

Zoonotic disease

Standards for care and storage of experimental animals and alleviation of suffering
Third Common Criteria

4 Acquisition of knowledge related to common infectious diseases between humans and animals

Laboratory animal managers, experimenters and breeders are **should be made to acquire sufficient knowledge and collect information on common infectious diseases between humans and animals**. In addition, managers, laboratory animal managers, and experimenters shall strive to develop a communication system with public health institutions, etc., so that **necessary measures can be taken promptly** in the event of an outbreak of a common human-animal infectious disease. matter.

National Center for Child Health and Development Research Institute
Hideki Tsumura



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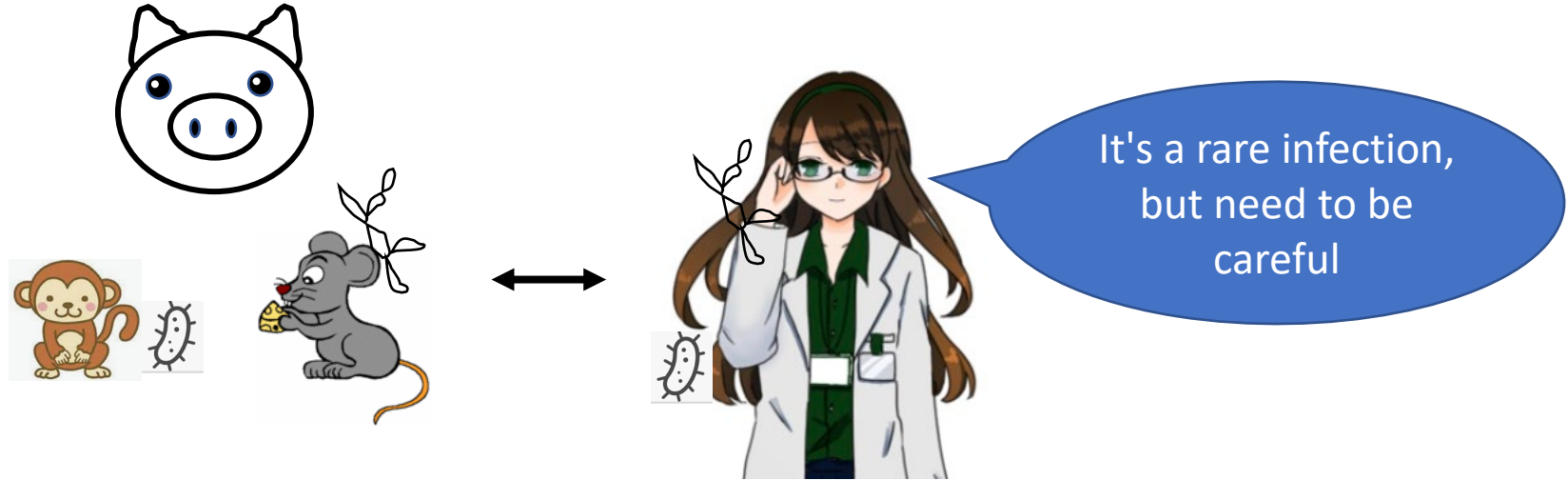
Knowledge of
zoonotic
diseases is
necessary



立ち絵：雨巻家

Zoonotic diseases from multiple animal species

Salmonella, dermatophytosis:
possible transmission from many animal species



Salmonella disease (non-typhoid): Salmonella typhimurium

Salmonella typhimurium, enteritidis S. enteritidis

Symptoms in laboratory animals : Mice and guinea pigs are highly sensitive, rabbits have various symptoms such as resistant fever and diarrhea, necrotic foci in the liver and spleen

Human symptoms : Infectious food poisoning symptoms such as abdominal pain, diarrhea, and fever

Cases : Meat animals, chickens, reptile pets, etc. may be infected, and asymptomatic infected persons may infect experimental animals



Tokyo Metropolitan Safety Research Center website



Infected Guinea Pig Spleen



Dermatophytosis :

Microsporum, Epidermophyton (Inkintamushi, athlete's foot)

Symptoms in laboratory animals : Parasitic on keratinized parts such as the stratum corneum of the skin of many experimental animals such as mice and rats, resulting in irregular hair loss

Human symptoms : Small ring rash, tinea vesicularis, athlete's foot, ringworm

Case : Human-to-human and pet-to-human transmission is common.



