

Assessment and management of food-borne pathogens in Japan including enterohemorrhagic *E. coli*

National Institute of Infectious Diseases
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Surveillance and management of food-borne infection in Japan(based on two laws)

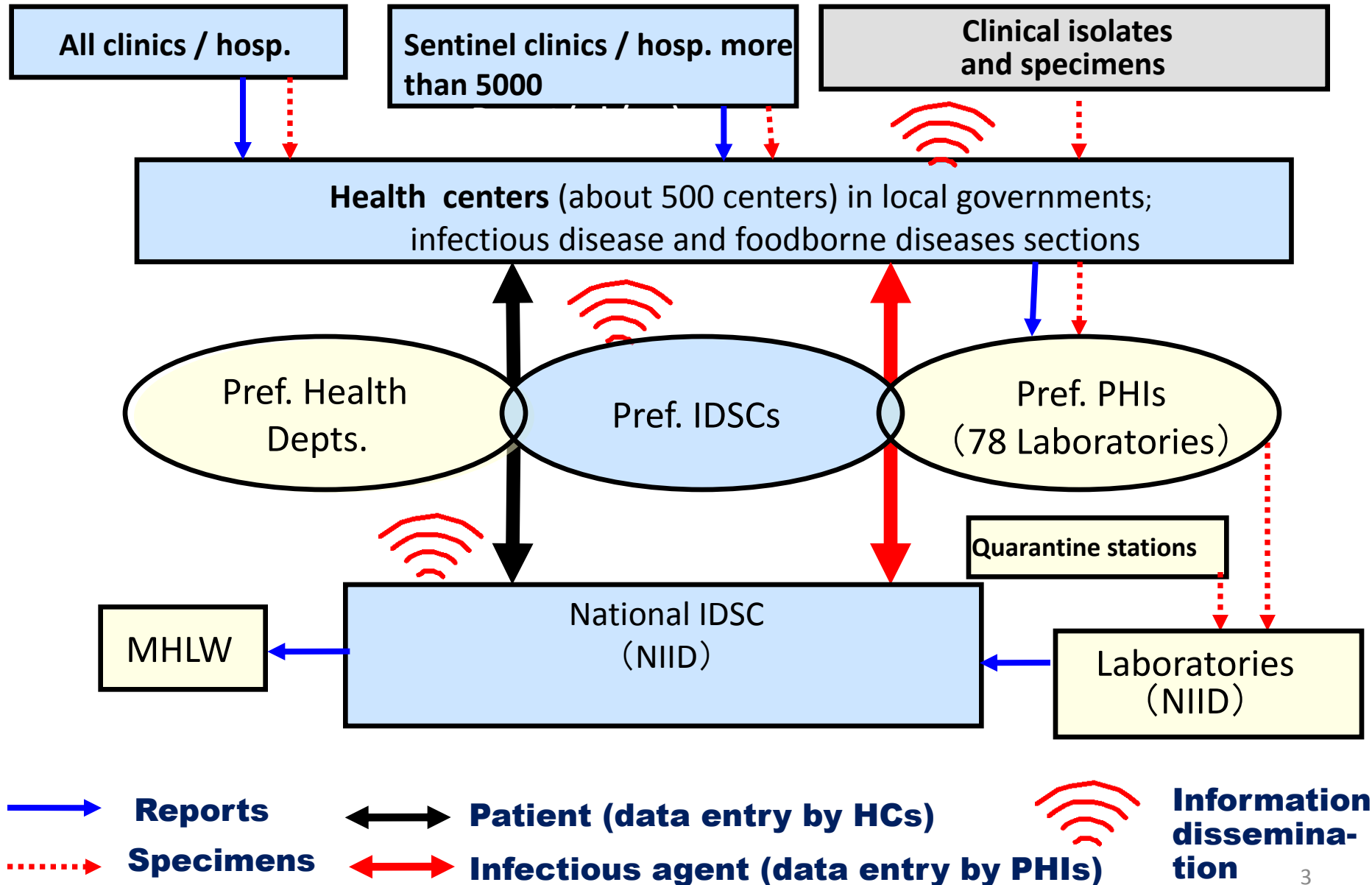
- **The Food Sanitation law:**

When an infection is notified as food poisoning by physicians or judged as such by the doctor of the health center, the local government investigates it and submits the report to MOH(section of food sanitation)

- **The Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infection (Infectious Diseases Law):**

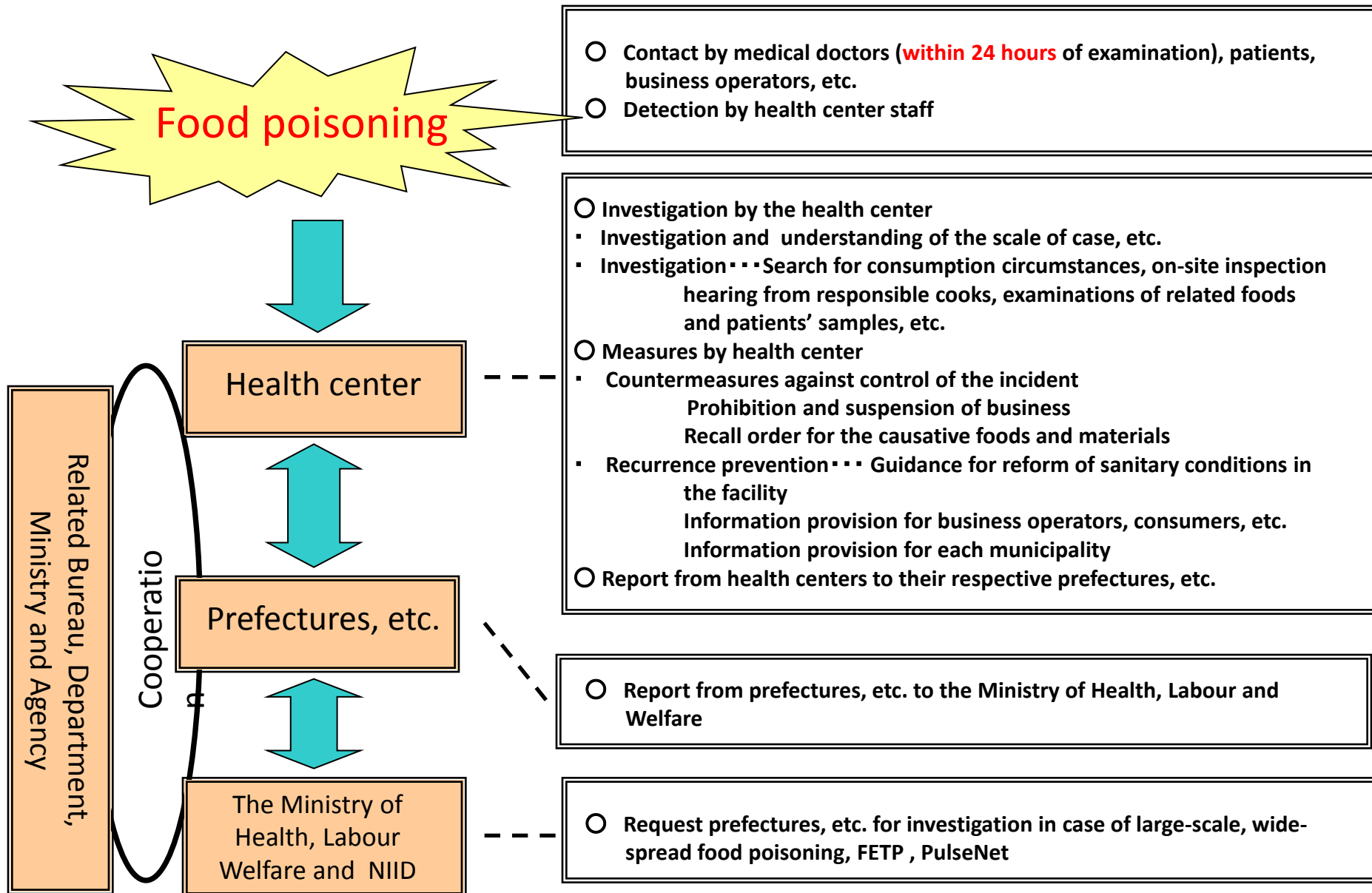
Physicians find patients with symptoms of infections and isolate the strain from the patients, physicians inform it to the local government, who submits the report to MOH(section of infectious diseases).

