NEWBORN SCREENING IN JAPAN

Kikumaro Aoki

Kagawa Nutrition University, Saitama, Japan

Abstract. In the 1970's, the government began to take steps for the treatment of congenital diseases. Mass newborn screening was started in October 1977 throughout Japan in order to detect five inborn errors of metabolism including phenylketonuria, maple syrup urine disease, homocystinuria, histidinemia, and galactosemia. In 1979, mass screening for congenital hypothyroidism was added to the original program. In 1989, screening for congenital adrenal hyperplasia was added and in 1992, screening of histidinemia was discontinued. Currently, screening covers six diseases. The government paid half the cost of screening tests initially and in 2001 this was raised to the full cost (~3000 yen). Parents pay for sample collection. The program is carried out according to law. A new activity involving screening for Wilson disease now necessitates taking dried blood specimens from children 1-3 years old.

INTRODUCTION

In the 1960s, Guthrie's method for screening newborns for Phenylketonuria was introduced into Japan. The data obtained on the effectiveness of newborn screening pushed the government to start newborn screening using Guthrie's method. In the 1970's, the government began to take steps for the treatment of congenital diseases to decrease the infant mortality rate. Priority was given to the prevention of congenital diseases. Thus, newborn screening began throughout Japan in October 1977 in order to detect five types of inborn errors of metabolism: phenylketonuria, maple syrup urine disease, homocystinuria, histidinemia, and galactosemia. In 1979, screening for congenital hypothyroidism was added to the original program. In 1989, screening for congenital adrenal hyperplasia was added and in 1992, screening for histidinemia was discontinued. Now, six diseases are being screened in Japan. Table 1 presents the Number of births and the corresponding screening rate.

Table 1. The number of newborns screened in Japan.

Year	Number of births	Screened	Rate (%)
1977-1993	24,163,633	22,326,111	92.4
1994	1,235,553	1,253,198	101.4
1995	1,183,716	1,196,068	101.0
1996	1,203,313	1,222,850	101.6
1997	1,194,510	1,215,649	101.8
1998	1,199,183	1,229,518	102.5
Total	30,179,908	28,443,394	94.2

Initially, the government and local authorities paid half the cost of about 3,000 yen per newborn infant. Since 2001, all expenses have been covered by the local budget. The cost to collect blood on filter paper is about 3,000 yen, which is paid to the obstetricians by the parents. With regard to the issue on whether the program is implemented as a policy or a law, it has been carried out as dictated by law.

The problems encountered in establishing and sustaining the program have included: (1) technical training of technicians in Guthrie's method (many European countries and the USA assisted with this training and we are greatly indebted to these countries, especially to the late Dr. Guthrie); (2) establishing a national quality control system; and (3) establishing a follow-up system for patients detected by screening. Present problems include: (1) development of new technologies for mass screening tandem mass spectrometry (MS/MS) or gas chromatography mass spectrometry (GCMS); (2) the maintenance of a quality newborn screening system; and (3) oversight of the cases reported (detecting any false negative result of screening). In 1999, questionnaires to detect cases missed by screening were sent to physicians throughout Japan. There were three cases of the intermittent type of maple syrup urine disease that were initially negative on screening, and one case of homocystinuria missed because of a low methionine cut-off point.

The role of the government in the screening programs is the completion of the initial steps. From this year onwards, the succeeding steps will depend on the local authorities of every prefecture. However, the government still has the responsibility of continuing the screening system as a whole. A new dried blood screening activity for Wilson disease involves children 1-3 years of age.

NEWBORN SCREENING IN KOREA

Young Ja Han[1], Dong Hwan Lee[2], Jong Won Kim[3]

[1]Korea Institute for Health and Social Affairs; [2]Department of Pediatrics, Soonchunhyang University Hospital; [3]Department of Clinical Pathology, Samsung Medical Center

Abstract. The Ministry of Health and Social Affairs adopted a newborn screening program in 1991 to cover low-income families. The system was extended in 1997 to cover all newborns. The number of screened conditions was reduced from 6 (CH, PKU, Gal, MSUD, HU, HIS) to 2 (CH, PKU) in 1995. The national newborn screening program was in need of an in-depth review for further improvement. Thus, a background survey was conducted at 241 health centers in June 2000 to assess the current status of the screening system and to identify characteristics of detected patients. Expert opinions on the effect and efficiency of the screening program were also gathered. The number of identified cases was 481 - CH (378 cases), PKU (73), MSUD (11), PA (7), UCD (9) and Gal (3). Most cases were identified after 1997. Of all cases, 83.5% were identified within 2 months after birth; discovery rate within 2 months after birth increased rapidly from 23.5% in 1994 to 90% in 1997; 17.7% of PKU and 4.2% of CH cases had associated family histories. Among the problems the present study revealed are: absence of an organization responsible for coordination and control of national newborn screening services, too many screening laboratories (76 laboratories as of 2000), inadequate follow-up treatments and services, complicated remuneration system. Further efforts should be made to establish an organization capable of coordinating newborn screening services; reduce the number of screening laboratories from the current 76 to 3-4 laboratories; implement Tandem Mass Screening; and simplify the remuneration system.