Quoted from Sugita Animal Hospital, Shiraoka City, Saitama Prefecture



Zoonotic diseases originating in small animals

Small Animal Microbial Monitoring Core Set of the Japanese Society for Laboratory Animal Science : Category A

Pathogens that may infect humans from experimental animals and cause disease

Salmonella, dermatophytosis: many animal species
Lymphocytic choriomeningitis: mouse, hamster
Renal symptomatic hemorrhagic fever (hantavirus): rat



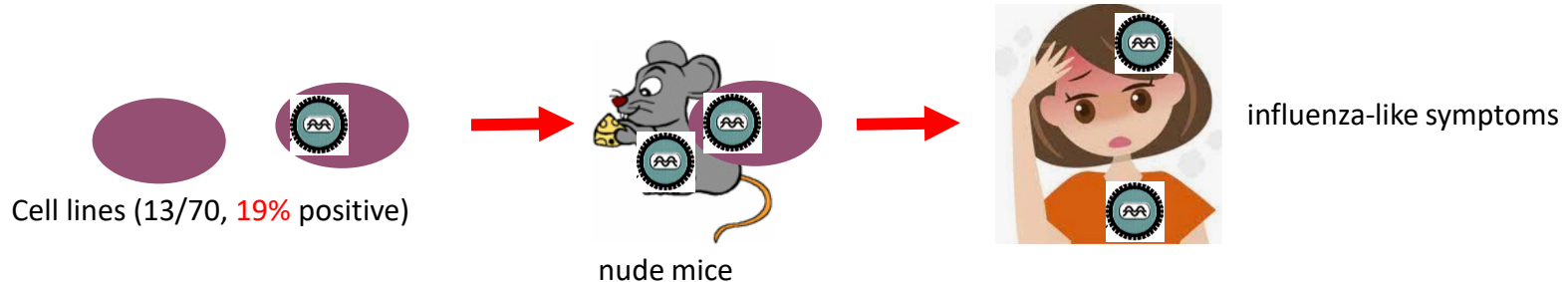
Lymphocytic choriomeningitis

Arenavirus, single stranded(-)RNA, Lymphocytic Choriomeningitis Virus(LCMV)

Symptoms in mice : Endemic, asymptomatic and persistent infection in wild mice of Europe and North and South America

Symptoms in humans : Asymptomatic, flu-like symptoms if developing

Cases : From 1965 to 1974, 3 outbreaks were reported at research facilities in the United States
In 1989, 7 of 82 (9%) US laboratory workers were antibody positive
2 out of 7 were hospitalized with acute fever, 7 of them were involved in breeding nude mice and experiments
13 out of 70 cell lines (19%) were positive for LCMV
In 2015, LCMV-infected mice were introduced from the Institut Pasteur in France at the RIKEN BioResource Center and bred without being detected by quarantine inspection.



Renal symptomatic hemorrhagic fever : Hantavirus, Bunyaviridae, single strand(-)RNA(-)

