衞生防護中心
Centre for Health Protection

Scientific Committee on Vector-borne Diseases

Prevention and control of urban typhus in Hong Kong

Purpose

This paper reviews the latest global and local epidemiology of urban typhus and examines the prevention and control measures in Hong Kong.

The causative agent, vector, and host

2. Urban typhus, also called, murine typhus, flea-borne typhus, or endemic typhus, is a rickettsial disease with a cosmopolitan distribution[1-6]. It is caused by the organism *Rickettsia typhi* (formerly called *Rickettsia mooseri*). *R. typhi* is a Gram-negative aerobic coccobacillus belonging to the family Rickettsiaceae. It is an obligatory intracellular parasite that infects the endothelial cells of blood vessels. They replicate by binary fission inside the host cells, and result in heavy damage and hence vasculitis.

3. Urban typhus is a zoonotic disease and the principal vector is the oriental rat flea *Xenopsylla cheopis*[7-10]. Rat flea is also the vector for plague. Fleas are jumping, wingless, blood sucking, light avoiding, terrestrial insects, with a bilaterally compressed body to facilitate their movement between hairs and feathers of their hosts. They are ectoparasites of animals such as domestic animals and rodents. Adult fleas are about 1 to 4 mm long. Their powerful hind legs allow them to jump up to 25cm high and 35cm horizontally, and enable them to move onto passing-by animal hosts. The preferred hosts of rat flea are the Norway rat (*Rattus norvegicus*, also known as sewer rat) and roof rat (*Rattus rattus*, also known as house rat), and to a lesser extent the house mouse (*Mus musculus*)[11, 12]. However, when these hosts die, rat fleas will leave and attack humans readily. This behaviour is of importance

when formulating the strategy for a rodent disinfestation program[10]. Fleas can survive months without feeding[13]. The nests of the hosts are the normal breeding places of all stages of rat flea. Fleas usually bite humans on the legs and ankles, and the bite is itchy.

4. Rodents are nocturnal social animals. They are good climbers (particularly true for roof rat), jumpers, and swimmers[11]. Their range of movement is about 30-50m for rats, and 5-10m for mice. They are most active when human activity is low, and their neophobic behaviour makes them avoid new and strange objects[14]. However, their exploratory behaviour make them explore the areas around and therefore the rodent infested area can expand rapidly if rodent activities are not in check.

5. The Norway rat (*Rattus norvegicus*), the roof rat (*Rattus rattus*), and the house mouse (*Mus musculus*), which are the hosts of the rat flea and the reservoir of urban typhus, are commonly found in the urban environments of Hong Kong[15]. The habitats of the Norway rat are mainly flower beds, sewers and holes on ground, while those of the roof rat include false ceilings, roof top and upper floors of a building. The house mouse mainly lives in store rooms and warehouses.

6. Both the rat flea and the rodent hosts constitute the reservoir. Infection by *R. typhi* in rodents is not fatal, and rickettsemia lasts for 1 to 2 weeks[6, 16]. In this time window, if a healthy flea takes a blood meal from the infected rodent, *R. typhi* will infect the flea's gut epithelial cells, and *R. typhi* will be excreted in flea faeces. This infection in the rat flea is not fatal and does not affect the life span (about 1 year) or the reproductive capacity[6]. *R. typhi* can persist for life in the flea. *R. typhi* can also be passed to offspring by transovarial transmission, thus bypassing the need for a mammalian host to maintain the bacteria in the environment.