Surveillance System in Japan

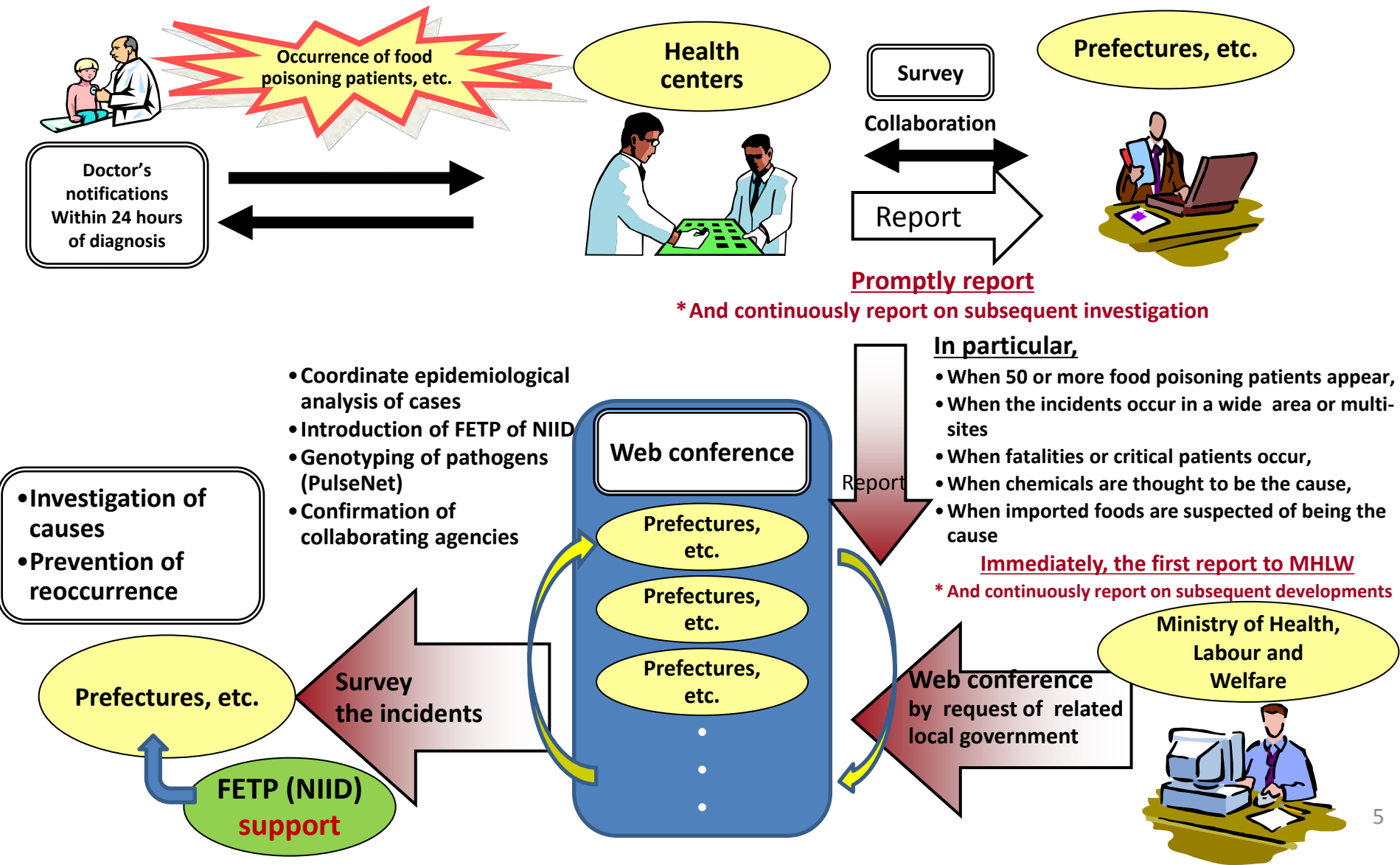


Local Government responses to food poisoning

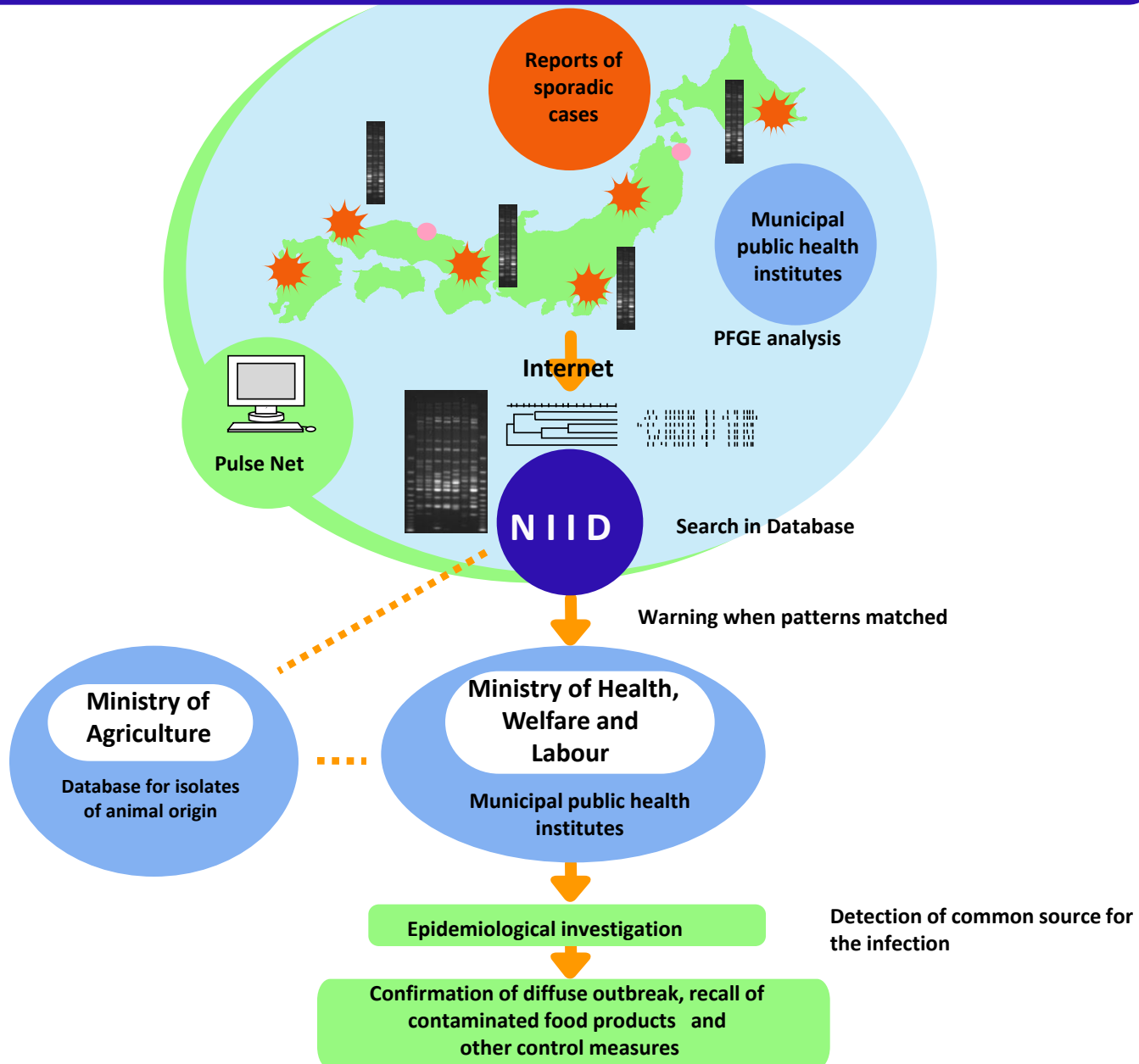
Food poisoning



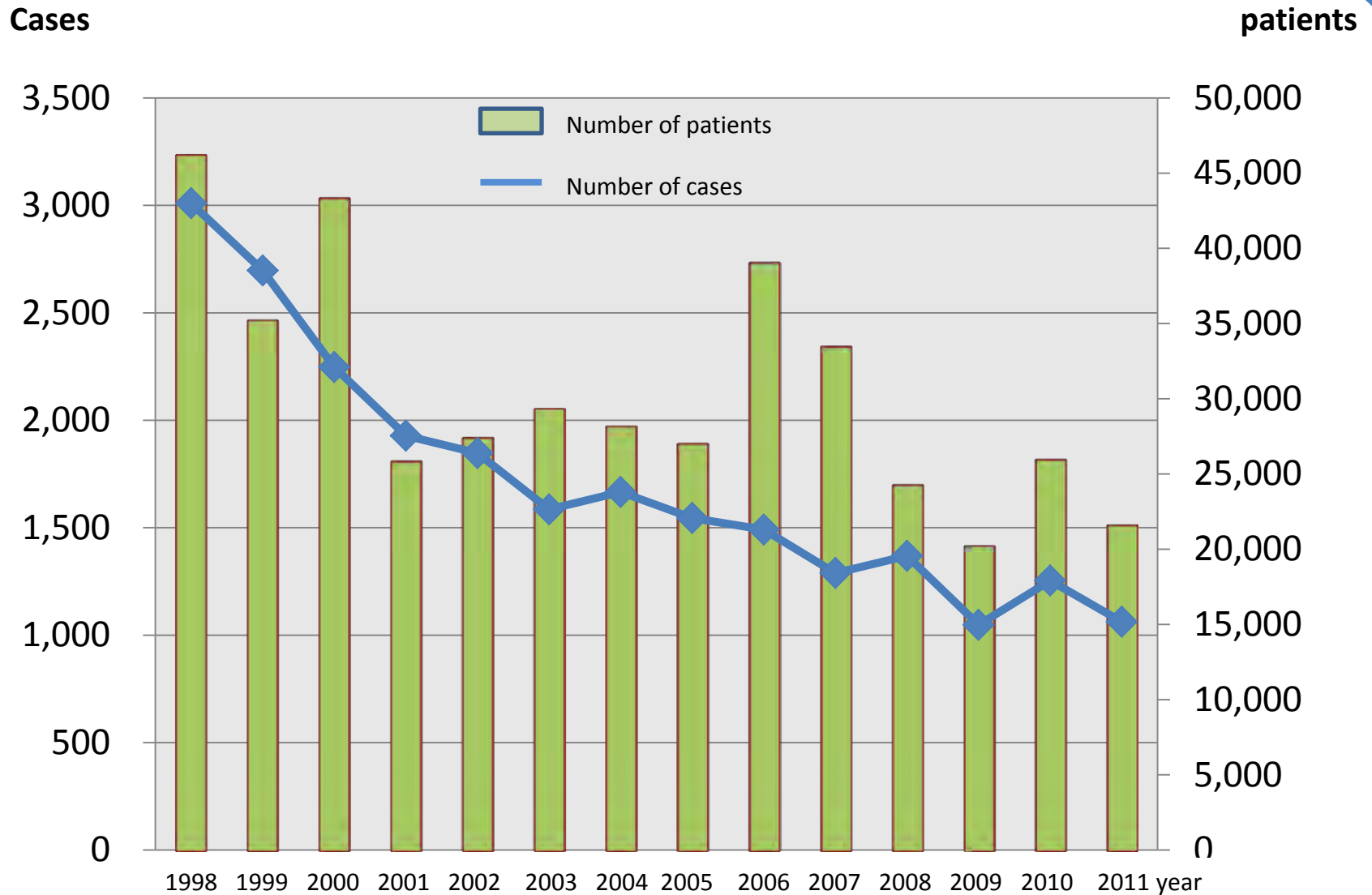
Response to food poisoning occurred in a wide and scattered area