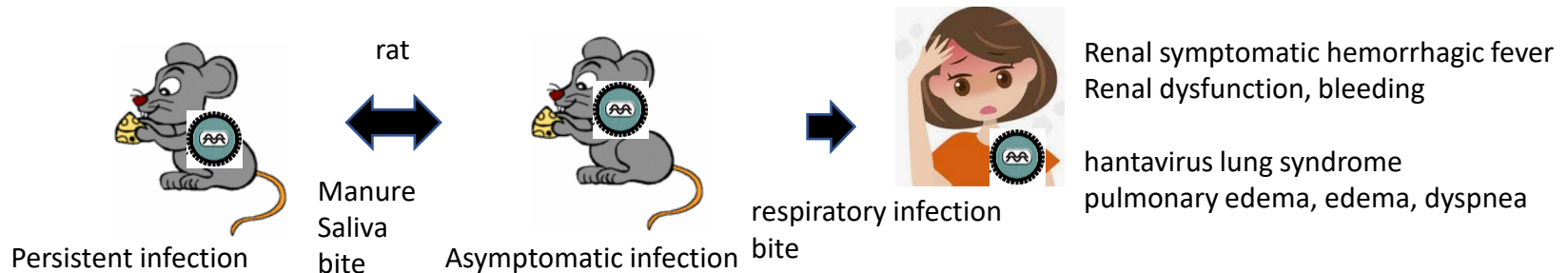
Symptoms in rats : Inapparent infection, virus excretion in feces and urine

Symptoms in humans : Aerosol infection, symptoms include fever, headache, renal dysfunction

Cases : From 1970 to 1984, 126 people developed symptoms at 22 research institutes in Japan, and one died.

In 1991, an antibody-positive rat was detected at Kyoto University.

Widespread use of antibody tests and a sharp decrease in reports of infection in rats



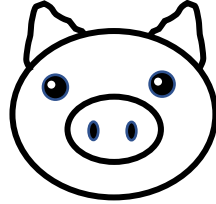
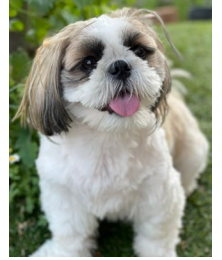
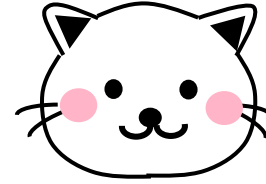
Zoonotic diseases originating from medium animals

Corynebacterium infection, Pasteurella infection: dogs, cats

Bartonella Infection (Cat-Scratch Disease): Cats

Capnocytophaga Infection: Dogs

Hepatitis E: swine



Infections from
pets are common



Corynebacterium infection

Corynebacterium ulcerans, Gram-negative bacilli

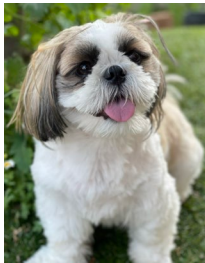
Symptoms in dogs and cats : Cold-like symptoms, asymptomatic

Human symptoms : Respiratory symptoms, white pseudomembrane in pharynx

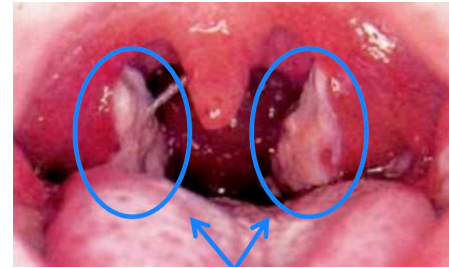
Cases : In Japan, a total of 19 cases from 2007 to the end of 2016

Diphtheria vaccine is effective for prevention

People with multiple
dogs and cats are at
higher risk of
infection.



Standing picture: Amamaki family



Pseudomembrane formation

From Ministry of Health, Labor and
Welfare materials



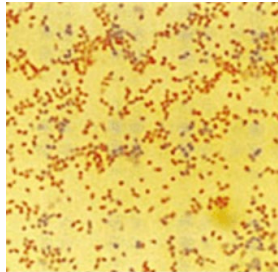
Pasteurellosis : Apart from *Pasturella multocida*, *Pasturella type3*, Gram-negative bacilli

Symptoms in cats and dogs : Invisible. Nearly 100% in the oral cavity of cats,
about 75% in dogs

Symptoms in humans : **Skin symptoms** such as bites (short incubation period),
redness, swelling