INTRODUCTION

The Ministry of Health and Social Affairs adopted newborn screening for low-income families in 1991 and expanded in 1997 to cover all newborns. Six disorders were initially included in screening – congenital hypothyroidism (CH), phenylketonuria (PKU), galactosemia (Gal), maple syrup urine disease (MSUD), homocystinuria (HU), histidinemia (HIS).

The disorders screened were reduced to two (CH and PKU) from 1995 onwards, because the other four were rarely detected and were not cost-effective. After 10 years, the program was reviewed for effectiveness, efficiency and equity so that policy measures could be presented for the further improvement of the national newborn screening program.

Table 1. Sources of funding for government screening program (Unit: thousand US$).

Year	Project budget			Source of funding
	Total cost	Test	Follow up	
1991	229	185	44	Social welfare fund
1992	246	216	30	Central government subsidy, Social welfare fund
1993	419	378	41	Central government subsidy, Social welfare fund
1994	583	541	42	Central government subsidy, local government budget, Social welfare fund
1995	644	590	55	Central government subsidy, local government budget, Social welfare fund
1996	494	432	61	Central government subsidy, local government budget
1997	4,129	4,057	72	Central government subsidy, local government budget
1998	3,008	2,899	109	Central government subsidy (40%), local government budget (60%)
1999	2,993	2,883	109	Central government subsidy (40%), local government budget (60%)
2000	2,961	2,801	160	Central government subsidy (40%), local government budget (60%)
2001	3,318	2,892	446	Central government subsidy (40%), local government budget (60%)
2002	3,313	2,962	351	Central government subsidy (40%), local government budget (60%)

Source: 1) MOHW, Internal material, 1991-1999
2) MOHW, Plan of Family Health and Welfare Program, 1991-2002

Current status of newborn screening in Korea

Table 1 shows the rapid funding increases from 1997 with 40% of the total cost being provided by the central government and 60% from local governments. Follow-up supports, including special milk, were given only to low-income families. Table 2 shows the budget allocation for management of the diagnosed cases. The cost of the program for inborn errors of metabolism was supported by both the central and local government on a 40-60% basis. The cost for testing was US$2,962,000 and US$351,000 for patient management. Table 3 shows that the cost of newborn screening was US$6.2 for 6 tests in 1991 and US$7.3 for 2 tests in 2002. Table 4 shows that a total of 2,222,110 newborns had been screened with 488 CH patients (1:4,558) and 49 PKU patients (1:45,349) detected from 1991-2001 (Table 4).

National fertility and family health survey

According to this survey, the newborn screening rate increased from 35.7% in 1994 to 88.8% in 2000. The rate has been higher for rural areas than that for urban areas since 1997, presumably due to the active program delivery by health workers at health centers in the rural area. The rate was high among women with a university degree and above (See Table 5).

Health center-based survey on the management of inborn errors of metabolism

A survey was conducted at 241 health centers in June 2000 to review the status of the screening system

Table 2. Budget for the inborn errors of metabolism (2002). (Unit: thousand US$)

Classification	Contents	Central government subsidy (40%)	Local government budget (60%)
Cost for test	2,962	1,185	1,777
Cost for management of patient	351	140	211
Total	3,313	1,325	1,988

Source: MOHW, Family Health Program Guideline, 2002.

Table 3. Cost for newborn screening (1991-2002) (Unit: won, US$).

Year	Cost	Test items
2002-1998	9,500 (US$7.3)	2 kinds: PKU, CH
1997	8,640 (US$6.5)	2 kinds: PKU, CH
1996-1995	8,000 (US$6.2)	2 kinds: PKU, CH
1994-1992	14,000 (US$10.8)	6 kinds: PKU, CH, HU, MSUD, GAL, HIS
1991	8,000 (US$6.2)	6 kinds: PKU, CH, HU, MSUD, GAL, HIS

Source: MOHW, Family Health Program Guideline, 2002.
Note: PKU (Phenylketonuria), CH (Chronic Hypothyroidism), HU(Homocystinuria), MSUD (Maple Syrup Urine Disease), Gal (Galactosemia), HIS (Histidinemia)

Table 4. Number of tested newborns and detected patients (1991-2001) (Unit: person).

Year	No. of tested	No. of detected patients	
	Newborns	CH	PKU
1991	28,286	7	1
1992	20,372	7	0
1993	35,094	8	0
1994	51,045	12	1
1995	74,880	8	2
1996	62,542	6	1
1997	345,013	62	6
1998	416,115	132	7
1999	398,444	88	9
2000	407,981	89	9
2001	382,338	69	13
Total	2,222,110	488	49

Source: MOHW, Internal Material, 1991-2001.

Table 5. Taking screening test of the last birth to 15- 44 year old married women (Unit: %, person).