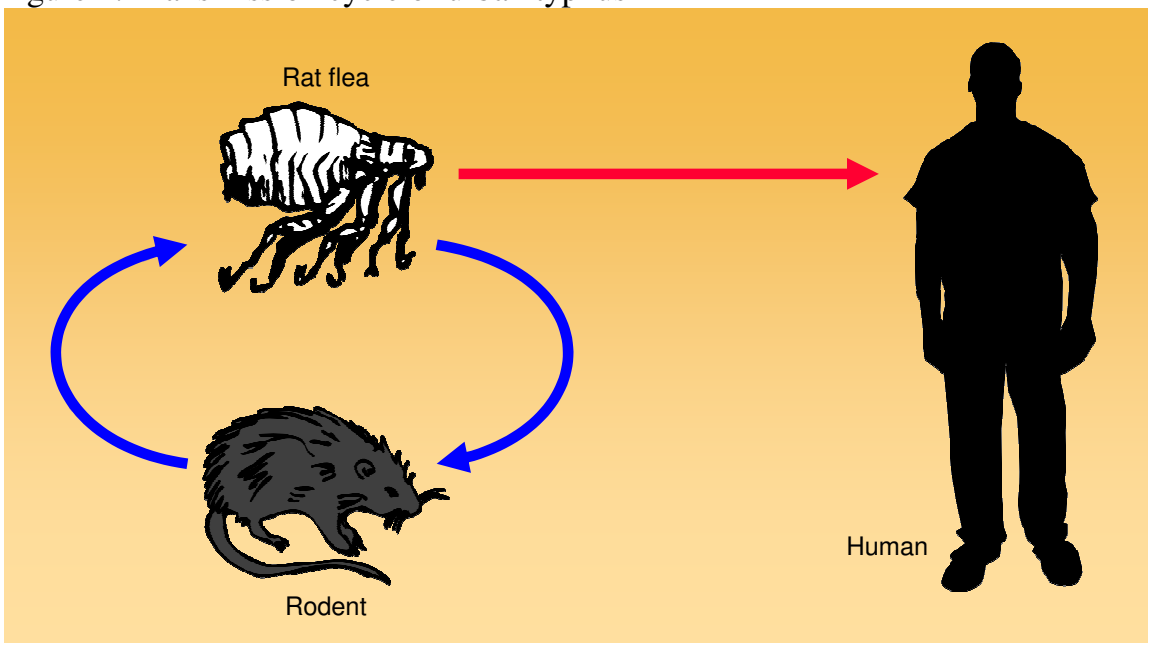
Mode of transmission

7. Urban typhus usually occurs between spring and autumn, when the rat flea is most abundant[16]. People working in sea ports, coastal areas, market, food storage areas, or granaries are at high risk.

8. The transmission cycle of urban typhus is shown in Figure 1. *R. typhi* bacteria multiply in the gut of a rat flea after it ingests blood from an infected host[17]. Unlike plague, the gut is not blocked and *R. typhi* bacteria are shed in the faeces by the rat flea which usually defecates while feeding[4, 6, 16, 18]. A healthy person becomes infected when the bacteria from the infective flea faeces enter the body through the bite wound. The bacteria can also enter the body when a person scratches the faeces into the skin wound or transfers the faecal material to a mucous membrane (e.g. conjunctiva). Air-borne dust particles contaminated by infective flea faeces from rat-infested building can

also result in infection if they are inhaled. There is also experimental evidence suggesting that infection can also occur through a flea bite[19].

Figure 1. Transmission cycle of urban typhus



Clinical presentation, laboratory diagnosis and patient management

9. The incubation period is commonly 10 to 12 days. The illness is characterised by acute onset of fever, together with headache, malaise, myalgia, nausea, and sometimes chills. In about 80% of patients a macular or maculopapular rash appears around 5 to 6 days after onset and spreads from the trunk to the arms and legs, but usually does not affect the face, palms, or soles. The severity of urban typhus is milder compared to epidemic typhus and is usually self-limiting[16, 18]. However, a small percentage of patients can develop severe illness resulting in neurologic symptoms, shock, organ failure, or death[20-22]. Untreated cases can last for several months, and the untreated fatality rate is 1-2% and increases with age. Infected persons develop permanent immunity.

