NEONATAL SCREENING AND MONITORING SYSTEM IN TAIWAN

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Abstract. Neonatal screening in Taiwan started as a pilot program in 1981. The coverage rate increased to 90% in 1990, and is currently more than 99%. Five diseases are covered in the screening program including congenital hypothyroidism, phenylketonuria, homocystinuria, galactosemia, and glucose-6-phosphate dehydrogenase deficiency. A monitoring system was established at the same time to ensure correct diagnosis and treatment for positive cases. Neonatal screening is not compulsory by law in Taiwan, but the government is very concerned about it. New tests for neonatal screening have recently been included as pilot programs. Parents of the newborns have to pay for these tests, for which informed consent has to be given. These additional tests include screening for congenital adrenal hyperplasia and tandem mass screening. The results of these pilot programs will be offered to the government for policy decision-making in the future.

INTRODUCTION

Neonatal screening in Taiwan started in 1981. The socio-economic condition in Taiwan at that time was not very good and health education for the people was inadequate. Therefore the initiation of neonatal screening was slow and stepwise starting from the two most important diseases: phenylketonuria (PKU) and congenital hypothyroidism (CHT). Other conditions were subsequently added. It took almost 10 years to raise the screening coverage rate to 70% (Table 1). The establishment of an efficient public health system was required to follow up the high-risk newborns identified by the screening system. The screen coverage rate increased to 90% in 1992 and is currently more than 99%. Five diseases are covered by the screening program — homocystinuria, galactosemia (GAL), and glucose-6-phosphate dehydrogenase (G6PD) deficiency. The cost for the laboratory tests is USD 6, but usually another 9 USD will be charged by the hospital for blood sampling and handling. The government gives 3 USD to each newborn. Neonatal screening is not a compulsory test by law in Taiwan, but the government is very concerned about it. There are three screening centers in Taiwan, one is in a public hospital, and the other two are private. All centers are under the coordination of the Department of Health.

Table 1. Year-specific coverage rate of neonatal screening in Taiwan.

Year	No. of live births	Screened	Rate
1984	371,008	24,657	6.7%
1985	346,208	38,792	11.2%
1986	309,230	71,666	23.2%
1987	314,024	117,739	37.5%
1988	342,031	192,601	56.3%
1989	315,299	214,477	68.0%
1990	335,618	266,312	79.4%
1991	321,932	282,453	87.7%
1992	321,632	302,571	94.1%
1993	325,613	314,780	96.7%
1994	322,938	315,952	97.8%
1995	329,581	317,921	96.5%
1996	325,545	323,551	99.4%
1997	326,002	322,835	99.0%
1998	271,450	267,089	98.4%
1999	283,661	282,395	99.6%
2000	305,312	304,394	99.7%
Total	5,555,728	4,015,939	-

RESULTS

The incidences of diseases discovered by the screening system were 1/2,879 for CHT, 1/34,921 for PKU, 1/62 for G6PD deficiency, 1/250,996 for homocystinuria and 1/1,003,985 for GAL. Compared with other countries, the incidence of CHT was similar, but the incidence of PKU was low (Tsai *et al*, 1995; Hsiao *et al*, 2001; Chien *et al*, 2001). Both homocystinuria and

Table 2. Monitoring of cases of congenital hypothyroidism.

Year	Followed	No record	Lost	Stop medication	Closed	Dead	Total
1984	2						2
1985	4	5	1	1			11
1986	8	19	0	1	1		29
1987	13	25	1	5	3		47
1988	8	54	6	6	1		75
1989	11	52	3	11			77
1990	20	29	3	9	3	1	65
1991	47		8	50	9	1	115
1992	42		6	40	0	1	89
1993	54		10	63	22	3	152
1994	67		11	73	10	3	164
1995	53		10	79	6	4	152
1996	71		8	67	9	4	159
1997	120		12	60	4	5	201
1998	140		4	17	6	6	173
1999	199		7	12	51	1	270
2000	243			3		1	247
Total	1102	184	90	497	125	30	2028
Percent	54.3	9.1	4.4	24.5	6.2	1.5	100

GAL were very rare in Taiwan, and most of the cases belonged to the mild or variant forms (Cheung *et al*, 1999). The occurrence of G6PD deficiency in Taiwan is very high as in some southeastern countries (Chiang *et al*, 1999).

From the early stages of the screening system, a monitoring system was developed. The aims of the monitoring system were to ensure proper diagnosis, proper treatment, and good outcome. The monitoring system was supported by the Department of Health. The program was run by one of the medical centers in Taiwan, and supervised by qualified geneticists and genetic counselors. Initially CHT was the targeted disease. In the recent two years, patients affected by PKU (including hyperphenylalaninemia), homocystinuria (including hypermethioninemia) and GAL were also enrolled. Parameters monitored include growth (body height, body weight, and head girth) for all cases; thyroid scan, thyroid function, and medications for CHT; plasma phenylalanine for PKU; plasma methionine for homocystinuria; and blood galactose for GAL.

The data were collected in two ways. The first method involved collection once each year by reviewing medical records. The second involved submission of data through the Internet using an electronic form available on the website. There was also an automatic alarm system that would send a message to the physician a week in advance of the patient's next visit. The physicians were encouraged to see patients according to the requested intervals. Through the web system, data came in immediately. Through the monitoring system, protocols for diagnosis and treatment could be unified and important data were made accessible. As shown in Table 2 for the follow-up of CHT, 24.2 % of patients had stopped their medications, and the other 6.1 % of patients were not cases and need not have been followed-up. A total of 30.3 % of all CHT cases detected by neonatal screening had transient disease. Many of the patients with transient type CHT had normal thyroid scans.

Many new screening advances have occured. The incidences of diseases targeted by those new tests are usually too low to be evaluated by research projects. Good clinical data were also lacking in Taiwan. Therefore, these tests were initiated as pilot programs. One screening center in Taiwan started screening congenital adrenal hyperplasia (CAH) in the year 2000 for almost all of

their babies. The same center started screening with tandem mass spectrometry (MS/MS) in August 2001, covering one-third of the babies. Another center screened part of their babies for CAH since 2001, and started MS/MS in 2002. Parents of the newborns had to pay for those tests after giving informed consent. The incidence of CAH from the pilot programs was 1/14,822.

DISCUSSION

Neonatal screening in Taiwan is directed by the Department of Health. All data from screening centers are collected and pooled. These data are complete and cover more than 99% of the total births. Through the monitoring system, all patients who screened positive for a disease were further followed-up. The immediate effect of the monitoring system was to ensure quality medical care for these patients. The studies of these cohorts provided important data. For example, the large fraction of transient CHT may be a specific finding in the Taiwanese population and suggests either gene polymorphisms or founder effects. However, the increase in transient type CHT also be related to over-diagnosis due to early treatment.

Adding new conditions to an ongoing neonatal screening program is always a problem. The advisory committee will ask for the efficacy or cost-benefit of screening for the new conditions. However, new diseases are usually rarer than the traditional ones like CHT; therefore, regular research projects do not have sample sizes large enough to provide the data. Neonatal screening is part of the public health system in Taiwan, and a significant portion of the budget comes from government funds. Therefore, adding any new condition will usually lead to a significant increase in government budget. This makes it difficult for the system to expand. A tentative solution is the concept of self-supported pilot screening programs. With time, such programs may provide reliable data on which policies can be based. There is a National Health Insurance System in Taiwan, but the system is not stable. Other commercial health insurance systems are still small. The insurance systems are as yet, not interested in the screening program.

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