptococcal toxic shock-like syndrome),<sup>a</sup> Syphilis, Tetanus,<sup>a</sup> Vancomycin-resistant *Enterococcus* infection,<sup>a</sup> Vancomycin-resistant *Staphylococcus aureus* infection,<sup>a</sup>

Viral hepatitis (excluding hepatitis A and E)

*Target diseases to be reported by the sentinel clinics and hospitals Category Vb*

## 'Influenza sentinel' (weekly report)

Influenza (excluding avian influenza virus infection)<sup>a</sup>

## 'Pediatric disease sentinel' (weekly report)

Chickenpox, Erythema infectiosum, Exanthem subitum, Group A streptococcal pharyngitis,<sup>a</sup> Hand, foot and mouth disease,<sup>a</sup> Herpangina,<sup>a</sup> Infectious gastroenteritis,<sup>a</sup> Mumps,<sup>a</sup> Pertussis,<sup>a</sup> Pharyngoconjunctival fever,<sup>a</sup> Respiratory syncytial virus infection<sup>a</sup>

## 'Eye disease sentinel' (weekly report)

Acute hemorrhagic conjunctivitis,<sup>a</sup> Epidemic keratoconjunctivitis<sup>a</sup>

## 'Sexually transmitted disease (STD) sentinel' (monthly report)

Condyloma acuminatum, Genital chlamydial infection, Genital herpes, Gonorrhoea

## 'Target diseases at sentinel hospital'

(weekly report)

Aseptic meningitis,<sup>a</sup> Bacterial meningitis,<sup>a</sup> Chlamydial pneumonia (excluding psittacosis), Mycoplasmal pneumonia (monthly report)

Methicillin-resistant *Staphylococcus aureus* infection, Multi-drug-resistant *Pseudomonas aeruginosa* infection, Penicillin-resistant *Streptococcus pneumoniae* infection

*Target disease of Syndromic surveillance designated by the government ordinance*

## 'Syndromic surveillance sentinel' (to be reported promptly after diagnosis)

Unknown fever ( $\geq 38$  °C) and respiratory symptom, Unknown fever and rash/vesicle

<sup>a</sup> Target disease of syndromic surveillance designated by the government ordinance.

and July.<sup>7</sup> The increase of imported Shigellosis in 2004 caused reportedly by the outbreaks among returnees from Hawaii due to an in-flight meal.<sup>8</sup> The number of EHEC cases that acquired infection in foreign countries, which until 2002 did not exceed 20–30, increased to 66 in 2003 and 151 in 2004. After a report from the Fukuoka Prefecture in 2003 of an outbreak during a school excursion to Australia, another outbreak among participants of a school excursion to Korea was reported from the Ishikawa Prefecture in 2004.<sup>9</sup>

Amebiasis tended to increase recently both in domestic and imported cases. And cases acquired infection through sexual contact represented 50% of the total cases.<sup>10</sup> There were continuous reports of imported disease of AIDS, syphilis and hepatitis B.

Dengue fever is increasing year by year, but malaria is decreasing gradually. Typhoid and paratyphoid fever and hepatitis A showed an increase and decrease throughout observation period. Although the outbreak among group

**Table 2** Number of imported, domestic and unknown origin cases for diseases with one or more imported one, 1999–2008<sup>a</sup>

