c) A patient who does not follow the direction of a doctor, or ignored a diagnosis made by the insurer without a justifiable reason.

d) A person who attempts to enjoy a benefit, through fraudulent means or other unjust action.

Furthermore, certain basis principles for insurance medical care are provided by the Ministerial Ordinance on Insurance Medical Institutions' and Insurance Doctors' Medical treatment under Health Insurance and the Ministerial Ordinance on Insurance Pharmacies' and Insurance Pharmacists' medical treatment under Health Insurance.

The Trends in the Medical Care Expenditure and the Reimbursement System

Present Situation Surrounding Medical Expenditure

Overview of the National Medical Expenditure for Fiscal Year 1995

- The national medical expenditure for the fiscal 1995 was 27 trillion yen, and the expenditure is growing at annual rate of more than one trillion yen in the recent years.
- The annual medical expenditure per person is about 215,000 yen. That means it is about 850,000 yen for a family of four per year and 70,000 yen per month.
- 83% of this expenditure is paid by various insurers and by the insurance schemes for the aged.
- Looking at the expenditure by the sources of finance, about 30% of the expenditure is covered by the public budgets, and 12% by the direct payment made by patients to the doctors.
- The share of the dental care services in the total medical cost is declining, compared with the cost of ambulatory care of hospitalization.

Trends in National Medical Care Expenditure

National medical care expenditure is increasing year by year (Fig. 3-3), and reached to nearly 27 trillion yen in 1995. The ratio of national medical care expenditure to national income is increasing to the level of 7%. All causes of this increase are not clear, but one of the well known causes is the increase of the aged population and the increase in medical care expenditures for the aged. The ratio of medical care expenditures for the aged to total medical care expenditure is increasing. This may be related to the increase of aged patients, suffered from several diseases, such as malignant neoplasms, coronary heart diseases, cerebrovascular attack, and so on.

Considering the continuing aging of the population and future advancement of medical technology, further growth in annual medical expenditure is inevitable.

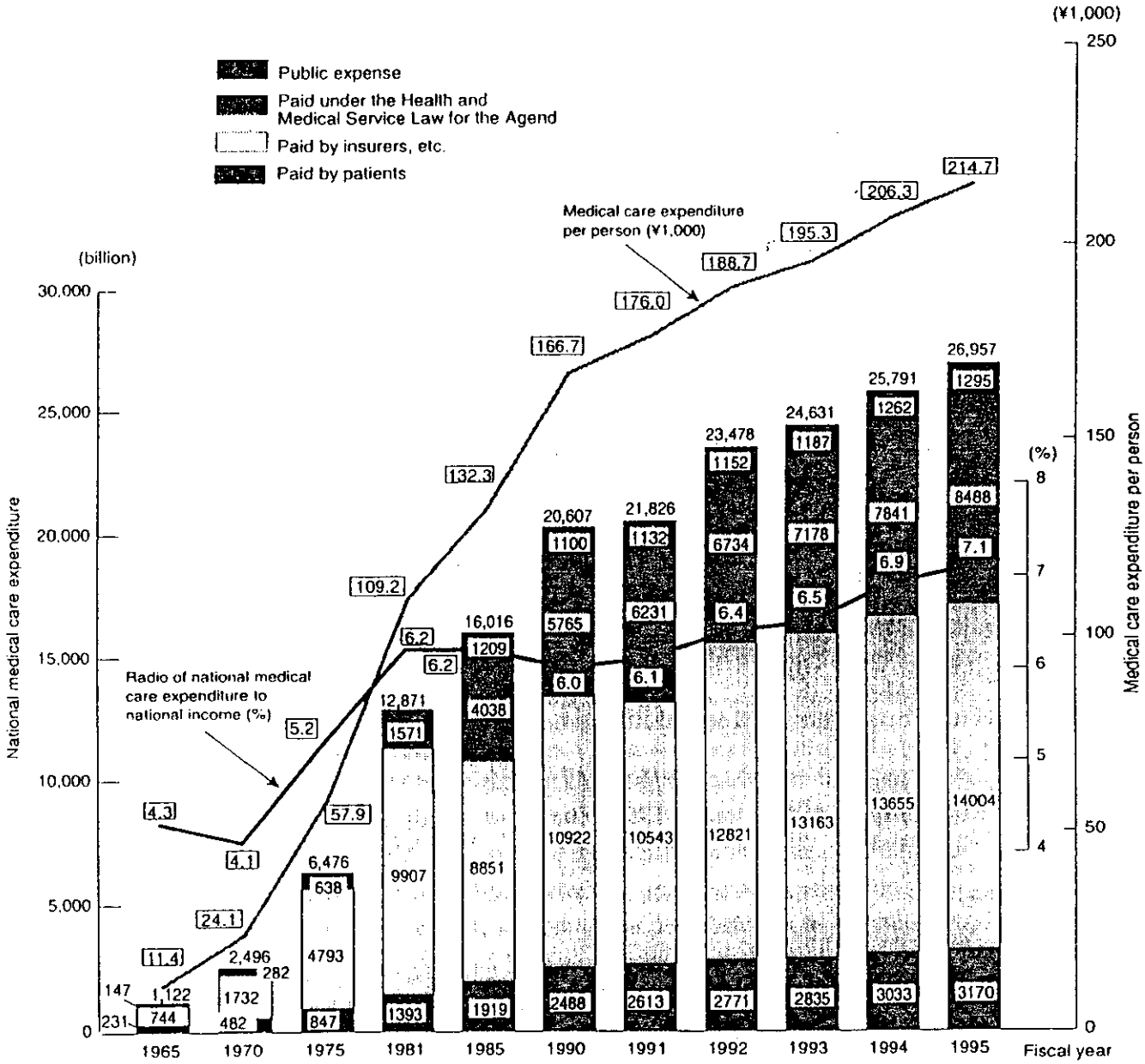
National Medical Expenditure

(Unit: billion yen, unless otherwise indicated)

