

Newborn screening and related policy against Phenylketonuria in China

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Summary

Phenylketonuria (PKU) is a treatable and preventable inherited metabolic disease. The overall incidence of PKU in China is 1/11,144. Newborn screening is an effective method of controlling PKU. In 1981, the Chinese Government initiated a newborn screening program and the number of newborns screened for PKU in China has risen each year. This review describes the current status of laws and regulations related to newborn screening for PKU in China and it identifies how China's newborn screening program has improved as a result of these laws and regulations. Specific measures and regulations, such as those implemented by government, follow-up services, and government coverage of expenses, have been implemented in different areas where they have yielded good results. These measures and regulations may serve as a reference for other areas of China. However, measures and regulations regarding newborn screening in China still face challenges. Prenatal health examinations and national financial support are expected to play a more significant role in newborn screening for PKU in the future.

Keywords: Phenylketonuria (PKU), inherited metabolic disease, incidence, newborn screening, measures and regulations

1. Introduction

Phenylketonuria (PKU) is usually caused by a deficiency of phenylalanine hydroxylase and results in severe mental retardation and neurobehavioral abnormalities. The overall incidence of PKU worldwide varies widely in different human populations. According to the National Institute of Child Health and Human Development, PKU occurs in approximately 1 in 15,000 births in the United States (1). However, incidence varies worldwide in different ethnic populations. A high incidence is reported in Turkey (1/2,600), while countries such as Finland and Japan have extremely low rates, with fewer than one case of PKU in 100,000 births (2,3). PKU is a treatable and preventable inherited metabolic disease (4). Newborn screening combined with a Phe-restricted therapeutic

diet throughout childhood can help to control PKU in most patients (5). Studies have shown that a higher rate of newborn screening and earlier treatment can lead to a better prognosis for patients (6-8).

In China, the overall incidence of PKU is 1/11,144 (9). In 1981, the Chinese Government instituted a newborn screening program by testing dried blood samples (DBS); this program is focused primarily on congenital hypothyroidism (CH) and PKU. From 1985 to 2006, a total of 13.66 million newborns had been tested for PKU and 1,170 cases had been confirmed, for a PKU rate of 1/11,680 (10). Prior to 2011, a total of 35.79 million DBS from newborns had been tested for PKU and 3,082 cases of PKU had been confirmed, for a PKU rate of 1/11,614 (11). According to available data (10,12), the number of newborns screened for PKU increased markedly after 1999 (Figure 1).

The current review has described laws and regulations related to newborn screening for PKU in China. Based on an analysis of the current status of and challenges faced by newborn screening for PKU, this review seeks to provide insight into the future prospects of newborn screening for PKU in China.

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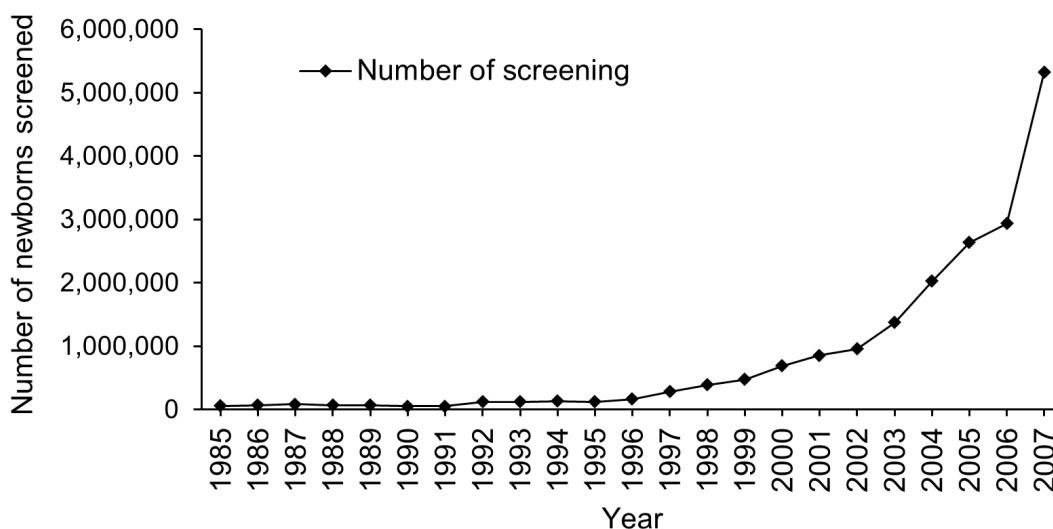


Figure 1. Annual number of newborns screened from 1985 to 2007.