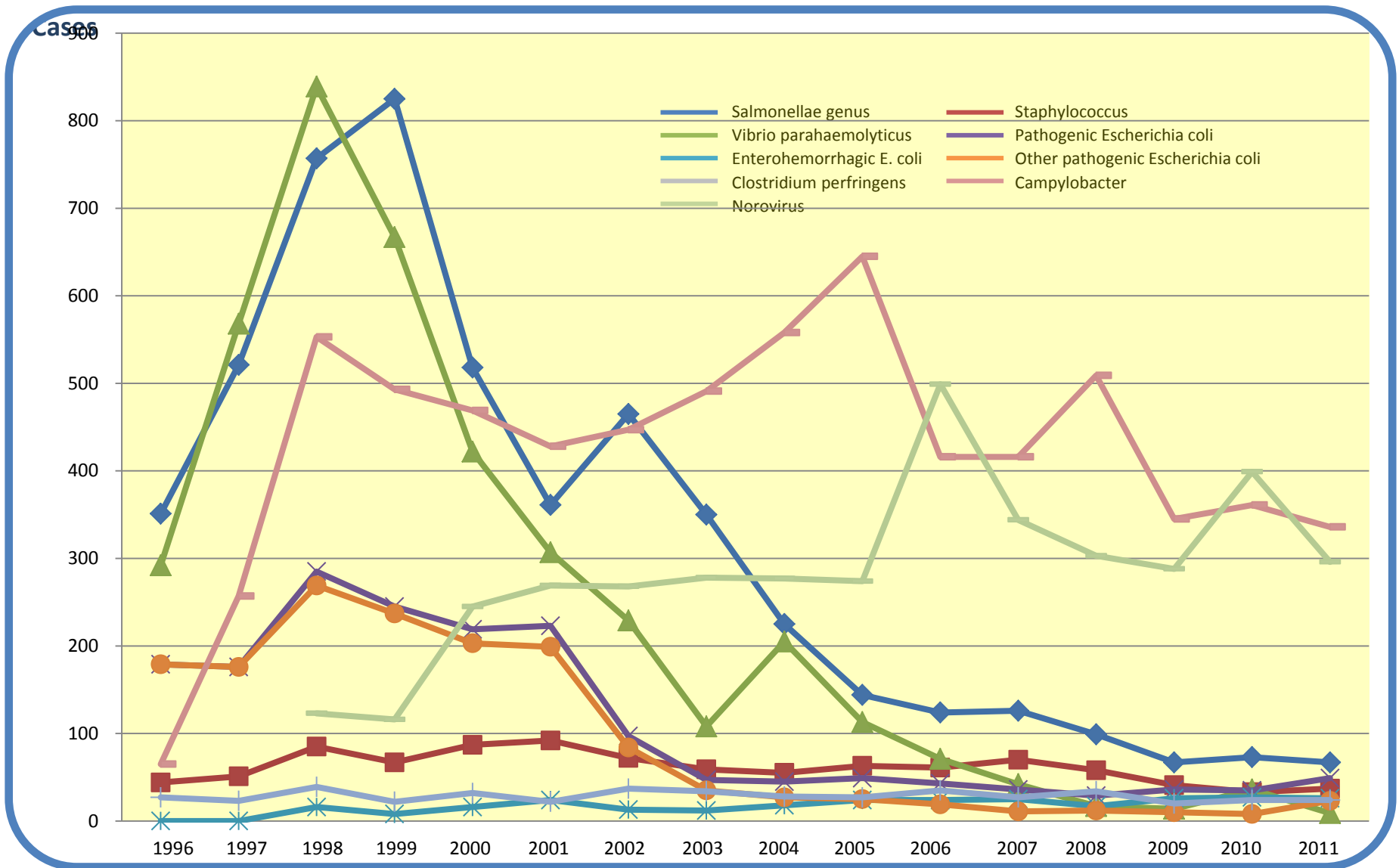
Schematic flow of Pulse Net Japan



Trend of annual food poisoning cases and patients



Annual reported number of food-borne diseases by each causative pathogen



* *Campylobacter* and norovirus cases have been increasing in recent years. However, *Salmonella* and *Vibrio parahaemolyticus* cases have decreased.

Reasons of decrease in the number of incidents and patients caused by *Salmonella*- and *Vibrio parahemolyticus*

Countermeasures taken to reduce food poisoning by

- ***Salmonella* (in 1998)**

- S. Enteritidis* is main serotype for Salmonellosis in Japan (mainly egg contamination:

- 2~4 eggs / 10,000 eggs)

- Setting expiration date of eggs in the case of raw-eating

- Setting standards for liquid egg chicken(zero viable number of *Salmonella* spp.)

- Creating guidelines of hygiene in the packaging facilities

- Awareness about the hygienic handling of eggs at home

- Storage criteria: store the eggs at below 10 °C at retail shops and at home

- ***V. parahemolyticus* (in 2001)**

- Setting standards of the display for raw-eating fresh fish and shellfish

- Standard set of criteria:

- Standard component: below 100 CFU/ g in raw-eating fresh fish and shellfish

- Processing standards: use of water comparable to drinking water in the processing of seafood

- Storage criteria: store the seafood at below 10 °C

At present, *Campylobacter* and norovirus infections are predominant food borne diseases, however in the point of diseases severity, enterohemorrhagic *E. coli* infection is a big concern in Japan

Trend of occurrence of EHEC infection

A) Food-borne diseases(Food Sanitation Law)

B) Infectious Disease Surveillance

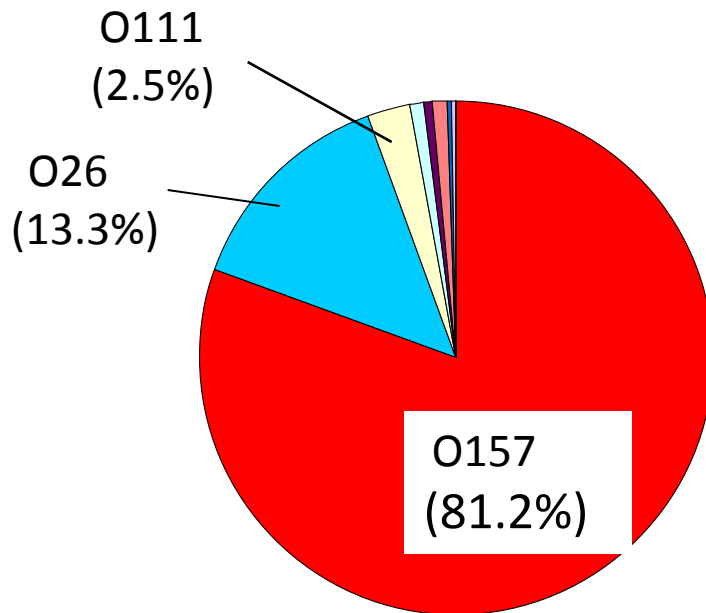
Year	No. incident	No. patients	No. death		No. of reports (patients)
2000	16	113	1		3,648
2001	24	378	0		4,435
2002	13	273	9		3,183
2003	12	184	1		2,999
2004	18	70	0		3,764
2005	24	105	0		3,589
2006	24	179	0		3,922
2007	25	928	0		4,617
2008	17	115	0		4,321
2009	26	181	0		3,879
2010	27	358	0		4,135
2011	25	714	7		3,938

No. of report in compliance with the Food Sanitation Law was smaller than that of the Law concerning the Prevention of Infectious Diseases. Incubation period of EHEC infection is around 4~8 days. When the incident is found, suspected food may have been discarded. So, it is difficult to identify contaminated foods.

Serotypes of EHEC isolated in Japan (Y1997-2008)

total ($n = 25,792$)

(O157+O26+O111=97%)



Major serotype:

O157:H7, O157:H-

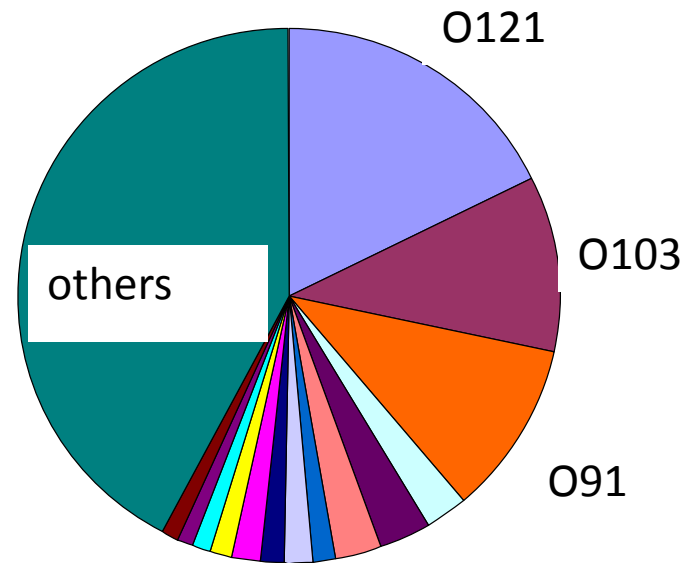
O26:H11, O26:H-

O111:H-

other than O157, O26, O111

($n = 1,406$)

(rest of 3%)