	1991	1992	1993	1994	1995
National medical expenditure	21,826.0 [+5.9%]	23,478.4 [+7.6%]	24,631.0 [+3.8%]	25,790.8 [+5.9%]	26,957.7 [+4.5%]
National income	363,054.2 [+5.0%]	369,088.1 [+1.7%]	372,464.4 [+0.9%]	373,034.5 [+0.2%]	379,720.4 [+1.8%]
National medical expenditure / National income	6.01%	6.36%	6.54%	6.91%	7.10%
National medical expenditure per head	176,000 yen [+5.6%]	188,700 yen [+7.2%]	195,300 yen [+3.5%]	206,300 yen [+5.6%]	214,700 yen [+4.1%]
Total population (in 1,000)	124,043	124,452	124,764	125,034	125,570
Paid by:	%	%	%	%	%
Public finance	1,111.3 (5.1)	1,151.9 (4.9)	1,187.4 (4.9)	1,261.8 (4.9)	1,295.3 (4.8)
The medical insurance	11,869.5 (54.4)	12,820.6 (54.6)	13,163.2 (54.0)	13,6545.8 (52.9)	14,004.2 (51.9)
The insurers for the aged	6,230.5 (28.5)	6,734.3 (28.7)	7,117.8 (29.5)	7,841.2 (30.4)	8,487.7 (31.5)
Patients' share	2,612.7 (12.0)	2,771.6 (11.8)	2,834.7 (11.6)	3,033.0 (11.8)	3,170.5 (11.8)
Paid from:	%	%	%	%	%
Government budget	6,810.4 (31.2)	7,147.3 (30.4)	7,486.2 (30.7)	8,035.9 (31.2)	8,539.8 (31.7)
National	5,353.3 (24.5)	5,591.6 (23.8)	5,775.8 (23.7)	6,167.5 (23.9)	6,513.2 (24.2)
Local	1,457.1 (6.7)	1,555.7 (6.6)	1,710.4 (7.0)	1,868.4 (7.2)	2,026.5 (7.5)
Premium	12,363.0 (56.6)	13,520.8 (57.6)	14,005.4 (57.5)	14,687.0 (56.9)	15,213.7 (56.4)
Patients share etc.	2,652.6 (12.2)	2,810.3 (12.0)	2,871.5 (11.8)	3,067.9 (11.4)	3,204.3 (11.9)
Breakdown by types of services:	%	%	%	%	%
General medical services	18,995.1 (87.0)	20,316.6 (86.5)	20,975.7 (86.1)	21,576.5 (83.7)	21,868.3 (81.1)
In-patient	8,849.3 (40.0)	9,646.5 (41.1)	9,897.6 (40.6)	10,007.8 (38.8)	9,922.9 (36.8)
Hospitals	8,341.6 (38.2)	9,123.4 (38.9)	9,347.6 (38.5)	9,510.2 (36.9)	9,454.5 (35.1)
Clinics	507.7 (2.3)	523.2 (2.2)	523.0 (2.1)	497.5 (1.9)	468.4 (1.7)
Out-patient	10,145.8 (46.5)	10,670.1 (45.4)	11,078.2 (45.5)	11,568.8 (44.9)	11,945.4 (44.3)
Hospitals	4,693.0 (20.0)	4,836.5 (20.6)	5,041.2 (20.7)	5,298 (20.5)	5,399.7 (20.0)
Clinics	5,452.8 (24.3)	5,833.6 (24.8)	6,037.0 (24.8)	6,269.9 (24.3)	6,545.6 (24.3)
Dental care service	2,119.0 (8.8)	2,296.6 (9.8)	2,315.5 (9.5)	2,351.3 (9.1)	2,383.7 (8.8)
Dispensary service	610.4 (4.7)	712.9 (3.0)	871.7 (2.6)	1,068.7 (4.1)	1,266.2 (4.7)
In-patient good supply				514.1 (2.0)	1,080.1 (4.0)
Geriatric health facility service, etc.	101.5 (0.5)	152.2 (0.6)	200.1 (0.8)	279.2 (1.0)	359.5 (1.4)

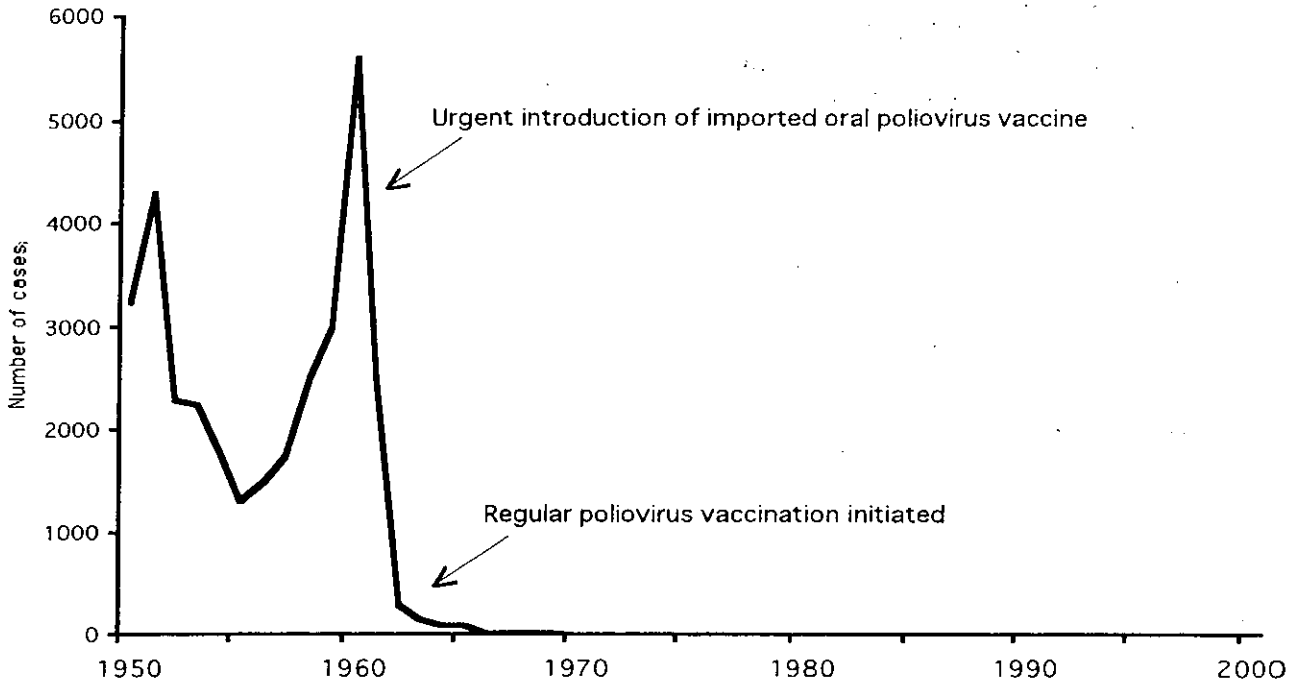
Note: The figures in brackets [ ] shows the growth over previous year.