2. Program of newborn screening for PKU in China

2.1. Laws and regulations related to the program of newborn screening for PKU

As mentioned earlier, a newborn screening program was instituted by the Chinese Government in 1981. Screening for PKU is a part of that screening program. The very first screening took place in Shanghai in October 1981, with 14 maternity hospitals participating (13). Since then, the Chinese Government has drafted a series of laws and regulations to enhance the extent of newborn screening (Table 1). These laws and regulations have identified the importance of newborn screening in law, stipulated that PKU be screened for, included newborn screening into basic maternal and infant health care services, established a protocol and technical specifications for China's newborn screening (in order to improve the quality of PKU screening and testing), and specified the objectives of newborn screening program, including PKU screening (14-18). The rate of newborn screening in Eastern China should reach 90% by 2012 and 95% by 2015, that in middle China should reach 50% by 2012 and 80% by 2015, and that in Western China should reach 40% by 2012 and 60% by 2015.

The program of newborn screening for PKU had made significant process with the help of those laws and regulations. There were only 3 screening centers in the 1980s, when newborn screening had just started, and yet the number increased to 46 in 2002 and then to 179 by the end of 2009 (11). The percentage of newborns covered by the newborn screening program also increased from 3.86% in 2003 to 59.01% in 2009 (11). In addition to these laws and regulations, specific measures and regulations regarding PKU that have been

implemented in cities and provinces of China warrant attention.

2.2. Implementation by government

Local government directives stipulating that newborn screening for PKU must be instituted helped to expand the coverage of newborn screening. Shanghai is one of first cities in China that instituted newborn screening for PKU; the percentage of newborns screened in Shanghai reached 97% in 2008 (19). In Guangzhou, the rate of newborn screening reached 99.0% and coverage by the city's Newborn Screening Network reached 99.3% in 2008 (20). One commonality of the measures and regulations regarding newborn screening in these two cities is that screening "must be instituted".

In 1996, the Standing Committee of the Shanghai People's Congress drafted Regulations on Maternal and Infant Health Care in Shanghai (21). According to article 35 of the Regulations, the Shanghai Government directed that a newborn screening program be instituted in the city. In Guangzhou, the Standing Committee of the Guangdong People's Congress also drafted Regulations on Management of Maternal and Infant Health Care in 1998 (22). Article 20 of Guangdong's Regulations stipulates that Guangdong Province must institute a newborn screening program and the Regulations also propose that screening include PKU testing. These two sets of regulations ensure that these areas are legally obligated to institute newborn screening including PKU testing. To some extent, implementation by government did enhance the rate of newborn screening for PKU in these areas.

2.3. Follow-up services

Follow-up services also play an important role during

Table 1. Features of laws and regulations related to newborn screening for PKU in China

Year	Law or regulation	Enacted by	Features	Ref.
<i>National laws or regulations</i>				
1994	Law on Maternal and Infant Health Care	The Central People's Government of the People's Republic of China	Identified the importance of newborn screening for the first time in law.	(14)
2001	Measures Implementing the Law on Maternal and Infant Health Care in China	The Central People's Government of the People's Republic of China	Included newborn screening in maternal and infant health care services.	(15)
2009	Measures for the Management of Newborn Screening	National Health and Family Planning Commission of the People's Republic of China	Specified that PKU be screened for and provided a protocol for China's newborn screening program.	(16)
2009	Plans for a Newborn Screening Program	National Health and Family Planning Commission of the People's Republic of China	Specified the objectives of the newborn screening program.	(17)
2010	Technical Specifications for Newborn Screening	National Health and Family Planning Commission of the People's Republic of China	Seeks to improve the quality of PKU screening and test.	(18)
<i>Local laws or regulations</i>				
1996	Regulations on Maternal and Infant Health Care in Shanghai	Standing Committee of the Shanghai People's Congress	Stipulated that the newborn screening program must be implemented in Shanghai.	(21)
1998	Regulations on Management of Maternal and Infant Health Care	Standing Committee of the Guangdong People's Congress	Stipulated that the newborn screening program must be implemented in Guangdong and proposed that screening include PKU testing.	(22)
2004	Working Proposal for Management of Maternal and Infant Health Care in Shanghai Major Projects and Components of Maternal and Infant Health Care in Shanghai	Health Bureau of the City of Shanghai	Indicated the time limit for PKU screening.	(23)
2006	Measures for the Management of Newborn Screening in Guangzhou	Health Department of Guangdong Province	Stipulated that children confirmed to have PKU can receive treatment for free until 8 years of age.	(26)
2007	Proposed Implementation of Newborn Screening for Genetic and Metabolic Diseases	Health Bureau of the City of Shanghai	Specified follow-up services for patients with PKU.	(24)