O128

O44

O146

O165

O119

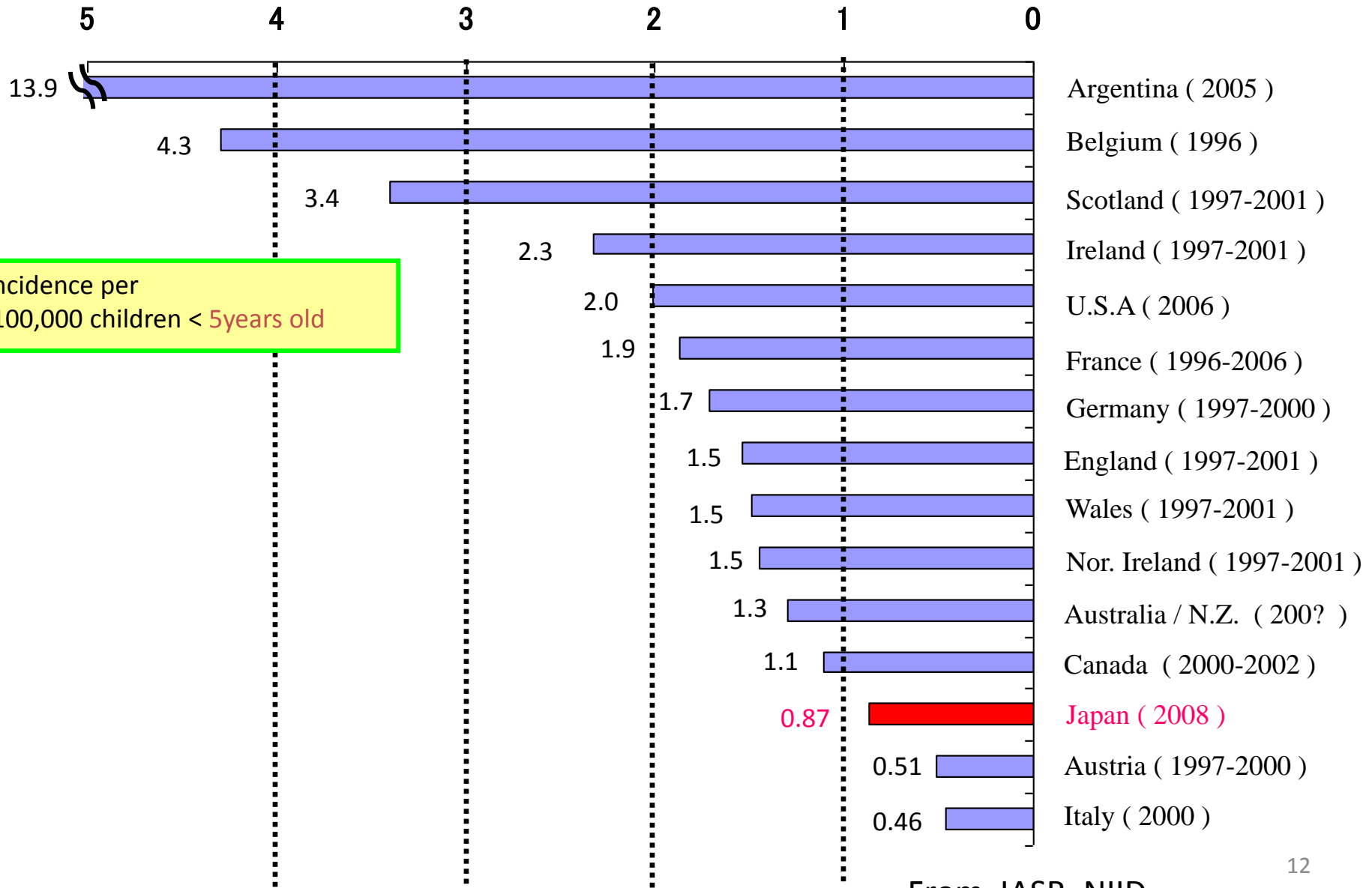
O145

O169

O8

O55

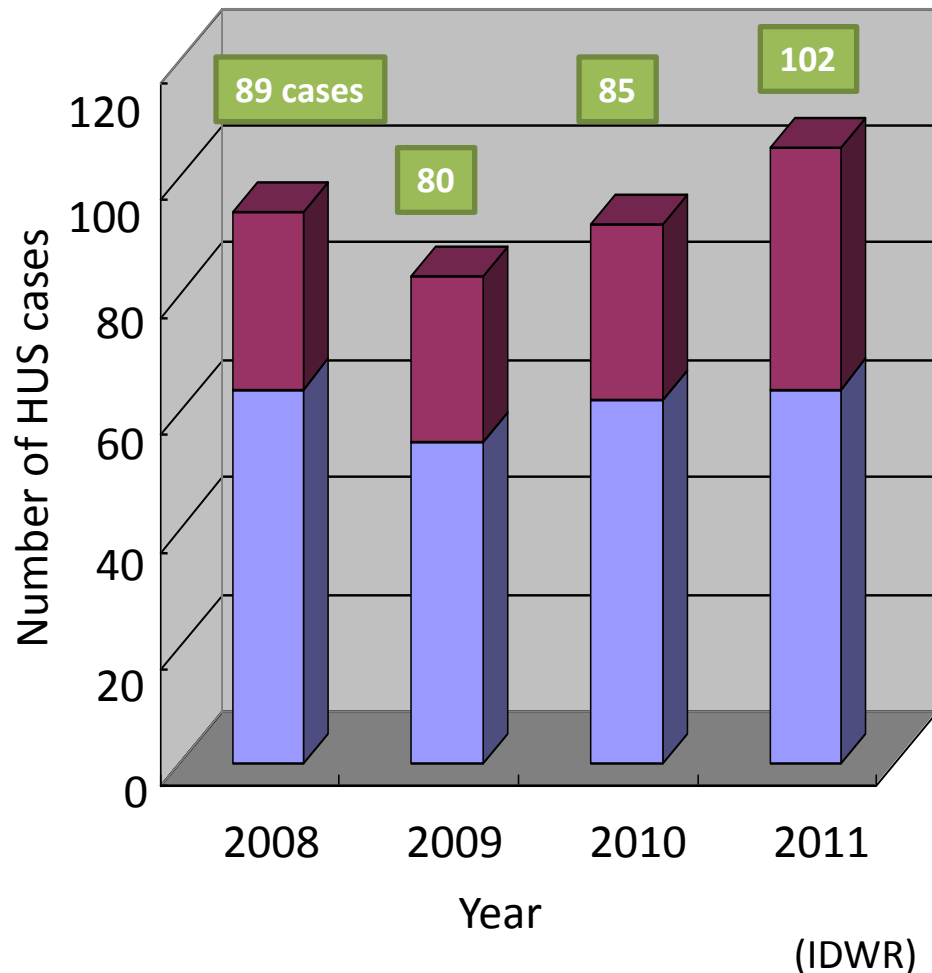
Comparison of HUS incidence



From IASR, NIID

Number of HUS cases with/without EHEC (2008-2011)

- # of culture-negative HUS cases (with %)
- # of culture-positive HUS cases



For EHEC culture-negative HUS cases:
detection of anti-*E. coli* O antibodies
in sera of HUS patients.

anti-*E.coli* antibody positive :
29 / 39-tested (74.4%)

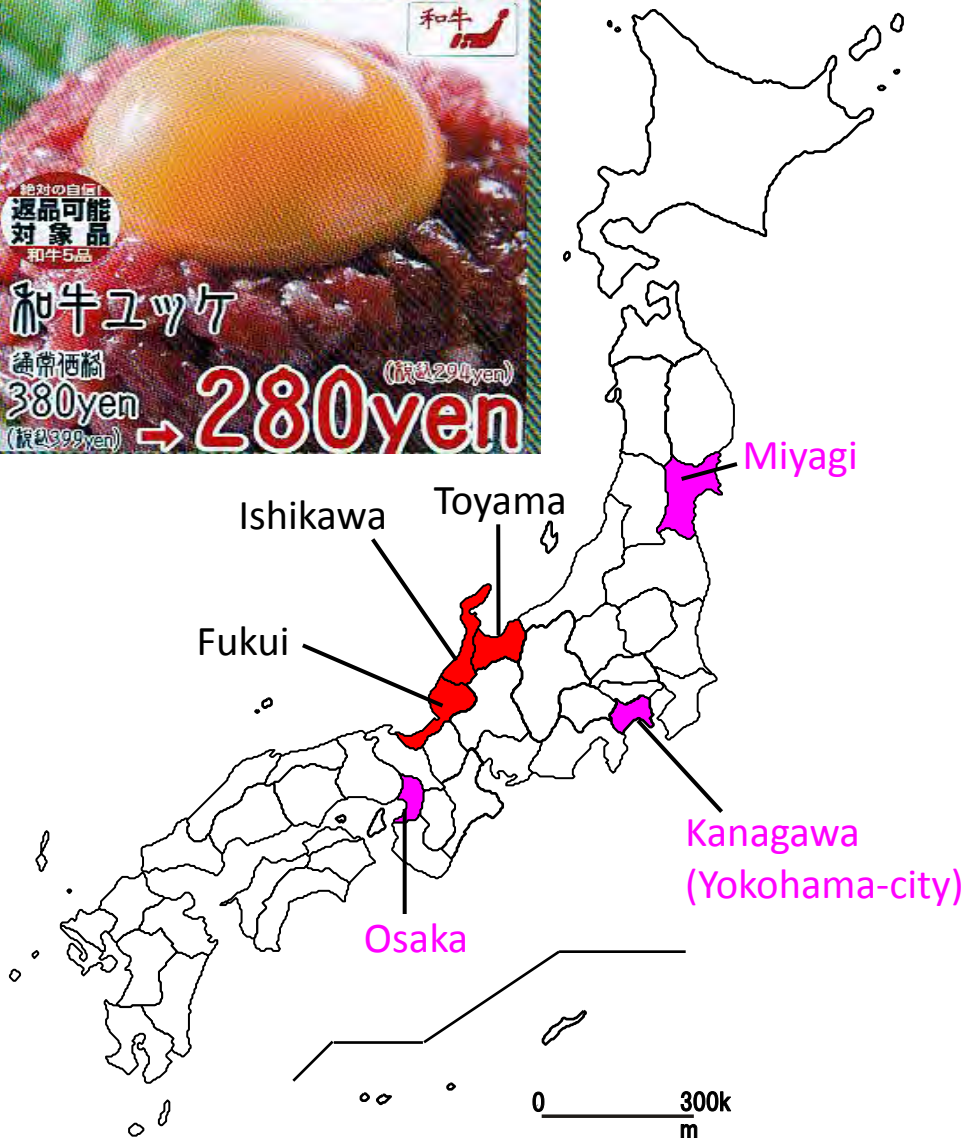
serotype of HUS
(% positive number)

O157 (85%)
O111 (5%)
O121 (2%)
O26 (2%)
O165 (1%)
O145 (1%)

EHEC outbreaks with more than 100 culture-confirmed cases, 2001-2012

Year	Prefecture/City	Setting	Serotype	VT type	Symptomatic cases	Culture positives	Likely mode of transmission	Reference
2001	Chiba P.	Patient's home	O157:H7	VT1&2	195	257	beef products	
2002	Fukuoka C.	Nursery school	O157:H-	VT2	74	112	lightly salted cucumber	
2002	Utsunomiya C.	Hospital and home for the elderly	O157:H7	VT1&2	123	111	Koumi-ae	
2003	Yokohama C.	Kindergarten	O26:H11	VT1	141	449	Foodborne	
2004	Ishikawa P.	High school	O111:H-	VT1&2	110	103	Foodborne	
2007	Tokyo M.	School refectory	O157:H7	VT2	467	204	Foodborne	
2007	Miyagi P., Sendai C. & Akita C.	Restaurant	O157:H7	VT1&2	314	173	boxed meals	
2009	Saga P.	Nursery school	O26:H11	VT1	N.D.	133	lettuce	
2010	Mie P.	High school	O157:H7	VT2	138	164	school lunch	
2011	Toyama P.	Chain restaurants	O111:H8	VT2, VT-	181	102	Yukhoe (raw be	
			O157:H7	VT1, VT2, VT1&2		38		
2011	Yamagata P.	Festival	O157:H7	VT1&2	287	189	Japanese rice cakes	
2012	Osaka C.	Nursery school	O26:H-	VT1	68	115	Foodborne	

An outbreak of EHEC O111:H8 in Yaki-niku chain restaurants by consumption of Yukhoe (raw beef dish), April 2011



- Confirmed **86 patients** including **5 death** and **34 HUS** were reported from **6** prefectures.
- **O111:H8** were isolated from patients and unopened package of raw beef meat.
- **O157:H7** were also isolated from some patients with O111:H8.

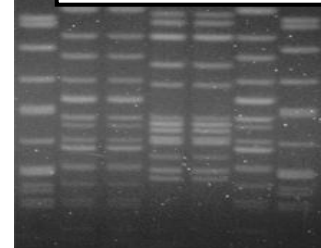
PFGE analysis for **O111:H8** and **O157:H7**

M Serodiagnoses detected higher O111 antibodies than that of O157 in sera of HUS patients.