Source: "*Kokumin Iryohi*, 1995" (National Medical Expenditure, 1995), Statistics and Information Department, Minister's Secretariat, MHW



Trends in National Medical Care Expenditure

5. Structure and history of polio eradication initiative



5-1 Description of polio eradication program

5-1-1 Introduction: Poliomyelitis has been a notifiable disease since 1947 in Japan and thereafter the cases have been grasped in the nation-wide scale. From around 1949, polio epidemics were reported from various parts of the whole country. In 1960, a large-scale epidemic broke out in Hokkaido and polio patients totalled more than 5,000 in one year. In 1961, emergency national immunization with regular, routine vaccination was started, resulting in abrupt decline in polio patients, and poliomyelitis has so far been brought under almost complete control (Figure 1). Mass vaccination with live oral poliovirus vaccine (OPV) has been carried out in spring and autumn (two doses for each infant).

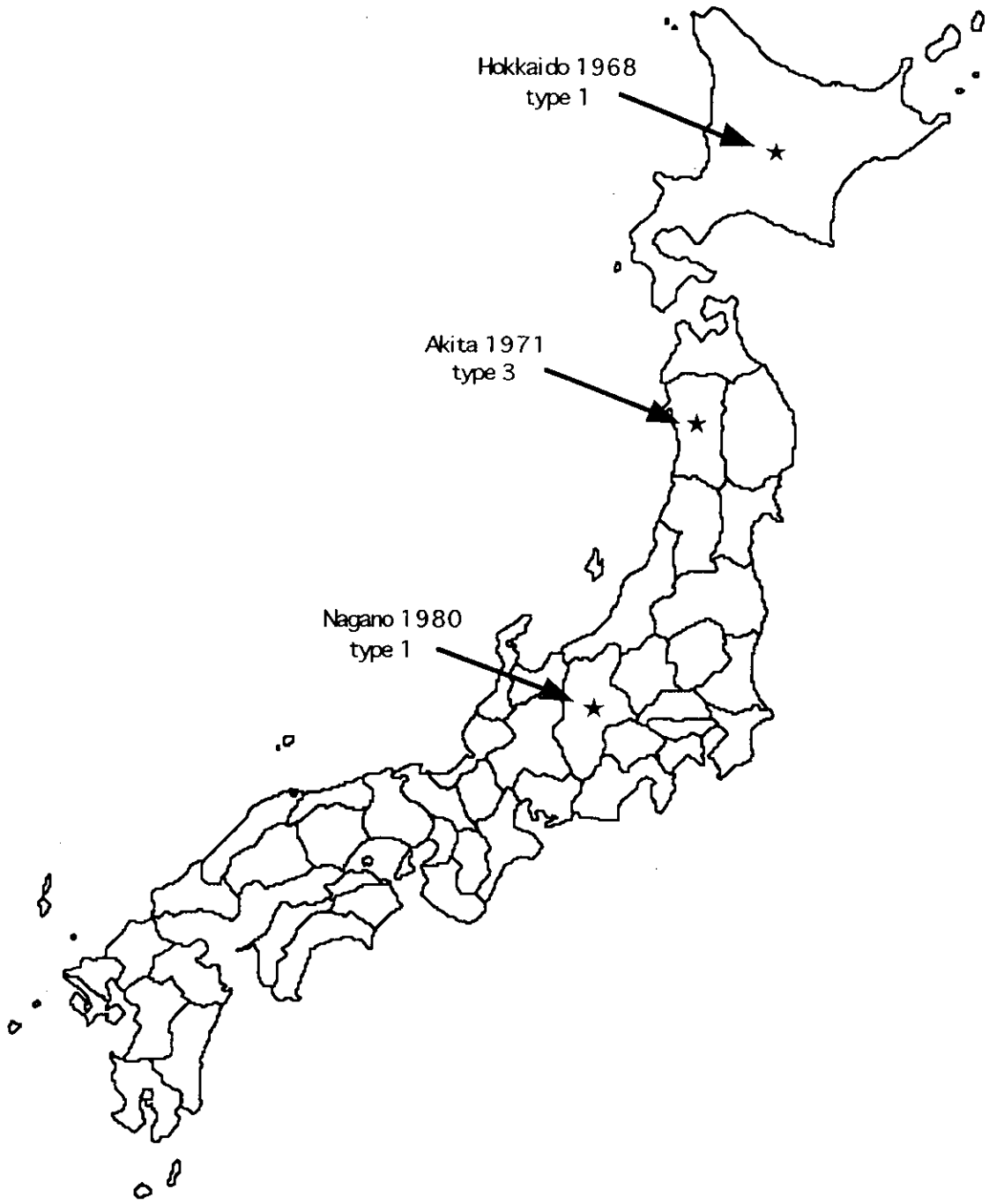
5-1-2: Annual incidence of confirmed polio cases.

Annual incidence of confirmed polio cases in Japan (1962-1999) is shown in the following table (Table 5-1). These numbers are derived from annual report of National Epidemiological Surveillance of Vaccine Preventable Diseases.