Respiratory symptoms due to respiratory infection

Cases : Mostly infected from cats, the most common infectious disease from pets



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From the blog of
Wakayama Animal
Hospital, Sakura City,
Chiba Prefecture

| Specimen | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 |
|---|------|------|------|------|------|------|------|------|------|------|
| Pus (scratches and bites caused by dogs and cats) | 10 | 102 | 17 | 19 | 29 | 23 | 60 | 61 | 94 | 144 |
| Respiratory system (sputum, respiratory secretions, bronchial lavage fluid, pleural effusion) | 7 | 26 | 15 | 39 | 34 | 49 | 48 | 60 | 88 | 110 |
| Others | 6 | 6 | 8 | 13 | 13 | 17 | 30 | 27 | 4 | 71 |
| Total | 23 | 42 | 40 | 71 | 79 | 89 | 138 | 150 | 224 | 325 |

As a result of a questionnaire survey conducted on the isolation status of *Pasturella* spp. in the laboratories of 478 hospitals designated for clinical training in Japan, the number of hospitals that responded was 291 hospitals (response rate 60.9%), of which 206 hospitals (70.8%), *Pasturella* spp. was isolated.
(Source) Yasutomo Arashima et al. "Isolation status Newspaper Vol. 57 No. 8 P. 668 Partially of *Pasturella* spp in Japan during the 10 years from 1992 to 2001" (2004) Veterinary and Livestock modified from Table 1
From the Ministry of Health, Labor and Welfare HP

Cat scratch disease : *Bartonella henselae*

Gram-negative bacillus bite (cat)

Symptoms in cats : Inapparent, transmitted by cat fleas, infected within red blood cells

Possessed by 5-20% of cats (7.2% of cats in Japan alone)

Symptoms of a person : Incubation period several days to 2 weeks, papules, pustules, fever, pain, prolonged lymphadenopathy

Cases : In Japan, a significant number of cat-scratch disease cases have occurred.



Flea control is critical.
Children are easily
infected.

Capnocytophaga infection :

Capnocytophaga canimorsus, Gram-negative bacilli

Symptoms in dogs : Asymptomatic, approximately 80% of dogs are colonized in the oral cavity

Symptoms in humans : Infection by bite, incubation period is 1 to 5 days, fever, headache, malaise, abdominal pain, nausea, etc.

Cheerful yesterday, shocked today! Proverb (If it becomes severe, it progresses quickly)
cases : In Japan, a total of 93 cases (including 19 deaths) from 1993 to 2017

2. Diagnosis at admission (n=70)

| Symptoms | Patients | % |
|-----------------------|----------|----|
| Septicemia | 29 | 41 |
| Unknown fever | 7 | 10 |
| Meningitis | 7 | 10 |
| Cellitis | 6 | 9 |
| Septic Shock | 5 | 7 |
| Respiratory infection | 4 | 6 |
| Others | 12 | 17 |



people with underlying diseases and the elderly should be careful.

people who work with animals are at higher risk of infection.



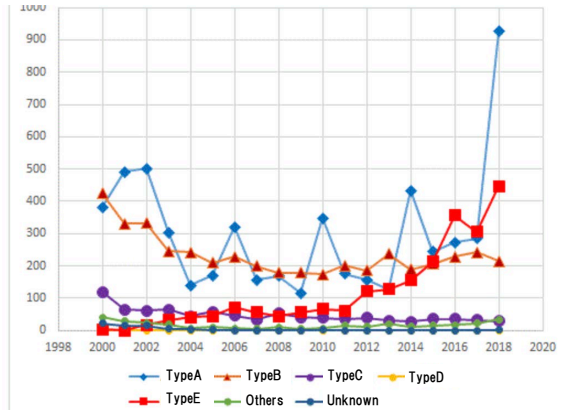
Hepatitis E : hepatitis E virus (Hepeviridae family, single strand(+)RNA)

Symptoms in pigs : High prevalence worldwide, asymptomatic, proliferates in intestine and liver Introduction of

Symptoms in humans : Incubation period 6 weeks, asymptomatic, hepatitis symptoms in some (1%) Abdominal pain, loss of appetite, fever, liver enlargement, jaundice, chills, nausea, vomiting

Cases : Caused by eating raw pork liver, etc., route unknown in about half

Figure 1. Number of reported cases of viral hepatitis in Japan (infectious disease trend survey: 2000-2018)



日本におけるウイルス性肝炎年間患者発生報告数推移(感染症発生動向調査:2000-2018年)



For pig experiments, you need to be careful.