the process of newborn screening for PKU. The Health Bureau of the City of Shanghai drafted a Working Proposal for Management of Maternal and Infant Health Care in Shanghai and Major Projects and Components of Maternal and Infant Health Care in Shanghai in 2004 (23). In 2007, the Health Bureau of the City of Shanghai drafted measures for Proposed Implementation of Newborn Screening for Genetic and Metabolic Diseases (24). These directives specified aspects of newborn screening for PKU and follow-up services: *i*) 1-2 visits must be made within 28 days of birth; *ii*) DBS for PKU testing must be collected within 72 hours of birth and the DBS must be sent to a designated laboratory within 24 hours; *iii*) PKU testing must be performed by the laboratory within 2 days of receiving the DBS and screening results must be submitted within 5 days; *iv*) parents must be informed of potentially positive results within 1 day, the newborn must be brought to the laboratory for further testing, and final results must be submitted within 7-10 days. By offering these follow-up services, Shanghai has more effectively screened newborns for PKU, and follow-up services have contributed somewhat to the percentage of newborns covered by the screening program.

2.4. Government coverage of expenses

Economic factors play an important role in newborn screening for PKU. HongKong has a screening rate higher than 95%, and the government covers expenses for newborn screening (25). The Health Bureau of the City of Guangzhou drafted its own regulations on newborn screening directing that children confirmed to have PKU can receive the treatment from the Newborn Screening Center of the City of Guangzhou for free until 8 years of age (26). According to a report by the Health Bureau of the City of Guangzhou, 15 patients with PKU had received free treatment prior to 2005, for a treatment rate of 100% (27). To some extent, government coverage of expenses can actually encourage parents to have their newborn screened. Experience in HongKong and Guangzhou may serve as a reference for other areas of China.

3. Challenges faced by and prospects for measures and regulations regarding newborn screening in China

The number and percentage of newborns screened

for PKU in China has increased significantly thanks to national laws and regulations and specific local measures and regulations. These specific measures and regulations, such as those implemented by government, follow-up services, and government coverage of expenses, may serve as a reference and can be implemented in other areas. However, there still are some challenges faced by existing newborn screening, and more effective measures and regulations need to be implemented in China.

Prenatal health examinations Prenatal health examinations are expected to play an important role in the prevention of PKU. Effective prevention of birth defects can be classified into three levels: primary prevention (avoiding causes of congenital abnormalities), secondary prevention (early detection of congenital abnormalities), and tertiary prevention (surgical intervention to repair congenital abnormalities) (28). The most important stage, primary prevention, has not openly contributed to the fight against PKU. Fees for prenatal health examinations are now completely covered by the state (29), but there are no reports of PKU being detected during prenatal health examinations.

National financial support National financial support is still relatively weak. Fees for PKU screening and treatment can significantly influence whether parents have their newborn screened, and yet only 40% provinces of China cover some of the fees for newborn screening for PKU. Funds to cover fees come from the new rural Cooperative Medical System (CMS) (such as in Guangdong, Guizhou, and Sichuan) or government expenditures (such as in Shanghai and Jiangsu) (30). In addition, the existing policy of free treatment should also be improved. The revenue from newborn screening in Guangzhou has been used to treat patients with PKU for free, and yet the cost of free treatment is only 5.5% of actual revenue (27). The duration of subsidized treatment could be lengthened from 8 years of age to a longer period.

In conclusion, the number and percentage of newborns screened for PKU in China increased significantly after 1981. Experience with implementation by government, follow-up services, and government coverage of expenses may benefit other areas in China. However, prenatal health examinations and financial support are expected to play a more significant role in newborn screening for PKU in the future.

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