Table 5-1

Year	No. of Cases			No. of Cases with Indicated Serotypes					
	Total Attempted for Poliovirus Virus Isolation	Positive Cases		1	2	3	1,3	2,3	1,2,3
1962	63	27	6	-	1	3	-	2	-
1963	20	19	3	-	-	3	-	-	-
1964	25	17	8	-	2	2	-	4	-
1965	27	18	8	1	1	2	1	3	-
1966	21	15	9	-	2	5	-	2	-
1967	16	15	8	-	2	3	-	3	
1968	13	12	10	1*	6	2	-	1	-
1969	14	13	8	1	4	2	-	1	-
1970	5	5	3	-	2	1	-	-	-
1971	2	2	2	-	1	1*	-	-	-
1972	2	2	2	-	1	-	-	1	-
1973	6	6	5	-	4		-	-	-
1974	3	3	2	-	2	-	-	-	-
1975	1	1	1	-	-	-	-	-	1
1976	1	1	0	-	-	-	-	-	-
1977	2	2	2	-	2	-	-	-	-
1978	1	1	1	-	-	-	-	1	-
1979	1	1	1	-	1	-	-	-	-
1980	4	4	4	1*	1	-	-	2	-
1981	4	4	2	-	1	-	-	1	-
1982	0	0	0	-	-	-	-	-	-
1983	2	2	1	-	1	-	-	-	-
1984	0	0	0	-	-	-	-	-	-
1985	1	1	1	-	1	-	-	-	-
1986	1	1	1	-	-	1	-	-	-
1987	0	0	0	-	-	-	-	-	-
1988	0	0	0	-	-	-	-	-	-
1989	0	0	0	-	-	-	-	-	-
1990	0	0	0	-	-	-	-	-	-
1991	1	1	1	-	-	-	-	1	-
1992	2	2	2	-	-	2	-	-	-
1993	3	3	3	-	2	1	-	-	-
1994	1	1	1	1	-	-	-	-	-
1995	0	0	0	-	-	-	-	-	-
1996	0	0	0	-	-	-	-	-	-
1997	0	0	0	-	-	-	-	-	-
1998	2	2	2	1	-	1	-	-	-
1999	0	0	0	-	-	-	-	-	-

* Non-vaccine-like



In 1962, stool samples were collected and examined for virus isolation only in less than half of the cases. However, from 1963 to 1969, stool samples were examined in most of the cases and since 1970 all cases have been examined their stool samples.

5-2. Wild poliovirus isolated from AFP cases

Since then two type 1- (1968 and 1980) and one type 3 (1971) wild type polioviruses were isolated in Japan. The following map indicates their locations.

Details of the last case of poliomyelitis due to wild poliovirus are as follows:

A 7 year- old boy developed paralysis on August 23, 1980. He had no history of vaccination. His travel history was not clear. Two different type 1 strains were isolated. Strain 1A was isolated a week after the onset of illness and the strain 1B a month after that. The neutralising antibody titer to type 1 reached to 1:128 in the convalescent serum. Detailed virological studies were reported by Hara et al., in Microbiol. Immunol. 27, 1057-1065, 1983. (**Annex-5-1**)

For type II, there were no wild type viruses isolated at least after 1962.
Non-Sabin type poliovirus type III was isolated from an AFP patient after 30 days of OPV in Akita prefecture on March 1,1971. The rct/40 marker of the isolated virus was negative, but showed different antigenicity from that of Sabin type 3. Unfortunately further virological analysis was not performed.

From the rest of the cases, Sabin vaccine type viruses (mainly types 2 or 3) have been isolated. Japan is thus considered to be one of the polio- non-endemic countries. However, it should be noted that from two non-paralytic cases, one from self-limiting encephalomyelitis case and the other from pharyngitis case, type 1 and type 3 wild polioviruses were isolated incidentally.

5-3. Wild poliovirus isolated from non AFP cases

Details of last wild poliovirus isolate from non-AFP cases are as follows:

Date of specimen (day/month/year): 19/01/1993

Type and source of specimen: throat swab

A 13- year -old boy visited a hospital because of his high fever (39.2C) and upper respiratory symptoms on January 19, 1993. Three days later, a throat swab was taken. The disease was transient and left no residual damages. No neurological abnormality was observed during the course of the disease. He had one OPV at one year and 4 month- old. Incidentally, he had a short trip to Taiwan from December 28, 1992 to January 1, 1993.

Geographical location of source of specimen: Nagahama city, Shiga Prefecture

Virological findings: Polio virus type 3 was isolated from the throat swab in the cultures of Hep-2 and RD cells. The nucleotide sequences in the regions VP-1 (300 nt) and VP1/2A (147 nt) indicated high homology with the wild- poliovirus type3 which was still isolated in Vietnam area. Virological details were published by Yoneyama et al., in Jpn.J.Med.Sci.Biol. 48, 61-70, 1995. (**Annex 5-2**)

Actions taken: Stool specimen family members and their contacts were extensively examined. At Nagahama Hospital routine stool examination were strengthened. For 6 months altogether stool samples from 240 people were tested. No polioviruses were isolated.

5-4. Wild poliovirus isolated from other sources

In addition, wild polioviruses were isolated from different sources and they were summarized in the following table.

Date specimen collected	Geographical location	Type of specimen
June 24, 1979*	Tokyo University, Animal facility	Stool from a chimpanzee
March 1981**	Narita International Airport	Waste of jet airliners from abroad

*Isolated from a paralysed chimpanzee. The animal was originally imported from Sierra Leone and kept for a year at Tokyo University, Animal Facility for the use of hepatitis B vaccine safety tests. On June 24, the chimp developed acute paralysis on his both lower limbs. Three days later, type 1 poliovirus was isolated from his stool. Markers indicated that this virus is not Sabin-type. No sequencing was performed. The virus was destroyed in March 1985.

** Isolated from wastes of two international airliners arrived in Narita Airport via Karachi, Bangkok and Manila. Two strains (both type 1) were isolated. Markers indicated the viruses were not Sabin type. Further virological examination was not performed and the virus was abandoned in March 1992.

6. Surveillance system for polio and poliovirus in Japan:

6-1. Surveillance for poliomyelitis

In Japan, nationwide surveillance for poliomyelitis was already initiated in 1947 under the communicable disease notification rule. In 1954, poliomyelitis was designated as a notifiable disease and since 1959 all physicians are required to immediately report poliomyelitis cases under the Infectious Disease Prevention Law. Whenever physicians encounter suspected poliomyelitis cases, they are required to fill out a special investigation form for which the format was modified in 1998 (**Annex 2-3**). Physicians are also required to obtain two stool specimens within 14 days of onset of paralysis for virological examination. Every suspected poliomyelitis case needs to be immediately reported to the Local Health Center (LHC). LHC will forward the investigation report to Department of Infectious Diseases (DID), Ministry of Health and Welfare.