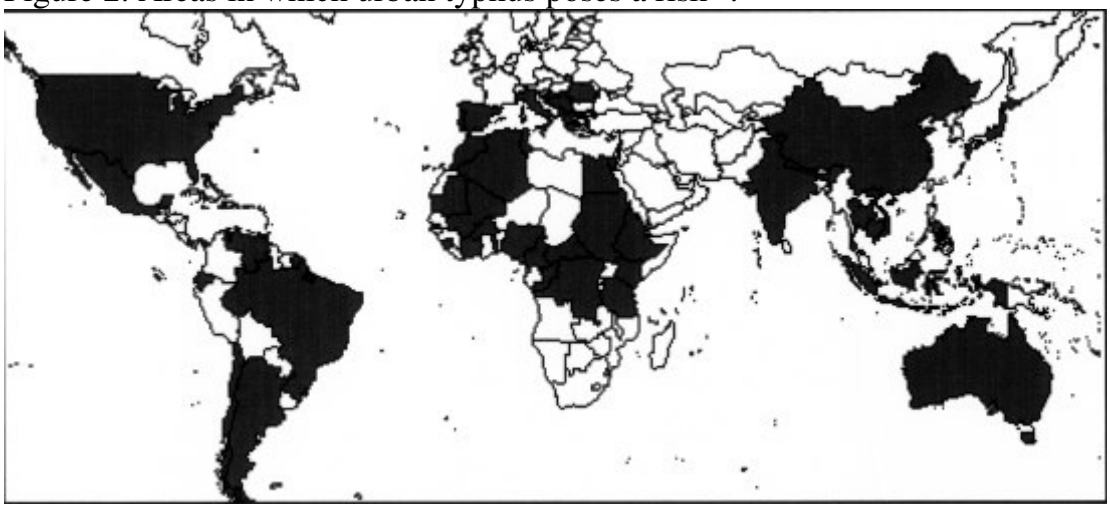
10. The laboratory diagnosis of urban typhus is made by demonstrating a four-fold rise in antibody titre against the typhus group antigen by immunofluorescence testing, or by demonstrating the presence of the DNA of *R. typhi* in EDTA blood specimen by polymerase chain reaction. However it should be noted that the former test cannot distinguish urban typhus from epidemic typhus[23], though epidemic typhus has not been reported in Hong Kong for decades. The latter test is more definitive and is required in case there is cross reaction to antigens of other rickettsial diseases. However the application of this test is limited by the fact that rickettsemia only occurs in a relatively narrow time window during the acute phase.

11. Doxycycline is the most common treatment, unless otherwise contraindicated[24]. Early empirical treatment is recommended for a suspected case, particularly when there is a compatible exposure history, because early treatment decreases case severity resulting in a shorter illness and decreased hospitalisation[20, 25].

Overseas epidemiology

12. The disease occurs worldwide chiefly in tropical and coastal regions and is found in areas where people and rats share the same habitat[4, 10, 26]. Figure 2 shows the areas in which urban typhus poses a risk, according to seroepidemiologic studies, case series, or imported cases in travellers[27]. The disease is prevalent in southern parts of USA (Texas, California), Hawaii, and also in Africa, Europe, and Asia[28-30].

Figure 2. Areas in which urban typhus poses a risk[27].



13. In the United States, the incidence of urban typhus was high (~2600 cases annually), with its peak activity from 1931 to 1946. Rodent and flea controls has led to a dramatic drop to less than 80 cases / year, and since 1994 it is no longer nationally notifiable [4, 31, 32]. Nowadays cases still occur in Hawaii[5] and the suburban areas[33] in southern regions like Los Angeles and Orange County of California[4], and south and central Texas[3, 18], where it is an important cause of fever and hospitalisation among children[25, 34, 35]. A seroprevalence test showed that 17 (9.7%) out of 176 homeless people in Houston, Texas had antibodies against *R. typhi*[36]. In 2008, there was an outbreak of 33 cases of urban typhus that clustered geographically in central Austin of Texas[37, 38]. In Texas, 9 to 72 cases were reported annually, while in California, 3 to 21 cases were reported every year[33]. There were 5 to 6 cases annually in Hawaii, but in 2002 an outbreak occurred across 5 islands and 47 cases were reported that year[39].