Classification	1994	1997	2000
Region			
Urban	35.7	73.4	88.4 (1,242)
Rural	35.8	74.4	93.0 (109)
Education			
Middle school	31.2	65.7	81.5 (53)
High school	33.5	71.6	86.7 (768)
University and above	43.2	79.0	92.5 (530)
Age of mother at delivery			
15 - 24	36.6	70.2	83.3 (201)
25 - 29	33.9	72.7	90.9 (695)
above 30	39.3	77.3	87.9 (455)
Mean	35.7	73.6	88.8 (1,351)

Sources:1) Hong *et al* (1994); Cho *et al* (1997); Kim *et al*, (2000).

Table 6. Distribution of inborn errors of metabolism identified (Unit: person).

Year of birth	CH		PKU		MSUD		Propionic acidosis		Urea cycle disorders		Galactosemia	
	M	F	M	F	M	F	M	F	M	F	M	F
2000[1)]	24	18	1	-	2	-	1	1	-	1	1	-
1999	44	44	9	1	3	-	3	1	3	3	1	1
1998	49	37	3	3	1	-	1	-	1	1	-	-
1997	34	41	4	3	3	-	-	-	-	-	-	-
1996	10	10	1	2	1	-	-	-	-	-	-	-
1995	5	12	4	4	-	-	-	-	-	-	-	-
1994	8	7	1	3	-	-	-	-	-	-	-	-
1993	9	4	0	0	-	-	-	-	-	-	-	-
1992	4	1	2	2	-	1	-	-	-	-	-	-
1991	1	2	0	5	-	-	-	-	-	-	-	-
Before 1990	6	8	11	14	-	-	-	-	-	-	-	-
Total	194	184	36	37	10	1	5	2	4	5	2	1

Source: Han YJ, *et al*. Measures to improve screening system for inborn errors of metabolism. KIHASA, 2000.
Note: 1) Only patients born from Jan to May in 2000 were included.

and to identify characteristics of the detected patients. In addition, a supplementary survey was conducted on the patient's family at the Patient's Family Association to gather information from them (Han, 2000). Information on the patients was gathered from the survey and various existing sources and was made into a duplication-free data set by utilizing patients' ID numbers. The total number of cases identified was 481, including 378 CHs, 73 PKUs, 11 MSUDs, 7 PAs, 9 UCDs and 3 Gals (See Table 6). Most of the cases were identified after 1997 when the government program was expanded.

IDENTIFIED PROBLEMS

A number of problems have been identified in the newborn screening system. There is no organization responsible for the coordination and the control of the national newborn screening services. There are too many screening laboratories. For the year 2000, there were 76 laboratories for newborn screening tests in Korea. Currently, the government supports screening for only two disorders (CH and PKU) so that the cost of additional tests is the parent's responsibility. Test selection is not based on prevalence of disease and the number of tests, and costs vary across medical facilities. Follow up treatment and services are not adequate and the remuneration system is very complicated requiring many administrative processes.

RECOMMENDATIONS

The following recommendations will help improve newborn screening in Korea as a whole:

1) Provision of an organization responsible for national newborn screening program, which should include quality assurance, accreditation of the screening laboratories, technical assistance and research.
2) Development of a newborn screening and patient management model, which should consist of specimen collection systems, screening laboratory work systems, follow-up retest systems and confirmatory, diagnostic and treatment systems
3) The number of screening laboratories should be reduced from the current 76 to 3 - 4 laboratories through cost competitiveness and the strict enforcement of standards/requirements.
4) Tandem mass spectrometry screening should be considered as an alternative for quality assurance and as a cost-effective way of improving the current screening program.
5) The number of test items that are supported by the government should be expanded from the current two items to more than five items. Costs may not increase very much if tandem mass spectrometry screening is introduced.
6) The current remuneration system should be simplified. Alternative methods include commissioning health insurance companies to handle payments and providing coupons.
7) Follow-up management of the identified patient should be strengthened. There will be little benefit to the health of the people if the patients are not treated properly even with money for screening tests. In order to improve patient management, activities of the health center should be strengthened and supported by the central government with patient management guidelines and health education materials.
8) As part of the research, dietary guidelines and a standard menu for patients with inborn errors of metabolism have been developed based on the analysis of components of favorite Korean foods selected by the patient family association. These guidelines should be supplemented and revised in the future.

REFERENCES

Cho NH, *et al.* 1997 National Fertility and Family Health Survey, KIHASA, 1997.

Han YJ, *et al.* Dietary instruction for the inborn errors of metabolism. KIHASA-MOHW, 2000.

Han YJ, Lee DH, Kim KS. Measures to improve screening system for inborn errors of metabolism, KIHASA, 2000.

Hong MS, *et al.* 1994 National Fertility and Family Health Survey, KIHASA, 1994.

Kim SK, *et al.* 2000 National Fertility and Family Health Survey, KIHASA, 2000

Ministry of Health and Welfare, Internal Material, 1991-1999.

Ministry of Health and Welfare, Family Health Program Guideline, 2000.

Ministry of Health and Welfare, Plan of Family Health and Welfare Program, 1991-2000.