LHC will also coordinate specimen transportation to District Public Health Laboratory (DPHL). Each of the 47 prefectures has one DPHL. In addition there are 24 government ordinance municipal DHPLs which totals the number of DPHL to 71 nationwide (**Annex-6-1**). DHPL are responsible for isolation and identification of polioviruses and have to send all isolates to the Section of Enteroviruses, Department of Virology II, National Institute for Infectious Diseases (NIID) for confirmation and intratypic differentiation. If necessary, original stool samples have to be sent to NIID. DHPLs are also requested to provide additional information of laboratory data on suspected poliomyelitis cases to NIID (**Annex 6-2**). Untypable enteroviruses need to be forwarded to NIID as well. NIID must report all findings to the DID.

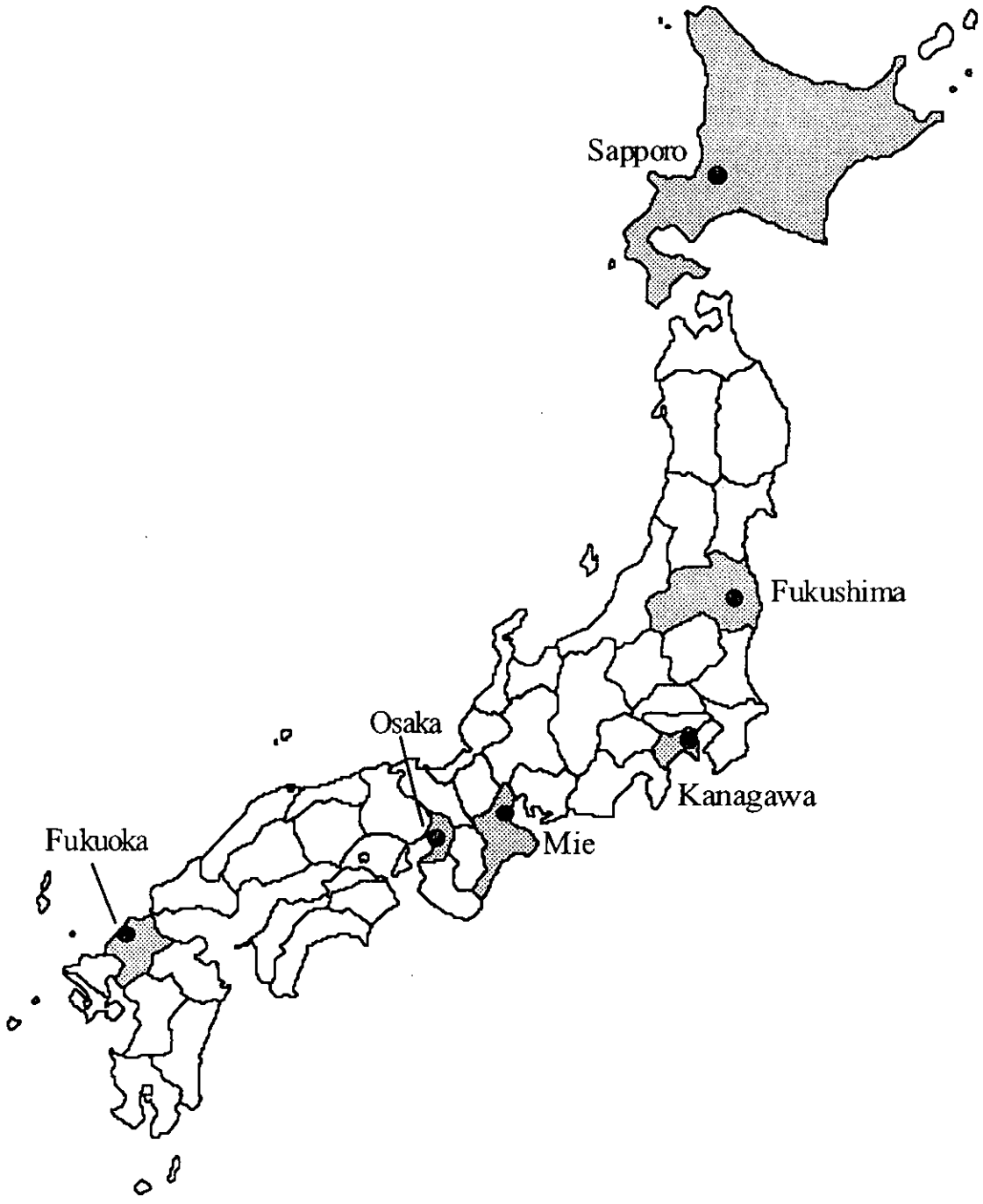
Under the National surveillance system for infectious diseases, laboratory and clinical data of several key infectious diseases including poliomyelitis, are collected and analysed at the Infectious Agents Surveillance Center, NIID, and monthly reports and annual reports are published. Annual summary reports have been published in supplement issues of Japanese Journal of Medical Science and Biology, an official publication of NIID.

6-2. Active surveillance for polio and polio-like diseases

Since April 1998, active surveillance for polio and polio-like diseases is conducted at all hospitals, clinics, DPHLs and LCHs. This surveillance system includes any clinical condition that could also represent poliomyelitis infection. For any such case, adequate stool specimens need to be collected and forwarded to the Public Health Laboratory Network. Up to date, **11** polio-like cases were reported and investigated. In **4** cases poliovirus vaccine type Sabin strain was isolated. All cases were reviewed by an expert committee of the Ministry of Health and Welfare and subsequently discarded as not wild poliovirus associated. Details of all cases are attached as **Annex 6-3**.

6-3. Supplementary surveillance activities for certification of poliomyelitis eradication

The study sites are illustrated in the following figure. The working group in six sites was organized (**Annex 2-3 and Annex 2-4**) and (I) prospective AFP surveillance study and (ii) retrospective record review was conducted.