14. Spread of urban typhus in the United States from urban areas to rural areas occurred and the epidemiology was different[31]. In the rural areas, there was a distinct summer peak, whereas in urban areas, cases occurred through out the year. This difference was attributed to occupational exposure of rural agricultural workers to rats and flea, whereas in urban areas, the rats and fleas activities were related to the temperature maintained in buildings and tended to be constant throughout the year.

15. The identification of urban typhus cases in endemic areas of United States in which the rat flea is absent lead to the discovery of the cat flea as a competent vector[31, 40-42]. The cat flea, *Ctenocephalides felis*, is the most prevalent flea species collected from opossums, cats, and dogs in southern Texas.

16. In Europe, the Health Protection Agency of the United Kingdom claimed that autochthonous urban typhus cases do not occur in the United Kingdom and any reported cases are acquired overseas[43]. There was only one case of laboratory confirmed urban typhus, with travel history to Viet Nam, from 1996 to 2005[44, 45]. In contrast, in Marseilles of France, 22% (63 out of 299) of homeless people had antibodies against *R. typhi* and there was an uptrend from 2010 to 2011, which was probably related to increased waste resulting from construction sites and a sanitation industry strike[46]. In Crete in Greece, urban typhus is a known cause of children hospitalization[47]. In the Canary Islands in Spain, the frequency of complicated cases, particularly renal damage, is higher[48].

17. In Australia, cases are regularly diagnosed only in south-west Western Australia. Recently the first case from New South Wales since the 1940s was reported in 2010[49]. In New Zealand, in contrast to the usual seasonality, cases occurred predominately over the colder months between April and October[50]. An increased number of cases were noted from the Waikato region, and it was confirmed that exposure to rural areas is the most important risk factor.

18. Urban typhus is endemic is Southeast Asia, particularly in Indonesia[51], as reported by surveillance networks such as the GeoSentinel Surveillance Network[27, 29, 52]. Around 11% of rodents captured in harbour areas in one study were seropositive[53]. In Laos, 9.6% of adult febrile patients were confirmed to have murine typhus[54]. Similarly, *R. typhi* DNA was detected in blood from 7% of adult febrile study samples from urban Nepal, and cases were more common in winter than in summer[55]. In Bangkok in Thailand, 8% of suburban blood donors had antibodies to *R. typhi*. In Malaysia there was an uptrend from 1991 to 1997[56]. Among blood donors and febrile patients in urban Malaysia, 9.2% and 22.9% of them were seropositive, respectively[57]. In rural areas, 28.1% of febrile patient were seropositive, with those working in agricultural sectors at higher risk[58].

19. Urban typhus is prevalent in South Korea, with a seropositivity of 32.6% in febrile patients[59]. 24% of these contained IgM, indicating a recent infection. On the contrary, only 4 cases of urban typhus were reported in Japan between 1958 and 2004[60]. Highly endemic area was found in the Hongta areas of Yuxi city, Yunnan province of mainland China, in which 28.9% of the general population were seropositive[61].

20. In Africa, cases have been reported in Algeria[62]. Cases with travel history to Tunisia have also been reported[63]. In Kuwait in the Middle East, an outbreak affecting 254 persons occurred in 1978[64]. In Latin America, in Mexico City, 17% of healthy blood donors are seropositive for *R typhi*[65]. In a study conducted in Caldas in Colombia in 2005, 14 out of 120 febrile patients with Weil-Felix positive samples were confirmed to be acute urban typhus cases[66].