Zoonotic diseases originating in primates

Ebola hemorrhagic fever, Marburg (Category 1 infectious disease, high mortality rate)

B virus (Category4)

Shigella (Category3), Tuberculosis (Category2) (Veterinary notification is required by law.)

| Classification and concept of infectious diseases | |
|---|---|
| Classification | Possible measures, etc. |
| Category 1 | <ul style="list-style-type: none">· Interpersonal: hospitalization (when the prefectural governor deems it necessary), etc.· Objective: Measures such as disinfection· Measures such as traffic restrictions are possible |
| Category 2 | <ul style="list-style-type: none">· Interpersonal: hospitalization (when the prefectural governor deems it necessary), etc.· Objective: Measures such as disinfection |
| Category 3 | <ul style="list-style-type: none">· Interpersonal: Employment restrictions (when the prefectural governor deems it necessary), etc.· Objective: Measures such as disinfection |
| Category 4 | <ul style="list-style-type: none">· Measures such as disinfection, including measures for animals |
| Category 5 | <ul style="list-style-type: none">· Incidence trend survey |

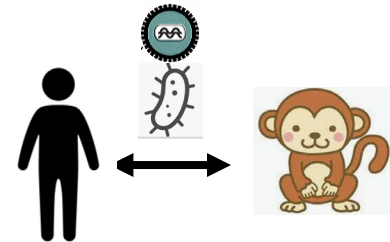


illustration : www.ac-illust.com



B virus : herpesviridae, double-stranded DNA

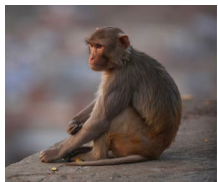
Symptoms in monkeys : The natural hosts are Asian cynomolgus monkeys, rhesus monkeys, Japanese macaques,
Usually asymptomatic or blistering in oral cavity

Symptoms in humans : Bite or droplet infection, local pustules, flu-like symptoms, encephalitis

50 people worldwide, fatality rate after infection onset is 40%

Cases : In 2019, two technicians handling monkeys at a pharmaceutical development contract company in Kagoshima City were infected with monkey-derived B virus (first in Japan). 9 months until a definitive diagnosis is made.

In 2021, a veterinarian at a monkey breeding facility was infected and died for the first time in China.



If you have a persistent fever of unknown origin, tell your doctor that you have been in contact with monkeys.



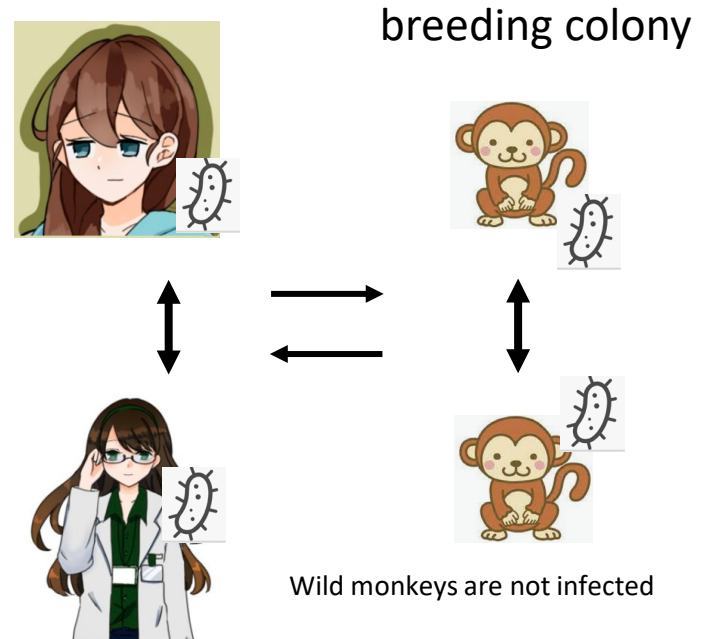
Shigellosis

Shigella spp. 4 bacterial strains

Symptoms in monkeys : asymptomatic infection, Diarrhea often leads to death within a few days.