The characteristics of the six regions were also shown in Table 6-1. In the investigation, the sum of the children under 15 years old in the catchment area of the hospitals investigated was 20% of the population size of total Japanese children under 15. If the area for the investigation was biased as to the abundance of wild type poliovirus or the access to the cases, the result of the current study cannot generalized to the whole Japan. If the selected areas for the investigation were biased as to the characteristics related to abundance of wild type poliovirus or the access to the cases, the results of the current investigation cannot be generalized to the whole Japan. The six regions, however, have high diversity from several perspectives. They differ in the degree of urbanization. They include highly urbanized areas such as Yokohama, Kanagawa and Osaka. Hokkaido, on the contrary, is the area with a lot of rural areas. Accordingly, the population density and development of transportation systems have great variety. Moreover, there is much diversity in the degree of urbanization within the region. Fukuoka prefecture, for example, includes two cities with the population over 1 million in its northern part and rural areas mostly in the southern part. The six regions locate from north to south of Japan. They also differ in the degree of access to the sea. Medical standard, on the contrary, is uniformly high all over Japan. The high diversity among and within the study sites along with uniformity in Japanese medical standard suggest that the bias in characteristics of the study regions is small, if exists, or even negligible. The full report of this study is attached as **Annex-6-4**. The major body of these results will be submitted to the Japanese Journal of Infectious Diseases.

Table 6-1. The population size[a] of the study regions for the investigation for the differential diagnosis and the response rate to the questionnaire study.

	Number of Hospitals	Questionnaire study		Population (X 1000)	Population under 15 years old (X 1000)
		Number of Hospitals responded	Response Rate		
Hokkaido	94	66	70.2	5,689	823
Fukushima	34	31	91.2	2,131	383
Yokohama	81	64	79.0	3,369	480
Mie	28[b]	25	89.3	1,862	293
Osaka + Hyogo[c]	36[d]	36	100.0	6,842[e]	974[f]
Fukuoka	54	54	100.0	4,999	767
Total	327	276	84.4	24,892	3,720
Japan (Total)	—	—	—	125,252	18,905

a: Population size in 1998 or 1999.
b: Although two hospitals situated in Aichi and Wakayama prefectures, the residents in Mie prefecture frequently visited the two hospitals.
c: 14 cities in Osaka prefecture and 5 cities in Hyogo prefecture.
d: Osaka University Hospital and the hospitals related to the Osaka University Hospital.
e: Population size corresponding to those of 64% of Osaka prefecture and 25% of Hyogo prefecture.
f: Population size of the children under 15 years old corresponding to those of 60% of Osaka prefecture and 24% of Hyogo prefecture.

6-3-1. Retrospective record review

A retrospective study was conducted covering the period from January to December 1998 for cases of GBS, transverse myelitis, Todd's paralysis and 6 other ICD-10 codes, which might present with acute flaccid paralysis (AFP). The study was conducted in 6 prefectures and 327 institutes (pediatric departments at hospitals in coordination with DPHL). A total of 46 cases were identified (zero cases of poliomyelitis, 13 cases of GBS, 3 cases of transverse myelitis and 25 others conditions). The summary is presented in Table 6-2. The performance of retrospective investigation in these 6 regions is summarized in Table 6-3. The

line listing of these cases is shown in detail in **Annex 6-5**. All cases were individually reviewed by responsible expert committee and finally discarded as non-poliomyelitis.

Table 6-2.

Diagnosis searched	**ICD Code** (ICD-10)	**Number of cases reported in the AFP surveillance system**
Acute poliomyelitis	A80.0 - 80.9	0
GBS	G61.0	22
Transverse myelitis	G37.3	3
Other (please specify)*		21

*Todd's paralysis	G83.8
Acute myelitis	G04.9
Myopathy	G95.9
ADEM	G04.9
Spinal cord tumor	C72.0
Recurrent hemiplegia	G81.9
Myositis	M60.0

Table 6-3. Performance of retrospective investigation conducted in 1998.

Study region	Population under 15 years old (X 1000)	Total AFP cases [a]	Incidence rate of AFP per 100,000 person years (95% CI)
Hokkaido	823	8	0.97 (0.42 to 1.92)
Fukushima	383	5	1.31 (0.42 to 3.05)
Yokohama	480	1	0.21 (0.005 to 1.16)
Mie	293	3	1.02 (0.21 to 2.99)
Osaka + Hyogo [b]	974 [c]	19	1.95 (1.17 to 3.05)
Fukuoka	767	10	1.30 (0.63 to 2.40)
Total	3,720	46	1.24 (0.91 to 1.65)

a: All AFP (acute flaccid paralysis) cases are non-poliomyelitis.
b: 14 cities in Osaka prefecture and 5 cities in Hyogo prefecture.
c: Population size of the children under 15 years old corresponding to those of 60% of Osaka prefecture and 24% of Hyogo prefecture.

6-3-2. Prospective study for cases of AFP

Furthermore, a prospective study for cases of acute flaccid paralysis (AFP) was conducted from January 1, 1999 to March 31, 2000 at the same 327 institutions in six prefectures. The performance of the prospective investigation conducted from January 1999 through March 2000. (Table 6-4).

Table 6-4.

Study region	Population under 15 years old (X 1000)	Total AFP cases [a]	Incidence rate of AFP per 100,000 person years (95% CI)	AFP cases with adequate stool samples [b]	
				Number	(%)
Hokkaido	823	6	0.58 (0.21 to 1.27)	4	(67)
Fukushima	383	6	1.25 (0.46 to 2.73)	3	(50)
Yokohama	480	3	0.50 (0.10 to 1.46)	2	(67)
Mie	293	1	0.27 (0.007 to 1.52)	1 [c]	(100)
Osaka + Hyogo [d]	974 [e]	19	1.56 (0.94 to 2.44)	19	(100)
Fukuoka	767	6	0.63 (0.23 to 1.36)	5	(83)
Total	3,720	41	0.88 (0.63 to 1.20)	34	(83)

a: All AFP (acute flaccid paralysis) cases are non-poliomyelitis.
b: Two stool samples collected at least 24 hours apart, 0-14 days after the onset of paralysis, and arriving at the laboratory with ice present with sufficient quantity for complete analysis and accompanied by proper documentation.
c: Specimen collected from cerebrospinal fluid.
d: 14 cities in Osaka prefecture and 5 cities in Hyogo prefecture.
e: Population size of the children under 15 years old corresponding to those of 60% of Osaka prefecture and 24% of Hyogo prefecture.