Local epidemiology

21. In Hong Kong, urban typhus is a statutory notifiable disease under the Prevention and Control of Disease Ordinance (Cap 599). The annual number of cases from 2005 to 2011 is shown in Figure 3. There is no discernible secular trend. However, it is notable that there were less local cases and more imported cases in recent years. There were a total of 25 confirmed cases from 2005 to 2011, making the average yearly number of cases 3.6 cases per year. Fifty-six percent (14 cases) of the cases were local cases, and 44% (11 cases) were imported cases. Local cases occurred through out the year, except from December to February, which are the coldest months in Hong Kong (Figure 4). For imported cases, more cases occurred from October to November.

Figure 3. Annual number of cases of urban typhus notified to the Centre for Health Protection, 2005 to 2011.

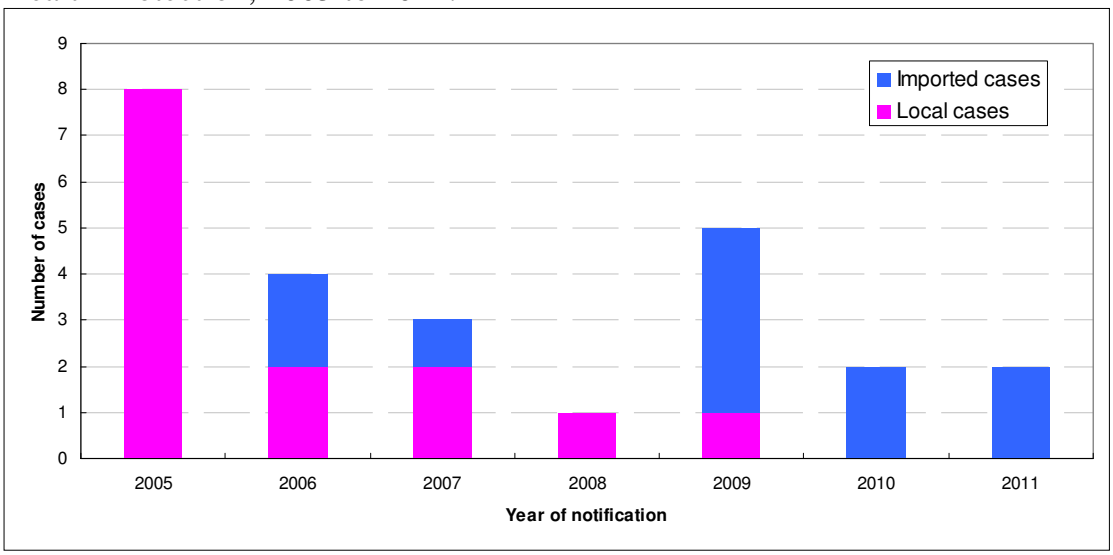
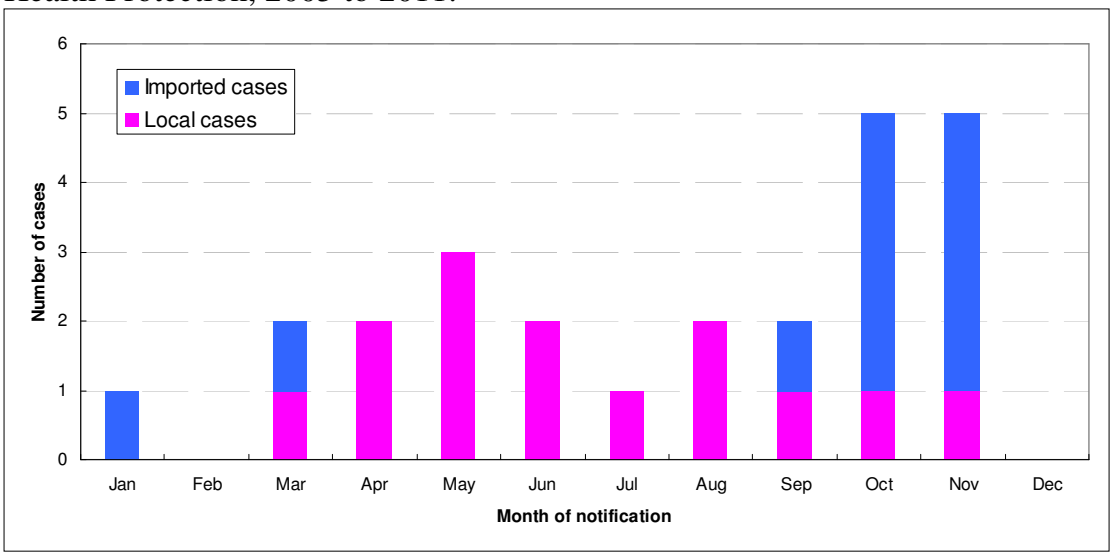
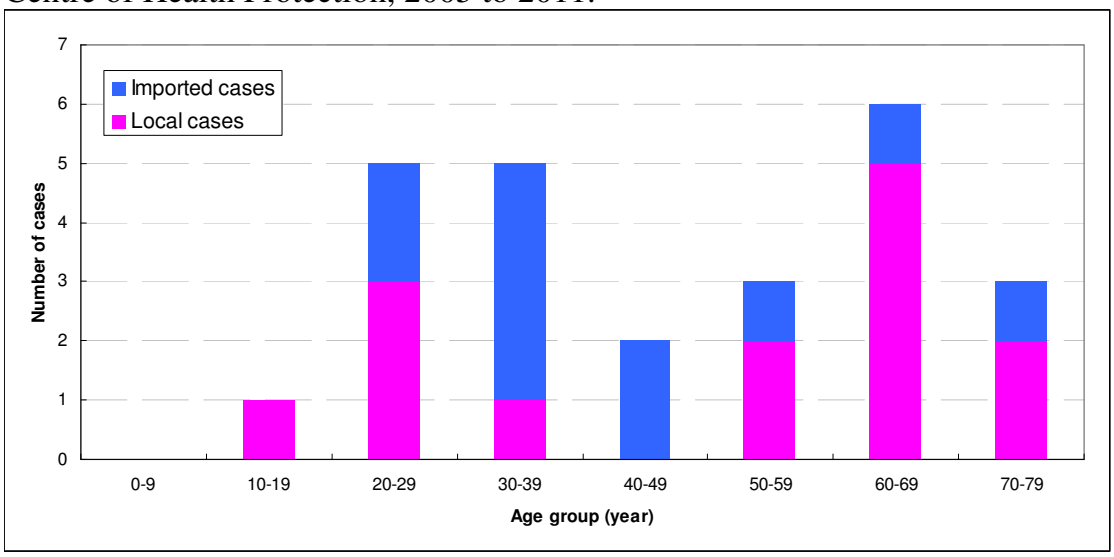