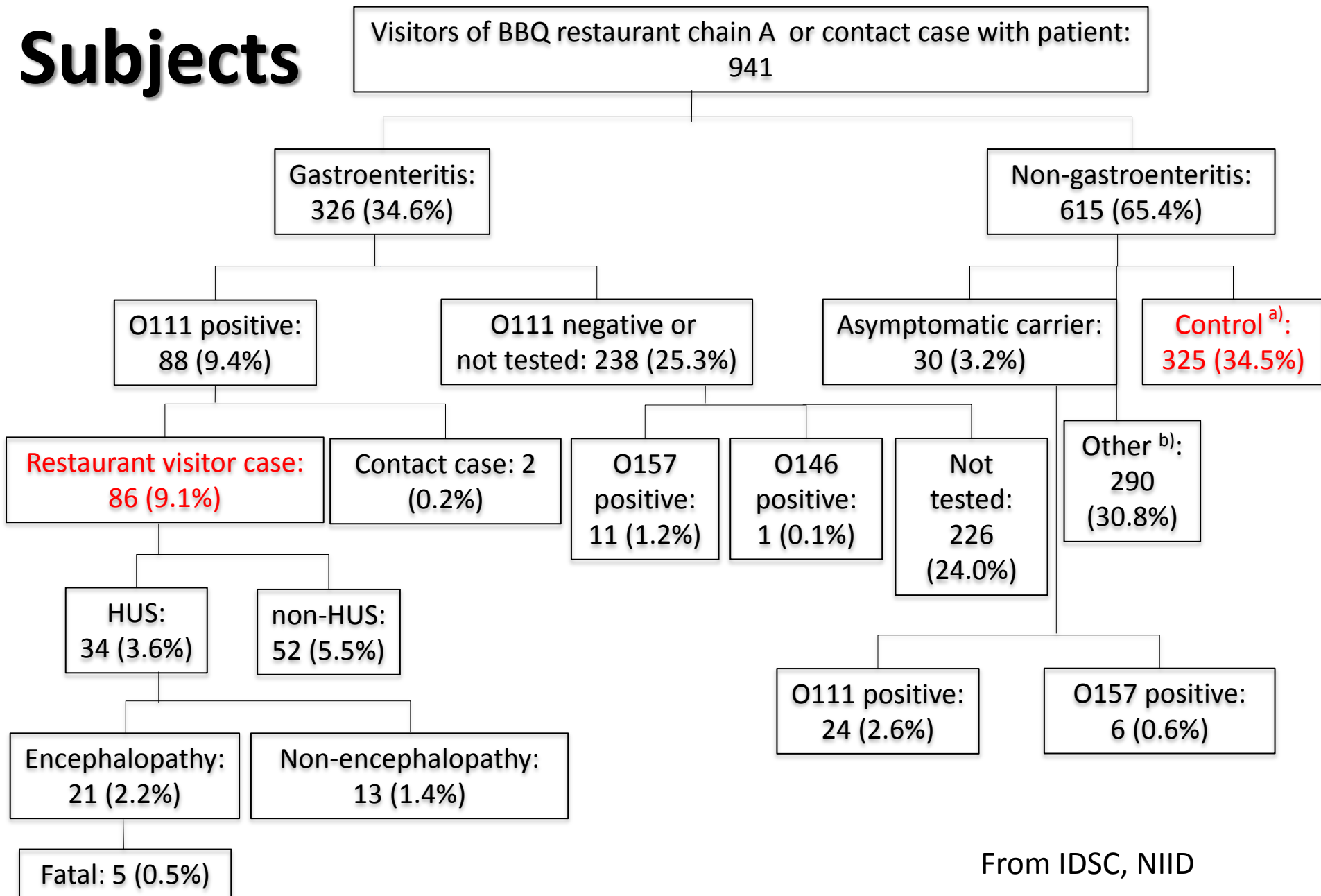


O111 is responsible for developing HUS.

5. O111:H8 VI-negative



Subjects



From IDSC, NIID

a) Eligible: no symptom and having record for intake menu as the group by public health sector

b) Other: included non-tested, inappropriate interview or not eligible group

Consumption of individual dishes among subjects

	Case (N=86)		Control (N=325)	
	N	%	N	%
BBQ				
Yukhoe (Raw beef)	82	95.3	166	51.1
Outside skirt	35	40.7	79	24.4
Chicken tail	25	29.1	54	16.6
Vegetable				
Been sprout	6	7.0	16	4.9
Kimuchi (Korean pickle)	15	17.4	43	13.2
Lettus	13	15.1	58	17.8
Salad	6	7.0	18	5.5
Lettus without pesticide	1	1.2	10	3.1
Ceaser salad	16	18.6	60	18.5
Sliced tomato	2	2.3	11	3.4
Other				
Cold noodle	24	27.9	60	18.5

a) One case: missing data of food consumption

From IDSC, NIID

Source of infection

- Yukhoe consumption: significantly high odds ratio (OR=19.64, 95%CI: 7.03-54.83), common source of material
- PFGE : distinguishable between isolates from patients and beef material
- Contamination setting:
 - No evidence of contamination in beef meats at a specific branch of the chain restaurant
 - Contamination at the meat processing company which provides chunks of meat to the restaurant or more upstream

Making Raw Beef Meat “Yukhoe (yukke)”