Altogether 41 AFP cases were reported. Polioviruses were not isolated from any of them. Majority was GBS (19 cases, 46%). Stool specimens were collected and examined in 34 cases (83 %). Non-polio AFP rate was calculated to be 0.88 with the 95% confidence interval of 0.63- 1.20. Additional clinical and laboratory information on each case is available upon request. Line listing of these AFP cases is shown in **Annex 6-6.**

6-4. Enterovirus surveillance

Enterovirus surveillance in Japan started in 1970 and has been playing important role for infectious disease surveillance system in Japan. The laboratory network is composed of 71 DPHLs, two laboratories from national hospitals and two private laboratories under coordination of NIID. The location of these public health laboratories is shown in a map in **Annex 6-7**. This network covers almost 100% of the total population. However, reports are information only from positive cases. All poliovirus isolates need to be immediately sent to the Laboratory of Enteroviruses, Department of Virology II, National Institute for Infectious Diseases (NIID) for confirmation and intratypic differentiation. Untypable enteroviruses are forwarded to NIID as well for further classification.

The enterovirus laboratory network is processing stool, CSF, respiratory, urine, skin, blood and genital specimens. Virus isolation is done by specific antibodies, isolation in L20B cells, PCR, monoclonal antibodies and nucleotide sequencing. The number of specimens processed and the numbers of specimens positive for enterovirus and poliovirus 1993-1999 is shown in the following Table (Table 6-5).

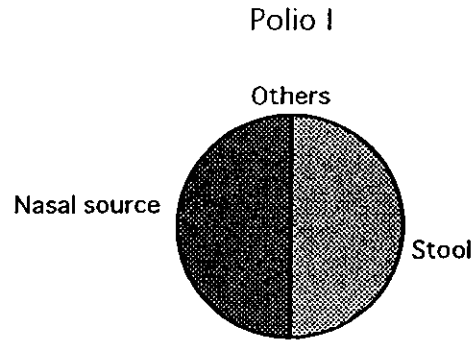
Table 6-5. Total number of specimens examined: (*total numbers of positives are listed)

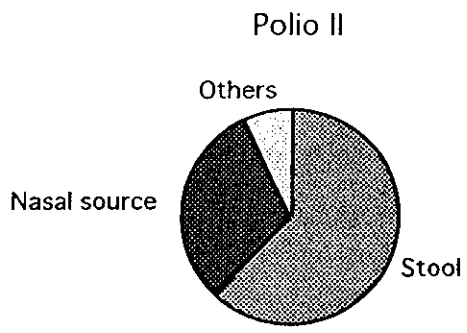
Year	Total no.*	Stool	CSF	Throat	Other
1999	7581	1567	2694	3259	61
1998	6513	1645	2719	3344	65

Isolation data of enteroviruses and polioviruses are collected and analysed yearly. Information for place of residence (geographical distribution), month (seasonal distribution), age, sex, type of specimen, clinical diagnosis, institution and other parameters are included. In **Annex 6-8**, distributions of place of residence and age are shown. Most of the polioviruses isolated are 0-1 year old.

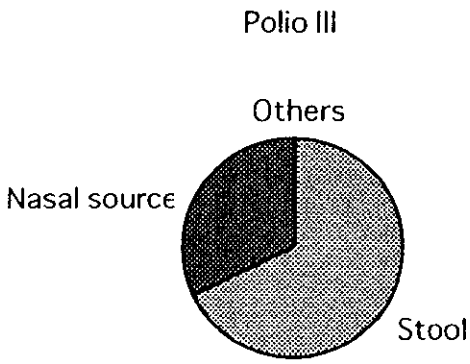
In the following figure, isolation/detection of polioviruses by source of specimens are shown (1996). Most of the polioviruses were isolated from stool specimen or nasopharygeal sourse.

Fig.6-1.



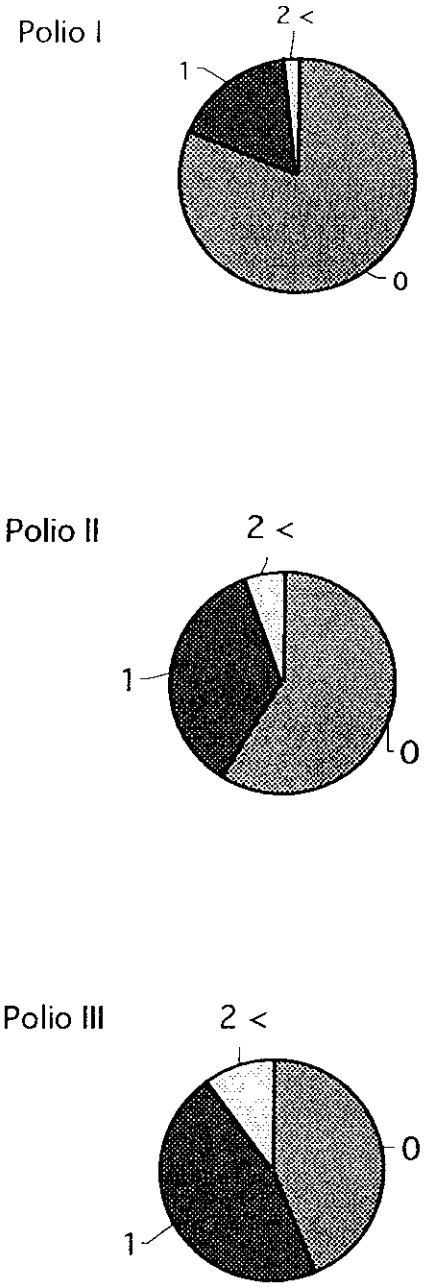


Others:
- Eye swab
- Spinal fluid
- Skin/Vesicle source
- Urine
- Blood
- Brain
- Lung
- Genital
- Other
- Unknown