Diseases	Imported	Domestic	Unknown	Total	Imported rate <sup>b</sup>	Incidence rate(1) <sup>c</sup>	Incidence rate(2) <sup>d</sup>
Shigellosis <sup>e</sup>	3847	1611	207	5665	0.70	1.40	25.87
Amebiasis	867	3648	667	5182	0.19	3.18	5.83
Malaria	802	0	0	802	1.00	0.00	5.39
Enterohemorrhagic <i>Escherichia coli</i> infection	552	31,774	1228	33,554	0.02	27.70	3.71
Acquired immunodeficiency syndrome							
Asymptomatic	479	4849	674	6002	0.09	4.23	3.22
AIDS	508	2160	540	3208	0.19	1.88	3.42
Others	62	547	72	681	0.10	0.48	0.42
Typhoid fever <sup>e</sup>	456	110	38	604	0.81	0.10	3.07
Dengue fever	449	0	0	449	1.00	0.00	3.02
Hepatitis A	431	2709	129	3269	0.14	2.36	2.90
Giardiasis	346	388	114	848	0.47	0.34	2.33
Cholera <sup>e</sup>	332	95	11	438	0.78	0.08	2.23
Paratyphoid fever <sup>e</sup>	283	26	13	322	0.92	0.02	1.90
Hepatitis B	186	2420	162	2768	0.07	2.11	1.25
Syphilis	153	5042	669	5864	0.03	4.40	1.03
Hepatitis E	65	211	2	278	0.24	0.18	0.44
Legionellosis	55	2389	37	2481	0.02	2.08	0.37
Cryptosporidiosis	34	230	1	265	0.13	0.20	0.23
Coccidioidomycosis	21	1	0	22	0.95	0.00	0.14
Scrub typhus	20	4075	7	4102	0.00	3.55	0.13
Meningococcal meningitis	17	102	8	127	0.14	0.09	0.11
Lyme disease	14	87	0	101	0.14	0.08	0.09
Echinococcosis							
<i>Echinococcus granulosus</i>	11	4	0	15	0.73	0.00	0.07
<i>Echinococcus multilocularis</i>	1	149	4	154	0.01	0.13	0.01
Leptospirosis	7	88	0	95	0.07	0.08	0.05
Psittacosis	7	292	2	301	0.02	0.25	0.05
Q fever	6	151	3	160	0.04	0.13	0.04
Hepatitis C	6	588	50	644	0.01	0.51	0.04
Brucellosis	4	4	1	9	0.50	0.00	0.03
Tetanus	4	847	7	858	0.00	0.74	0.03
Acute encephalitis <sup>f</sup>	3	824	21	848	0.00	1.08	0.03
Rabies	2	0	0	2	1.00	0.00	0.01

<sup>a</sup> The data in 1999 is from April to December, 2008 from January to March.

<sup>b</sup> Rate of imported/(imported + domestic) cases.

<sup>c</sup> Incidence rate is per year per 1,000,000 population in 1999–2008.

<sup>d</sup> Incidence rate is per year per 1,000,000 outbound travelers in 1999–2008.

<sup>e</sup> The cases includes clinical ones with epidemiological links without laboratory confirmation only consistent with clinical case definition were reported, but the number of cases per sentinel was not calculated.

<sup>f</sup> Acute encephalitis had been reported as a sentinel reporting disease until November 4, 2003.

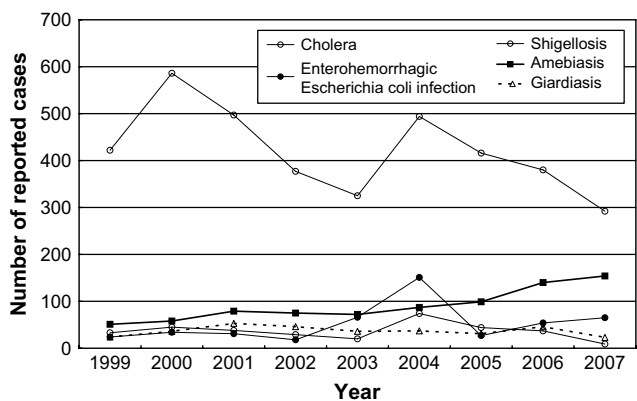
tours to endemic countries was reported to account for the increase of imported diseases,<sup>11</sup> investigation of attributable events or causes were not always made in a timely manner. Retrospective investigation could recognize the increase of cases returning from certain countries, but it was difficult to seek further risk factors because limited information was listed on line.

## Discussion

Public health surveillance is defined by the World Health Organization as the "Systematic ongoing collection, collation, and analysis of data and the timely dissemination of

information to those who need to know so that action can be taken." The basic principle for disease control and prevention is the same no matter where it is acquired. But target groups who need to know differ. The precautionary information should be communicated to travelers with the risk assessed properly. Of course rapid detection of cases can lead to rapid response and early containment and finally to prevention of indigenous transmission of exotic pathogens. In this respect, effective infectious disease surveillance is essential.