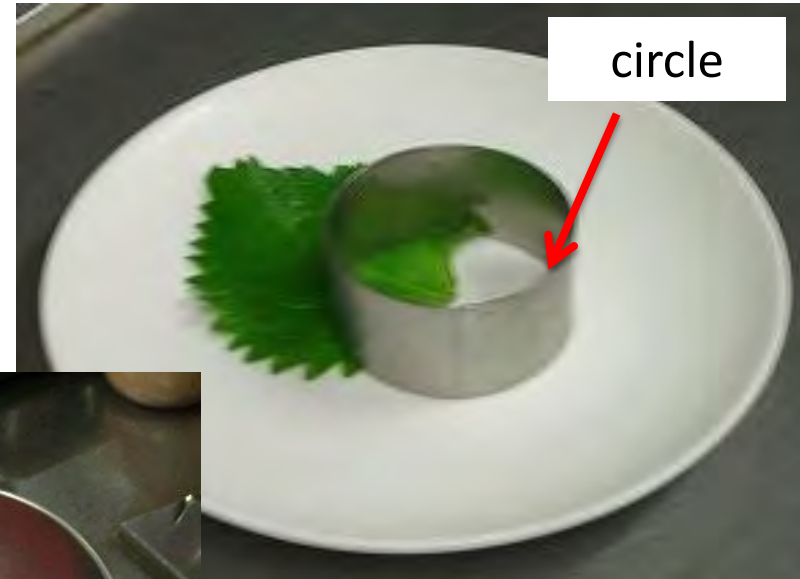
Cut chunks of meat to small pieces



Mixed with sauce

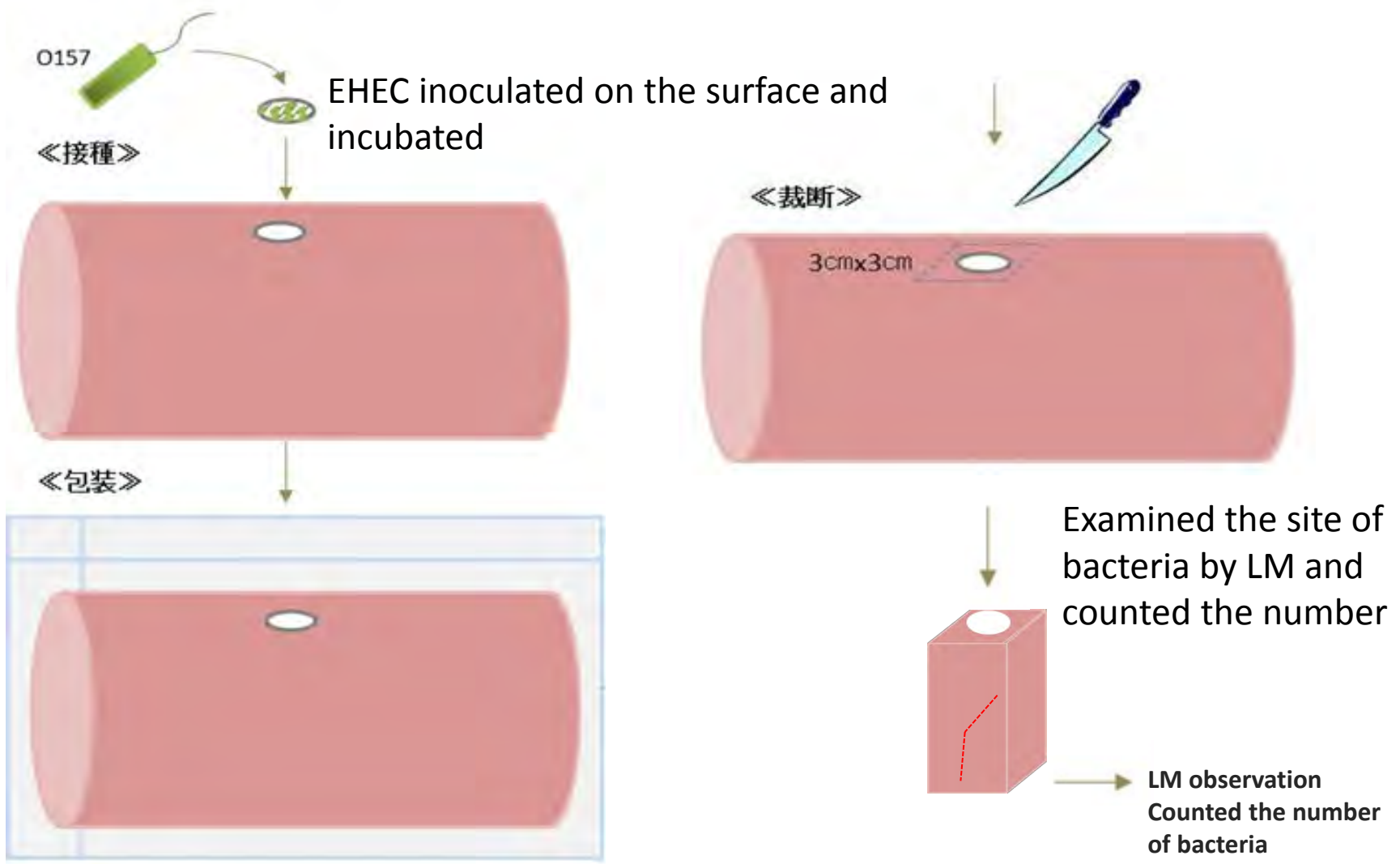


pull into shape



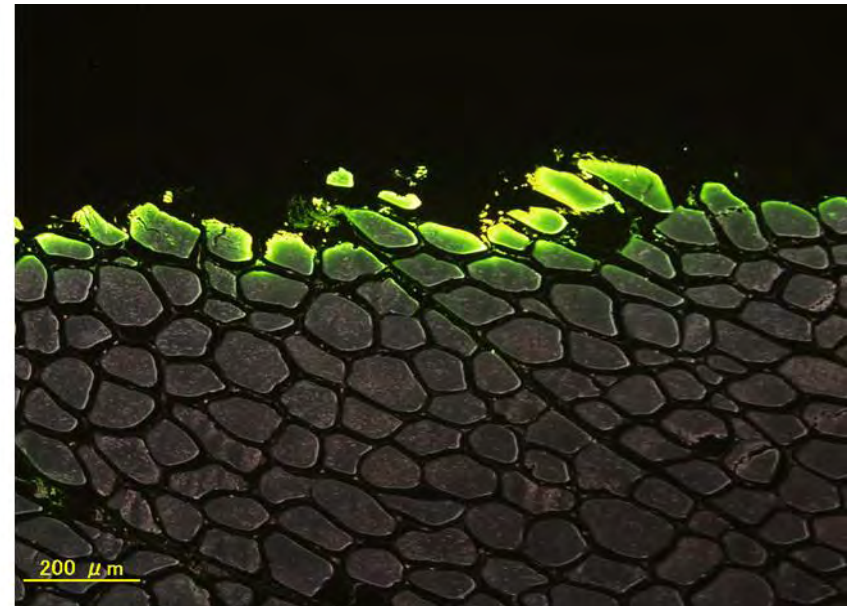
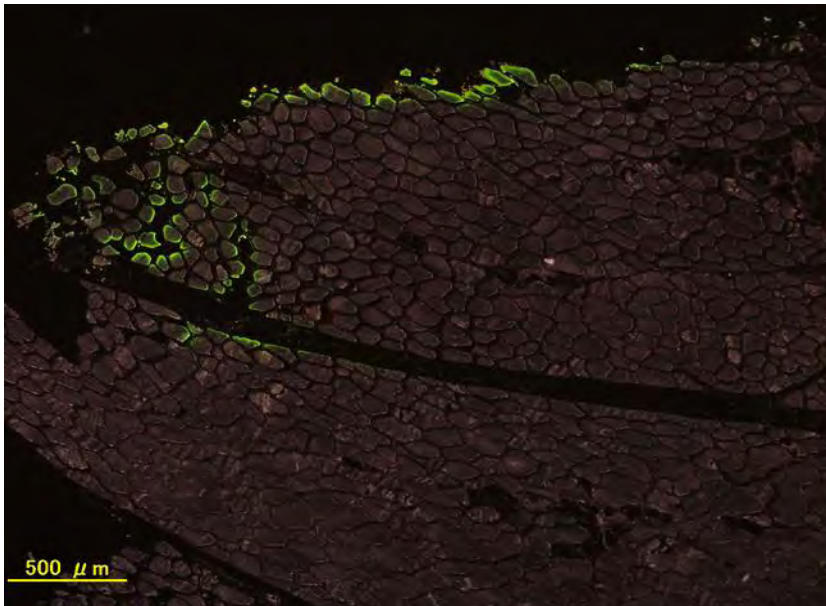
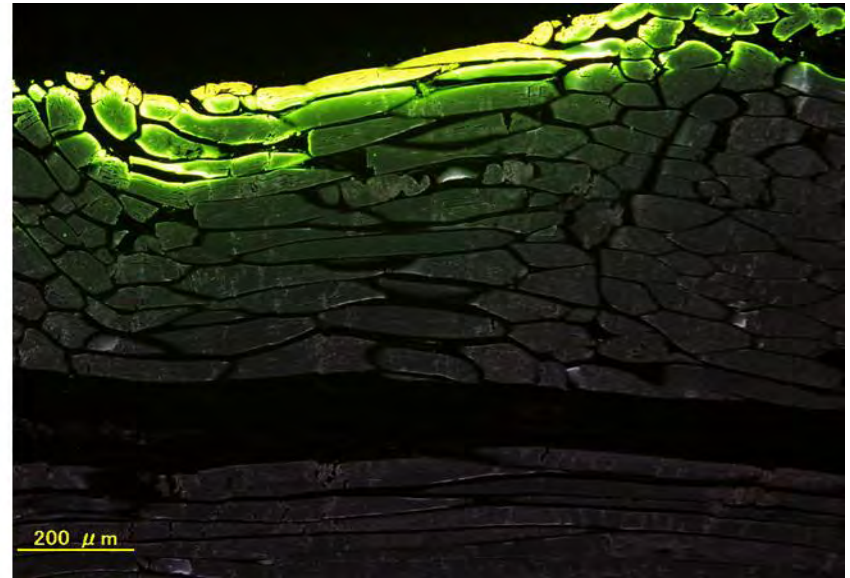
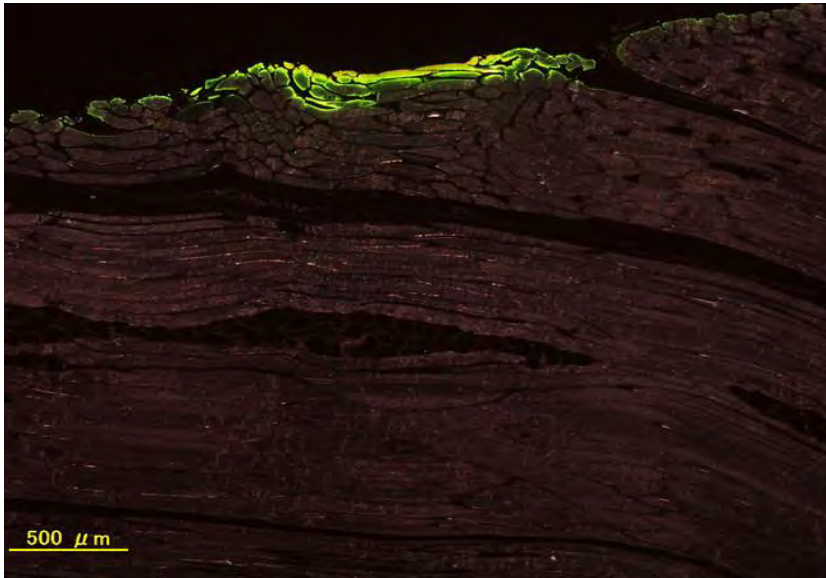
From Dr. Igimi, NIRS

Localization of EHEC after inoculated on the surface of beef meat chunk



The EHEC strain(1×10^4) was inoculated on the surface of chunk of meat.

Localization of EHEC strain after inoculation in the surface of meat:



The bacteria was detected at the depth of 10 mm under the surface;
the bacteria invades inside the beef.

Heating the surface of chunk of beef meat at 85°C

1 min



3 min



5 min



10 min



After heating the surface at 85°C for 10min, temperature at the depth of 10mm reached to 60°C and kept for 2min . Bacteria at the depth were killed .

Countermeasure by MHLW: Establishment on criteria and standards related to eating raw meat taken

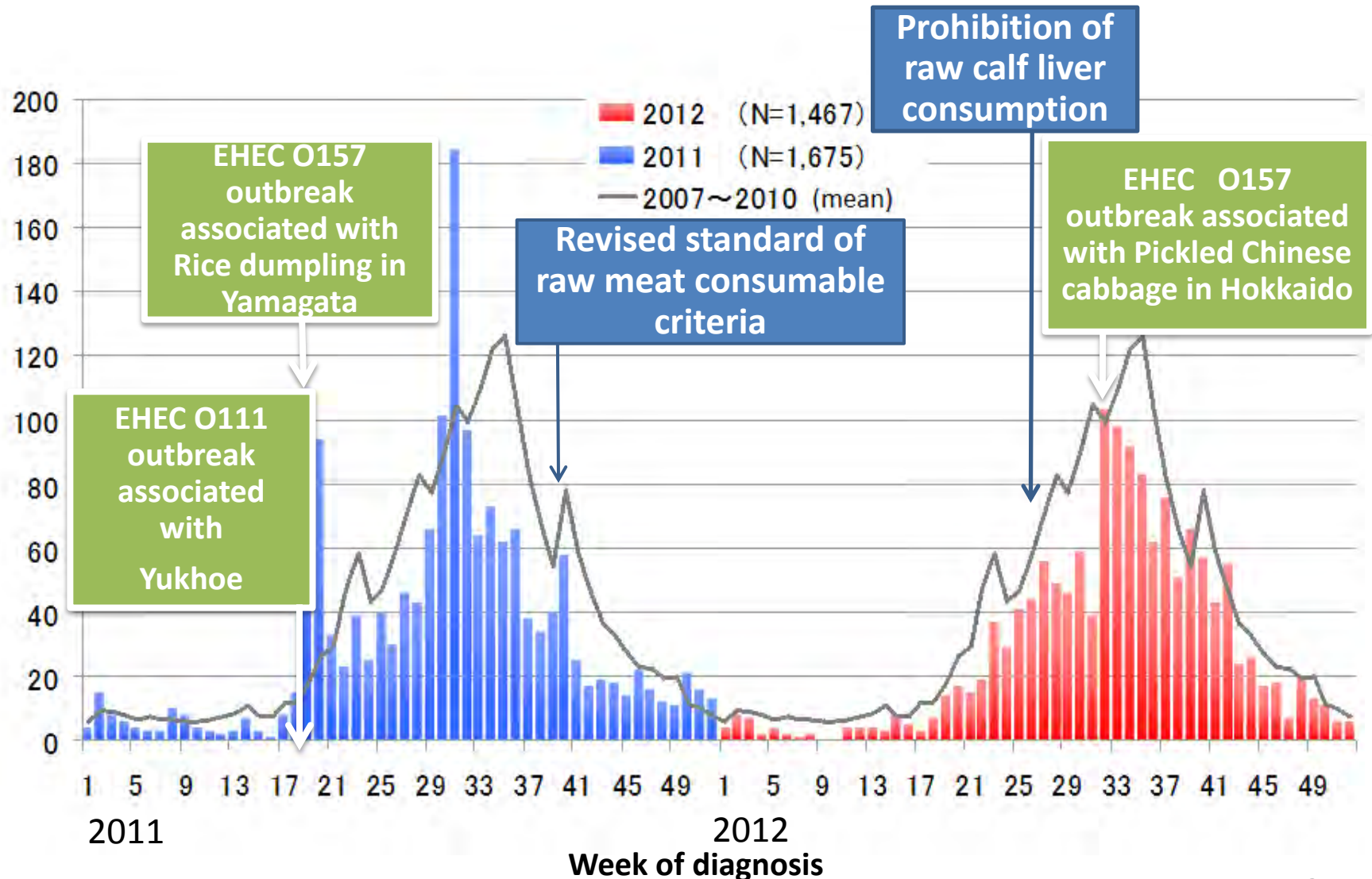
- 1) Component standard of raw-eating meat:
 - negative for *Enterobacteriaceae* bacteria in 25 g of sample
- 2) Processing standards:
 - Thorough hygiene facilities
 - Sanitary equipment
 - Sanitary handling
 - Prevention for the spread of contamination inside
 - Heating a portion of depth of more than 10 mm from the surface of meat chunk for more than 2 min at 60°C
(surface of meat chunk should be heated at 85 °C for 10min.)
- 3) Storage criteria:
 - raw meat should be stored at 4°C or less