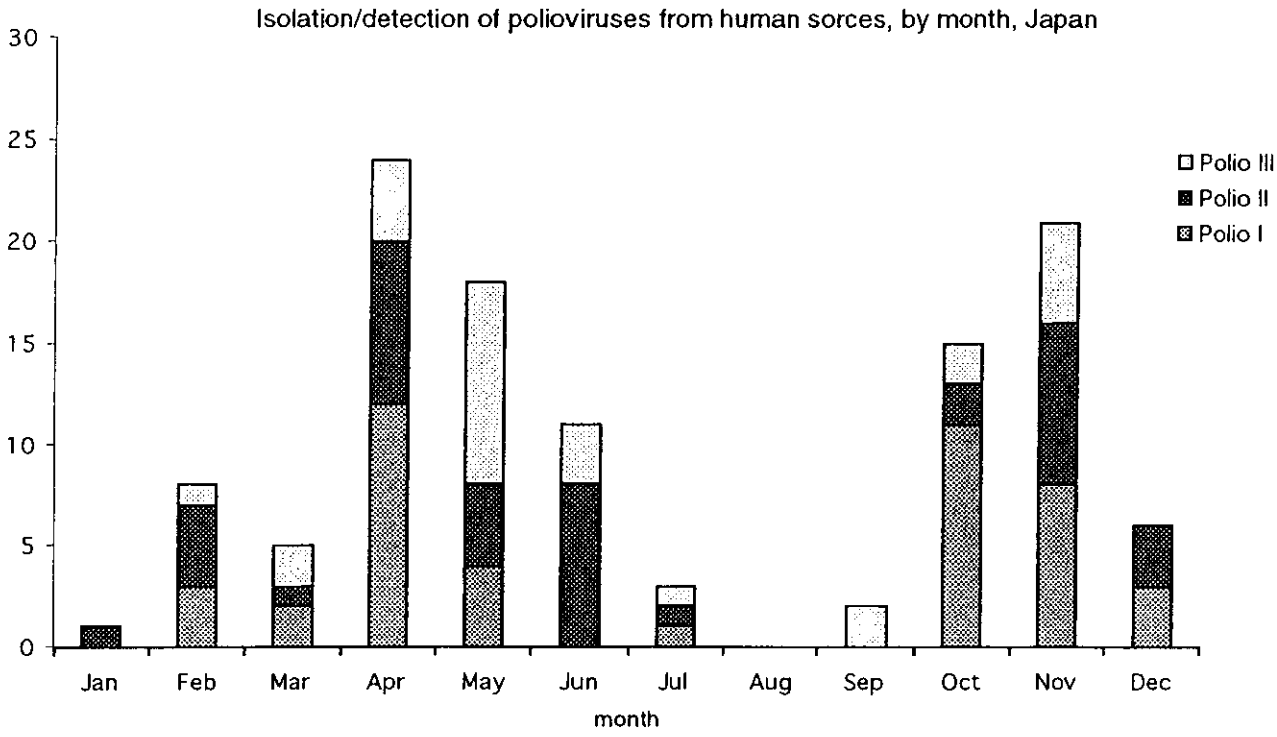


Age distribution are shown in the Fig.6-2. Data obtained 1996 are shown, but basically no yearly changes were noticed. Most of the polioviruses were isolated from 0-1 year babies.
Fig.6-2.

Age groups



The monthly distribution of poliovirus isolation is illustrated in the Fig.6-3. In Japan routine OPV immunization is performed in spring and fall. Consequently the monthly distribution of poliovirus isolation is reasonable.



External quality control for all laboratories is provided by NIID through annual training courses for personnel with special emphasis on poliomyelitis eradication. In 1998, a special training course was conducted for the reliable and timely isolation of polioviruses and L20B cells were distributed.

6-5. Environmental surveillance

Monthly sampling of river and seawater is conducted in 3 prefectures (Toyama, Hiroshima and Miyagi) with a total population of 1.12 million, 2.9 million and 2.4 million respectively. Results of this environmental surveillance were published for 1993-1995 for Toyama, 1990-1992 for Hiroshima and 1994-1999 for Miyagi. Membrane or cellulose filters were used for concentration of samples. All samples were tested at local DPHL. Summaries are shown in Table 6-6. The publication for Miyagi prefecture is attached as **Annex 6-9**. The two other publications are only available in Japanese.

Since 1995 one poliovirus isolate (Sabin strain) and one enterovirus were isolated from environmental surveillance as shown in **Annex 6-10**.

A special study has been conducted by Matsuura et al. on genomic analysis of polioviruses isolated from river water and sewage in Toyama Prefecture. Seventy eight strains of polioviruses were isolated during 1993-1995 (16 serotype 1 isolates, 31 serotype 2, 3, respectively). Most of the polioviruses were isolated up to three months after routine OPV immunization for children in May and October every year. All these isolates were characterized by PCR restriction fragment length polymorphism (RFLP) method and by partially sequencing VP3/VP1 region of viral genome. Of these isolates, 36 were identified to be Sabin vaccine strains, and 42 to be vaccine-variant strains that had less than 1.4% of nucleotide divergence, derived from Sabin strains, including seven isolates with patterns different from those of Sabin strains by PCR-RFLP analysis. Seventy six percent (32/42) of variants had 1 to 3 amino acid substitutions. Moreover, the mutations in the loci adjacent to neutralization antigenic site 1 were found in 10 isolates of type 1 and 3 isolate of type 3, respectively. All variants were completely neutralized by Sabin type-specific polyclonal antisera. This suggested that OPV immunization is effective against the variants.

This paper has been submitted for publication in the Journal of Applied and Environmental Microbiology. Once excepted, this publication can be made available for review.

Table 6-6. Summary of environmental surveillance results:

Year	Total no. samples examined	Total no. entero-viruses isolated	Total no. Polio-viruses isolated	Type 1 results		Type 2 results		Type 3 Results	
				Wild	Sabin	Wild	Sabin	Wild	Sabin
1999	18	0	0						
1998	41	0	0						
1997	42	1	1						1
1996	27	0	0						
1995	6	0	0						

6-6. Stool survey of healthy children

Since 1962, 10 DPHLs per year have been nominated by turns to conduct active epidemiological surveillance on seven vaccine- preventable diseases. They attempt to isolate polioviruses from randomly selected healthy children (20 each, for three age groups; 0-1, 2-3, and 4-6) two months after the annual vaccination.

Form 1996-1998 a total of 2,660 healthy children age (0-6) from 10 different prefectures were randomly surveyed and stool specimens analysed at DPHLs. A total of 15 poliovirus isolates (all Sabin strains) and 452 NPEV were found. Results are summarized in Table 6-7.