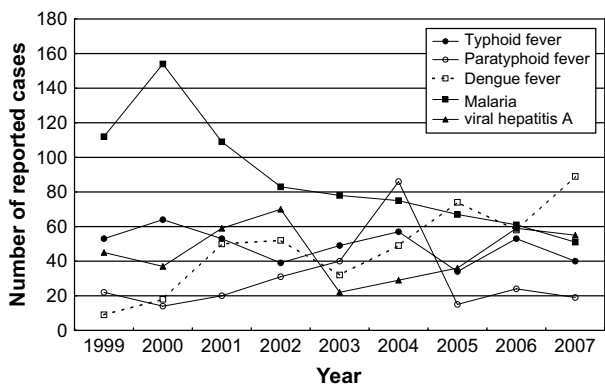
In this study it was not difficult to overview the situation of imported infectious diseases because the current Japanese surveillance system requires the presumptive place of infection including the specified country if possible. But



**Figure 1** Annual trends of imported cases of selected diarrheal infectious diseases. \*The data in 1999 is from April to December.

there have been no studies on the evaluation of reporting rate. Before April 1999 when the infectious disease control law was revised, 50–80 cases of malaria were reported annually in the framework of the old infectious disease prevention law, but the Research Group on Chemotherapy of Tropical Diseases reported by their field investigation that approximately 120 patients have been confirmed with malaria annually.<sup>12</sup> It means that cases notified to the Ministry of Health and Welfare were about 50% in those days. Reports of malaria peaked in 2000 one year after the new law enactment and steadily decreased to the same level before 1999. On the other hand, Dengue fever is increasing. It is not possible to determine whether the reporting rate of malaria has decreased recently or not, it will be necessary to evaluate the surveillance system including assessment of missed opportunity for diagnosis and treatment. It might be better to report febrile illness with travel history abroad for effective detection and evaluation.

It is natural that reported imported cases of malaria, dengue fever and rabies are complete. Domestic case of coccidioidomycosis is reported to be caused from imported materials. A proportion of typhoid/paratyphoid fever, cholera and shigellosis are acquired inside the country



**Figure 2** Annual trends of imported cases of selected febrile infectious diseases. \*The data in 1999 is from April to December.

without doubt because there is no travel history abroad. As there is a report of *Vibrio cholerae* from imported food,<sup>13</sup> further is required investigation of the source of infection in each cases.

Most of the imported cases were reported with the suspected country of infection. Analysis using 2006–2008 data showed suspected countries of infection for cholera are India, Philippine, and Indonesia (in descending order); India, Indonesia, and China for shigellosis; India, Indonesia and Nepal for typhoid/paratyphoid fever; Philippine, Thailand and India for dengue fever; Papua New Guinea, Nigeria, India and Indonesia for malaria. But it depends upon the number of travelers and the local situation in certain countries which might change year by year. More detailed analysis using country specific travelers is necessary.

AIDS, syphilis, hepatitis B, and giardiasis are part of imported infectious diseases. As they have the unique feature as sexually transmitted diseases (STD), it might be better to handle these separately. But it is important to monitor imported STD because they could increase local infection rates, and to provide information for travelers.

In the current study, it was noted that unusual increases of reported imported infectious disease were not fully investigated for attributable events or causes in a timely manner although several events affecting the number of reports were identified. Retrospective analysis can provide the country of infection, but more timely information is necessary for travelers. The capacity of timely investigation and risk assessment should be enhanced further.

The results of investigation of an outbreak among a tour group sharing common source of infection or cluster in time and of travel place of individual tourists not related each other will be reflected or involved in a local epidemic, which can be linked to international investigation and control activities. Under the current circumstances of pandemic alert, the timely sharing of imported infectious disease at the global level will also be necessary.

**Conflict of interest**

The author has no conflict of interest.

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