Figure 4. Monthly number of cases of urban typhus notified to the Centre for Health Protection, 2005 to 2011.



22. The male-to-female ratio was 0.6:1. The affected persons were aged from 14 to 78 years, with a median of 48 years. The age group distribution is shown in Figure 5. Interestingly, there are more local cases in the older age groups. Clinical presentations include: fever (25 cases, 100%), deranged liver function test (19 cases, 76%), headache (14 cases, 56%), rash (13 cases, 52%), myalgia (11 cases, 44%), conjunctivitis (2 cases, 8%), lymphadenopathy (1 case, 4%). Four of these patients recalled a history of insect bite during the incubation period. All patients were hospitalised, with a median length of stay of 8 days. A 69-year-old male patient developed gastric bleeding and cardiac arrest, and then succumbed.

Figure 5. Distribution by age group for urban typhus cases notified to the Centre of Health Protection, 2005 to 2011.



23. The occupations of housewife (6 cases, 24%), retired person (6 cases, 24%), and domestic helper (16%) together made up more than half (64%) of the cases. For the 11 imported cases, the places of origin include: Indonesia (5 cases, 45%), Mainland (4 cases, 36%), and Nepal (1 case, 9%). The place of origin of one of the imported case remained undetermined as the patient travelled to Mainland, Lhasa, and Nepal during the incubation period. For the local cases, judging by epidemiological and environmental investigations, 2 of the most common sources of infection are urban residential area (4 cases) and rural residential area (2 cases). Other exposure histories include golf club, hiking, poultry farm, and market. One other case was related to either rural residential area or market, and 3 other cases sources of infection remain unknown due to lack of information. Clusters of urban typhus cases have not been reported to the Centre for Health Protection (CHP).

Prevention and control measures in Hong Kong

24. To prevent and control urban typhus, a coordinated approach encompassing environmental hygiene, personal protection, health education, rodent / flea monitoring and infestation control, disease notification and surveillance, and source investigation have been adopted.

Environmental hygiene

25. The major way to prevent and control urban typhus is to control the rodent and the flea. The most fundamental and effective way of rodent prevention and control is to eliminate the food, harbourage and passages[15]. This can be achieved via proper handling of refuse, storage of food, and keeping of articles. Blockage / elimination of rodent passages through installation of gratings, wire mesh or metal plates etc are structural rodent-proofing measures essential for successful rodent disinfestation with rodenticides or trapping.

Personal protection

26. When handling dead rodents, attention should be paid to personal and environmental hygiene[11]. Wear gloves and face mask when handling dead rodents and avoid direct contact with them. All areas, clothes and items contaminated by dead rodents should be disinfected thoroughly using general household disinfectant or diluted bleaching solution. Before taking off gloves, wash them with water and then cleanse with general household disinfectant or diluted bleaching solution. Hands should be washed thoroughly with soap and water after removing the gloves. No vaccine is available for urban typhus.

Health education

27. Community education is regularly done by the CHP and Food and Environmental Hygiene Department (FEHD). Health information related to prevention of urban typhus is available in the CHP website[67]. Health

education to patients and their contacts is provided by the CHP upon notification of urban typhus.

28. Every year, FEHD will hold a territory-wide interdepartmental anti-rodent campaign to enhance the public alert on rodent prevention, and to enlist support from the community in controlling rodents[68, 69]. A spectrum of publicity instruments were used for public education including display of banners and posters, distribution of leaflets, talks, exhibitions, broadcasting of TV announcement of public interest and organizing health education activities at public markets.

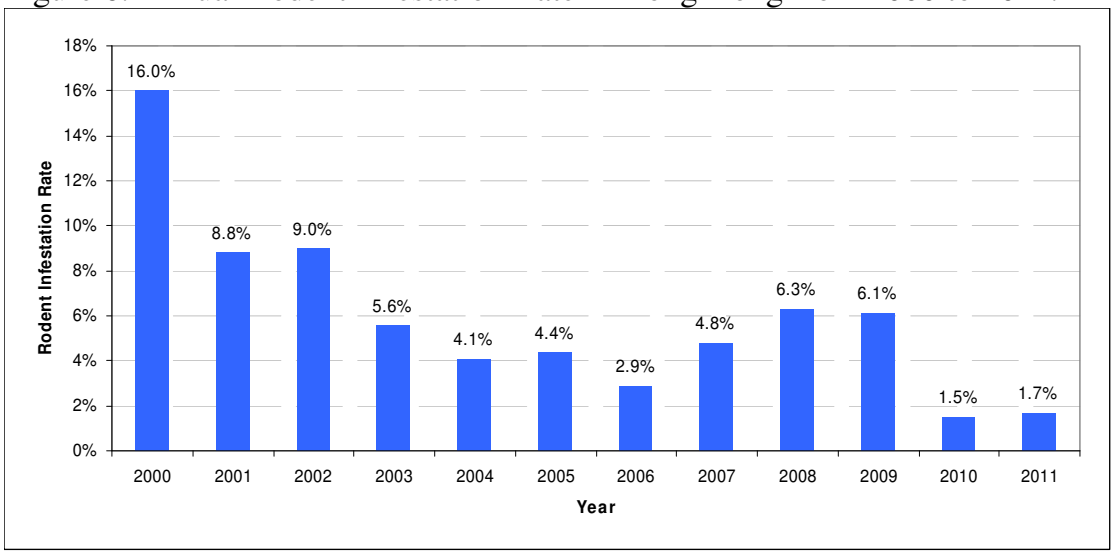
Rodent / flea monitoring and infestation control