Symptoms in humans : Diarrhea, vomiting.

Cases : People often get infected while traveling to Southeast Asia. Overseas, there have been cases of infection in breeding workers and zoos.



Importation and quarantine of monkeys

Pet monkey import ban (July 2005)

Only experimental research and exhibition animals are allowed.

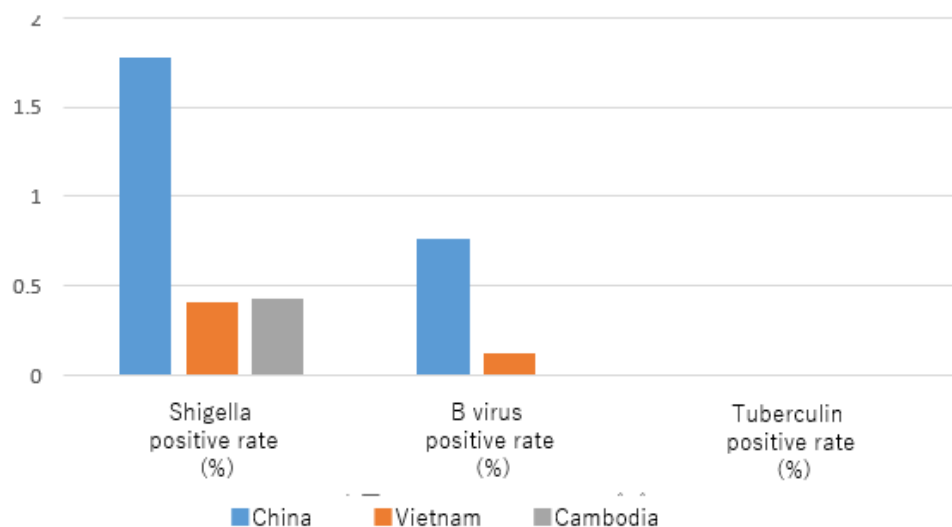
Importable Countries: United States of America, Cooperative Republic of Guyana, Republic of Suriname, People's Republic of China, Republic of Indonesia, Republic of the Philippines, Socialist Republic of Vietnam, Kingdom of Cambodia

Import quarantine certificate (Ebola hemorrhagic fever, Marburg disease), mooring inspection **for at least 30 days in Japan**



Hamley Co., Ltd. inspection results by major exporting country 2004-2021

| Production area | Shigella positive rate (%) | B virus positive rate (%) | Tuberculin positive rate (%) | Average weight (Kg) | Number of target animals |
|-----------------|----------------------------|---------------------------|------------------------------|---------------------|--------------------------|
| China | 1.78 | 0.76 | 0 | 2.79 | 8,125 |
| Vietnam | 0.41 | 0.12 | 0 | 2.31 | 1,925 |
| Cambodia | 0.43 | 0 | 0 | 2.73 | 1,086 |
| | | | | | 11,136 |



Preventive measures against zoonotic diseases

If bitten or scratched by an experimental animal

First aid measures

Sufficient washing of the affected area with a large amount of tap water, etc.

Disinfection with rubbing alcohol or iodine disinfectant

Follow-up

Call emergency services in case of urgency or anaphylaxis



Human-to-laboratory animal transmission

Parainfluenza type 3, B. bronchiseptica: small animals?



Dermatophytes, Staphylococcus aureus, Pseudomonas aeruginosa: animals in general? ?



Tuberculosis, Measles, Dysentery: Primates



Health management
of experiment workers
is also important



Summary

Zoonotic disease

1. Knowledge of zoonotic diseases is necessary
2. It is important to handle animals that do not transmit diseases from experimental animals, and vice versa.