Identified causative foods of EHEC O157 incidents

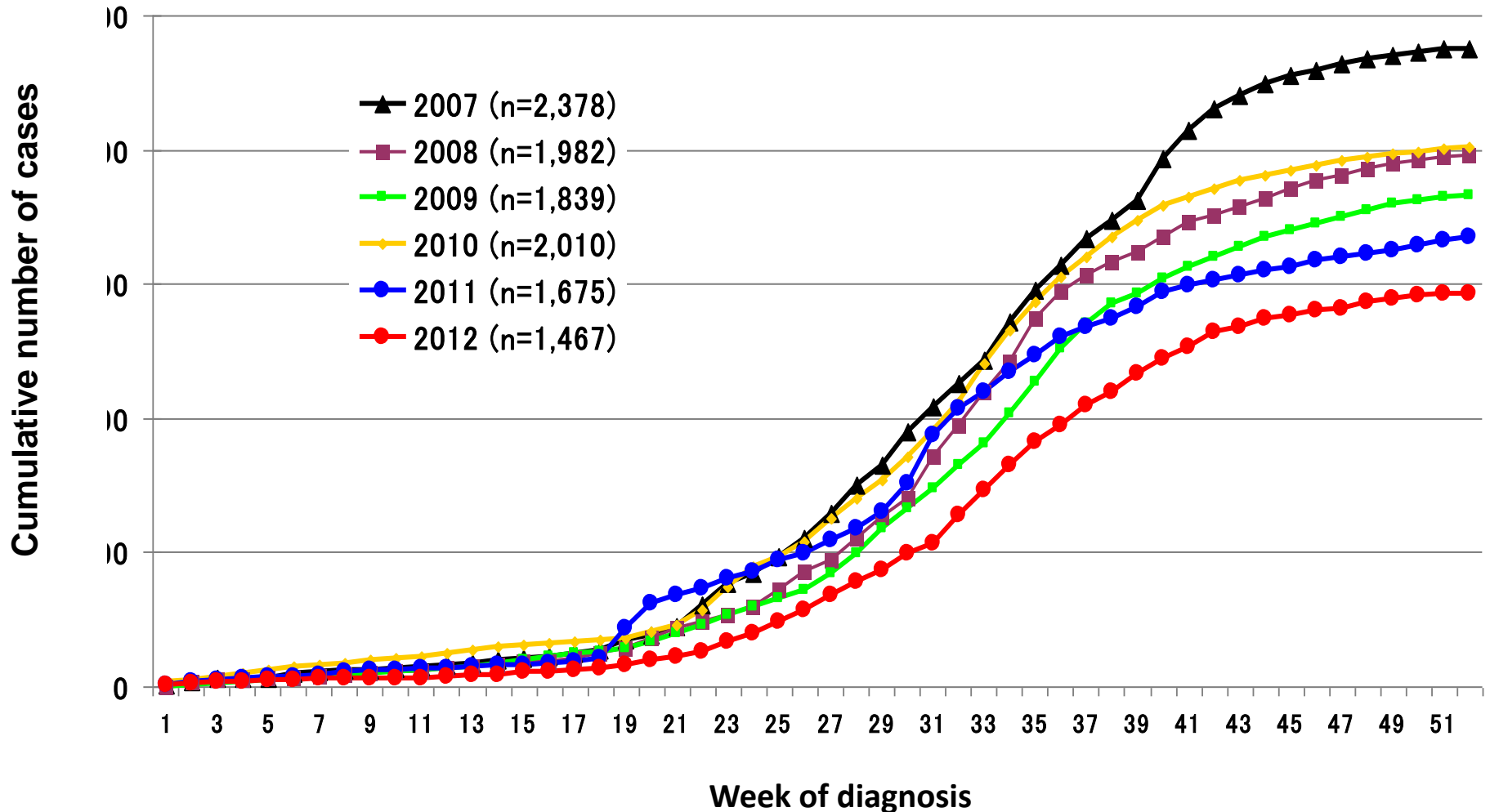
(from 2003 to 2009 year, Report from Annual Statics of Food-borne diseases)

Causative foods	No. of incidents	Facilities occurred	No. of incidents
Grilled meat	36	restaurant home other	32 2 2
Calf liver	18	restaurant home other	15 2 1
Yukke (Yukhoe)	8	restaurant	8
Steak/ hamburger	4	restaurant other	3 1
Broiled calf innards	3	restaurant	3
Other meat	1	home	1
Others(include unknown, vegetable suspected, etc)	69	restaurant home school others	56 3 1 9
Total	139		

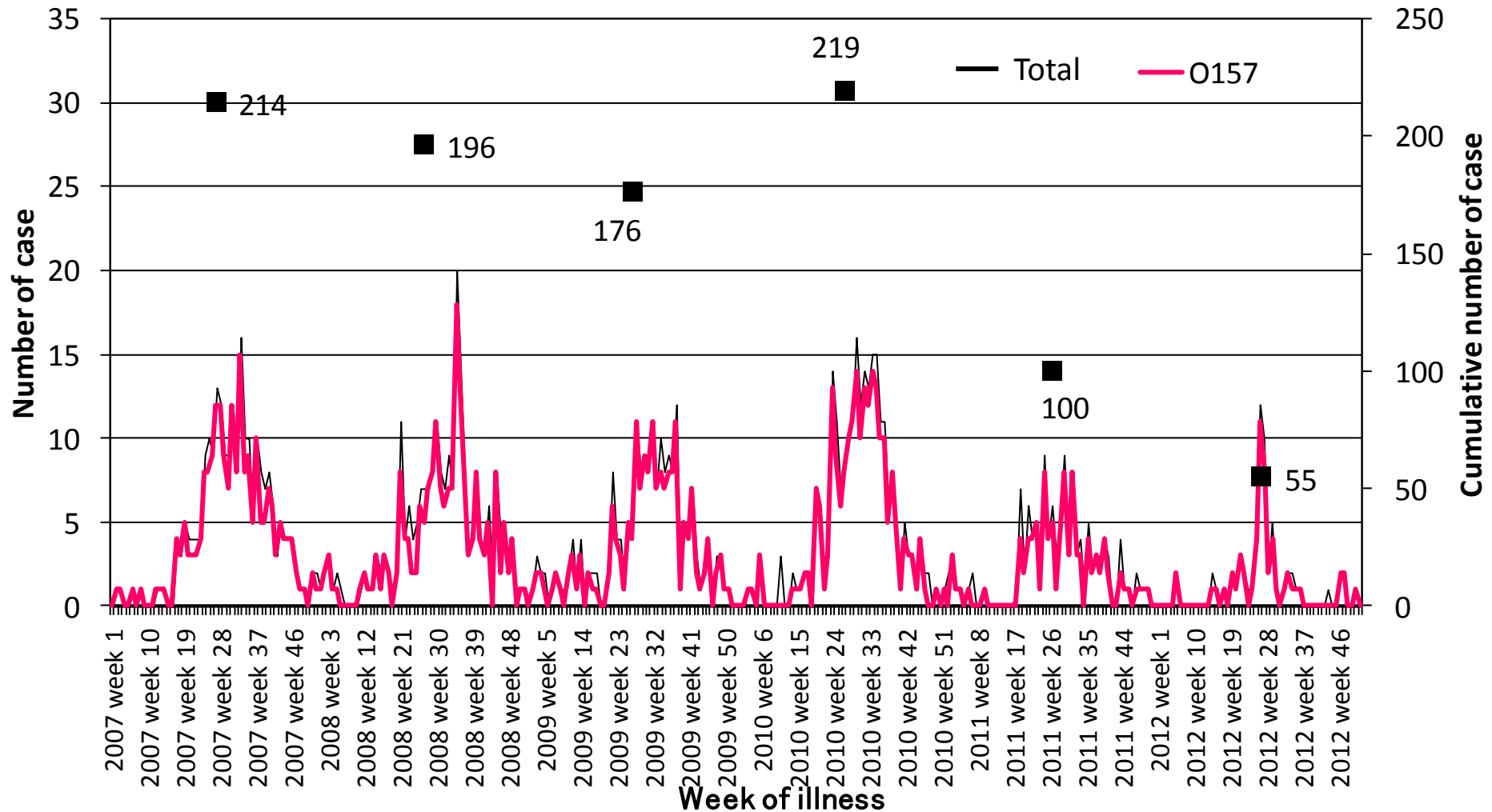
Number of EHEC O157-symptomatic cases and countermeasures for the control, 2011-2012



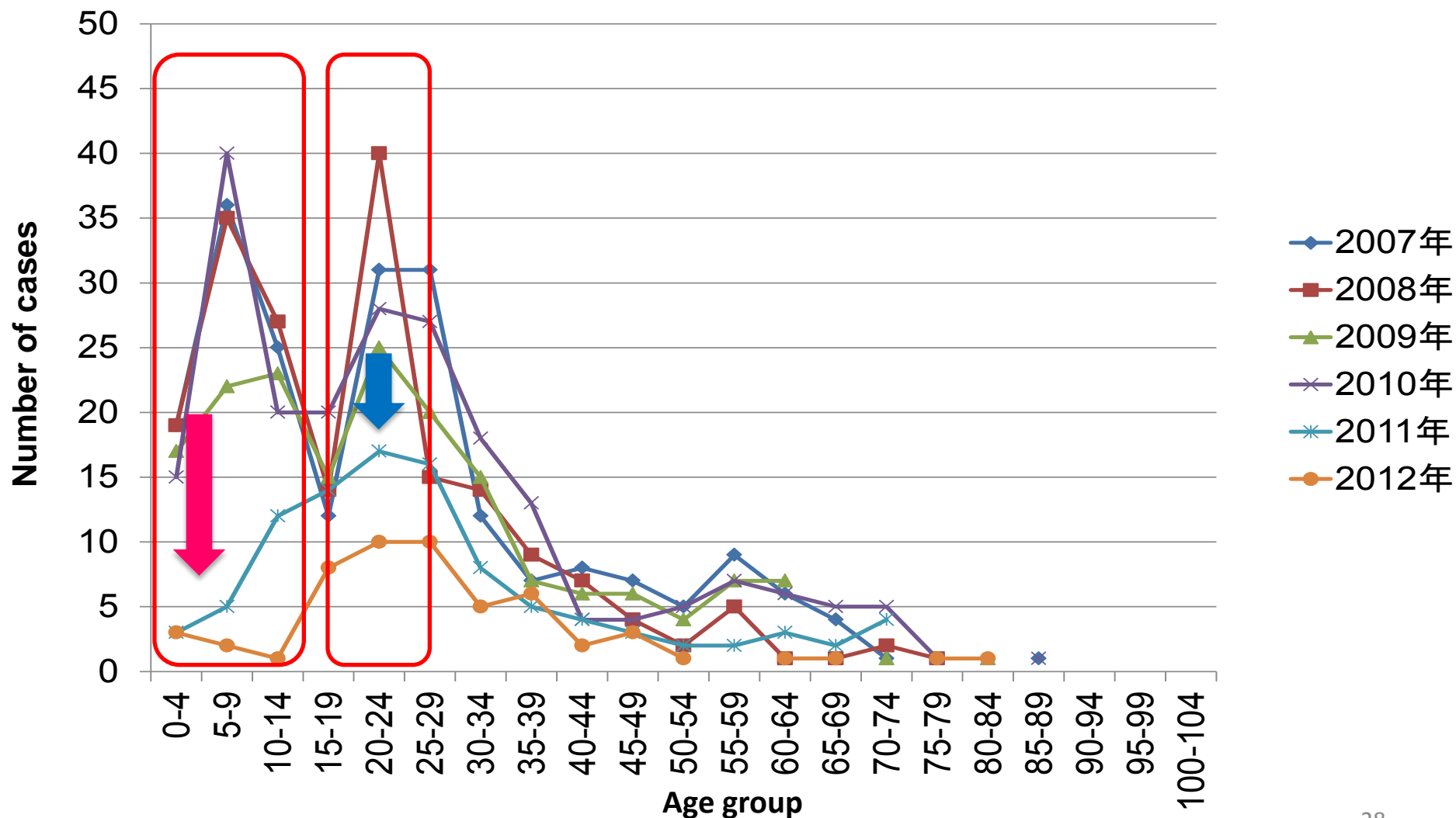
Cumulative number of EHEC O157-symptomatic cases, 2007-2012