29. To facilitate the planning of rodent prevention and control strategies, the Pest Control Advisory Section of FEHD has, since 2000, regularly performed a routine, territory-wide Rodent Infestation Survey to monitor the rodent infestation situation[11, 15, 70, 71]. It helps to determine rodent problematic spots so that prompt action can be taken to prevent proliferation of the rodent population. Rodent Infestation Survey is a scientific and objective method to determine the degree of rodent infestation in areas of interest. It is conducted twice a year in all districts by using census baiting. About fifty bait stations of at least 50 metres apart were set in each study area. The Rodent Infestation Rate (RIR) is then calculated by the percentage of bait consumed by rodent.

RIR = (Number of bait consumed by rodent / Total number of bait set retrieved) x 100%.

Information from PCAS has showed that the RIR has been decreasing from 16.0% in 2000 to 1.7% in 2011 (Figure 6)[72]. Meanwhile, FEHD also carries out regular anti-rodent operations at strategic locations over the territory[11, 15].

Figure 6. Annual Rodent Infestation Rate in Hong Kong from 2000 to 2011.



30. On the other hand, the severity of flea infestation of rodents is monitored using annual rat-flea surveys[11, 15, 73]. Such surveys on selected rodent biotopes have been conducted in the community for over thirty years, whereas those on rodents found in the airport and other port areas were started in 1998 and 2004 respectively. During rat-flea survey, rats captured alive by cage trap would be examined to determine the species and examined for any signs of plague infection. The number of rat flea(s) collected from the rat examined per total number of rats examined gives the Rat-flea Index (RFI). When Rat-flea indices are greater than 1, pest control staff will carry out flea disinfestation in addition to rodent control operation.

31. The Port Health Office of the Department of Health conducts inspections at airports, seaports, and ground crossing to monitor the hygiene and sanitation condition and coordinates efforts of the respective managements for rodent infestation prevention and control.

Disease notification and surveillance

32. In Hong Kong, urban typhus has been a notifiable disease since 1951. All registered medical practitioners are required to report suspected or confirmed cases to the CHP for investigation and public health control measures. Cases are defined as persons with compatible clinical features and laboratory confirmation. CHP continues to monitor the trend of the disease and disease statistics are uploaded to CHP's website regularly.

Source investigation

33. After receiving report of human infection, the CHP will carry out investigation to collect epidemiological information about places they have visited. Travel collaterals and household members are contacted and put under medical surveillance. Health education is also used as a tool to alert the parties concerned on the prevention and control of rodent and the disease. The case will also be notified to the PCAS for prompt investigation of rodent activity at and around the patients' homes and their vicinity, workplaces, markets, and other places they have visited to determine the source of infection. PCAS would inform and advise the district pest control staff of FEHD and parties concerned to eliminate the breeding site of rodents when necessary.

Conclusion

34. Urban typhus is a disease that is found worldwide. The rat flea is the principal vector of urban typhus. There were less local cases and more imported cases in recent years. The number of cases reported in Hong Kong remained at a low level of around 3.6 cases every year. Nonetheless, the disease remains a potential threat to the public health of Hong Kong. Various government departments and the community should continue to participate in the coordinated effort of environmental hygiene, personal protection, health education, rodent / flea monitoring and infestation control, disease notification

and surveillance, and source investigation in order to achieve the prevention and control of the disease in Hong Kong.

Centre for Health Protection

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