Cumulative number of EHEC O157-symptomatic cases with the history of raw beef or raw calf liver consumption , 2007-2012 (note: outbreak-related cases were excluded)



Annual age distribution of EHEC O157-symptomatic cases with the history of raw beef or raw calf liver consumption, 2007-2012 (note: outbreak-related cases were excluded)



PAR(population-attributable risk) % with EHEC infections in eating raw beef , raw calf liver, etc. between 2010 and 2012

Exposure (Consumption)	Exposure/EHEC case		Exposure/Control case		aOR	PAR%
	N	%	N	%		
In 2010 Y						
Raw calf liver	10/53	18.9	7/345	2.0	9.8	16.9
Raw/uncooked beef	18/53	34.0	52/344	15.1	9.4	30.3
Enough cooked ground beef	7/46	15.2	15/212	7.1	1.5	4.9
In 2012 Y						
Raw calf liver	0/65	0.0	0/269	0.0	NC ^{a)}	NA ^{c)}
Raw/uncooked beef	4/63	6.3	8/256	3.1	NC ^{b)}	NA
Enough cooked ground beef	8/65	12.3	13/269	4.8	4.4	2.5

a) NC: Not able to calculate crude Odds Ratio (too low)

b) NC: Not able to calculate Multiple Logistic Regression (too low)

c) NA: Not able to calculate PAR% (too low)

Comparison of the attributable risk among EHEC O157 cases for consumption of raw/uncooked beef meat and raw calf liver before and after the introduction of enhanced restrictions

- Raw/uncooked beef (**PAR% ^{a)}: 16.9%**)
OR=13.3, 95%CI: 4.4-39.8
- Raw beef liver (**PAR% 30.3%**)
OR=28.2, 95%CI: 3.0-infinity

- Raw/uncooked beef (**PAR%: too low**)
OR=1.6, 95%CI: 0.4-6.9
- Raw beef liver (**PAR%: too low**)
OR: Not available

1st October 2011

Revised the standard of
raw meat consumable
criteria

1st July 2012

Prohibition of raw
calf liver
consumption

Investigation
July-December,
2010

Case: 53
Control: 221

Case: 63
Control: 257

Investigation
July-December,
2012

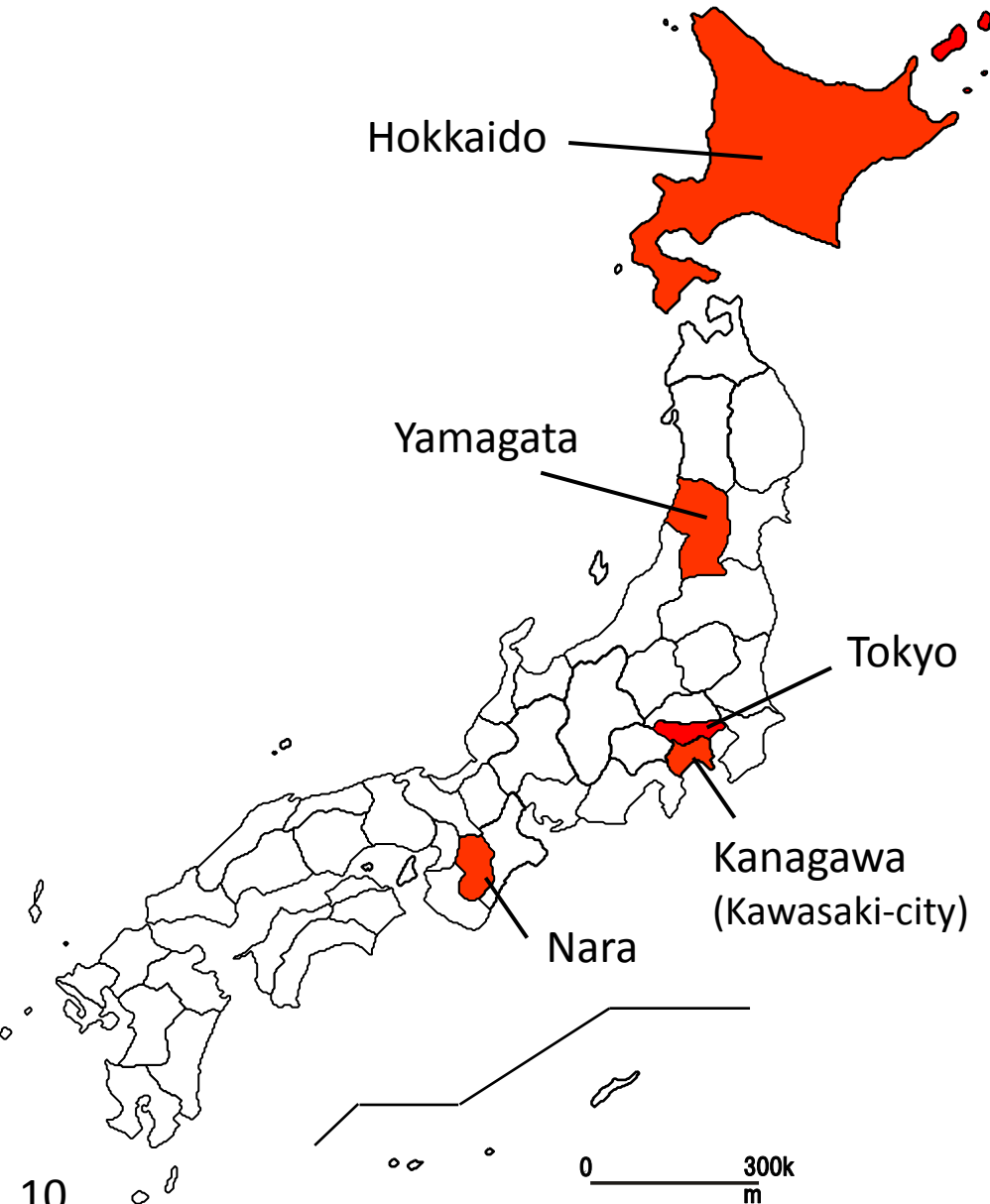
Comparison between both years

From IDSC, NIID

Conclusion

- Information on food-borne diseases are collected based on the two laws in Japan
- Incidents have been decreasing in *Salmonella* and *Vibrio parahaemolyticus* food-borne infections probably due to the effective countermeasures taken
- The reported total number of EHEC O157- symptomatic cases decreased after several countermeasures were taken in 2011 and 2012.
- The number of sporadic EHEC O157-symptomatic cases with the history of raw beef or raw calf liver consumption decreased , especially among age groups of both less than 10 years and 20-24 years old
- The decrease of EHEC O157 infection attributes to the restriction of consumption of either raw beef meat or raw calf liver

An outbreak of EHEC O157:H7 due to consumption of pickled vegetable occurred in Hokkaido Pref, August 2012



- **169 patients** including **8 death** were reported from **5** prefectures (Hokkaido, Yamagata, Tokyo, Kanagawa, and Nara).
- **11** facilities for elder care in Hokkaido were involved in the outbreak.
- **O157:H7** were isolated from patients and unopened package of pickled vegetable.
- **IS-printing system** was very effective for early detection of diffused outbreak.

Identified causative foods of EHEC O157 incidents

Problem: about half of incidents are caused by contaminated vegetables and others

Causative foods	No. of incidents	Facilities occurred	No. of incidents
Grilled meat	36	restaurant home other	32 2 2
<u>Calf liver</u>	18	restaurant home other	15 2 1
<u>Yukke (Yukhoe)</u>	8	restaurant	8
Steak/ hamburger	4	restaurant other	3 1
Broiled calf innards	3	restaurant	3
Other meat	1	home	1
Others(include unknown, vegetable suspected, etc)	69	restaurant home school others	56 3 1 9
Total	139		

EHEC outbreaks with more than 100 culture-confirmed cases,

Problem:

Person to person transmission in nursery school and kindergarten

Year	Prefecture/City	Setting	Serotype	VT type	Symptomatic cases	Culture positives	Likely mode of transmission	Reference
2001	Chiba P.	Patient's home	O157:H7	VT1&2	195	257	beef products	
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2011	Yamagata P.	Festival	O157:H7	VT1&2	287	189	Japanese rice cakes	
2012	Osaka C.	Nursery school	O26:H-	VT1	68	115	Foodborne	

Colonization status of EHEC in cattle in Japan

Problem: Colonization frequency of EHEC in cattle is quite high

		O157			O26	
Species of cattle	No. examined	No. isolated	Positive frequency (%)	No. examined	No. isolated	Positive frequency (%)
Japanese beef	256	43	16.8	246	4	1.6
Crossbred	527	80	15.2	512	9	1.8
Holstein	209	23	11.0	209	0	-
Japanese shorthorn	27	0	-	27	1	3.7
Jersey	4	1	25	4	1	25.0
Alien	2	1	50	2	0	-

Acknowledge

- 1) National Institute of Infectious Diseases
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- 2) National Institute of Health Sciences
- 3) Local Public Health Institutes
Especially, Toyama Prefectural PHI
- 4) Ministry of Health , Labor and Welfare
- 5) Food Safety Commission of Japan

Thank you for your attention