

DEVELOPMENT OF A NEWBORN SCREENING LABORATORY QUALITY ASSURANCE SYSTEM IN SHANDONG, CHINA

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Abstract. Shandong is a large province in northeastern China with a population of over 80 million. There are over 800,000 births annually with newborn screening testing currently being performed in 15 laboratories in city maternity and child health care hospitals. Since 1996, the number of newborns screened has steadily increased until the number screened annually now exceeds 600,000 (over 70%). During the period from 1996-2000, there were 97 cases of classical PKU confirmed and 399 cases of congenital hypothyroidism giving incidences of 1:11,644 and 1:2,831 respectively. The large number of newborns screened and the relatively large number of screening laboratories presents a quality control challenge since ideally each newborn should receive identical newborn screening services and the laboratories should be of equal abilities. With assistance from the US Centers for Disease Control (CDC), a provincial laboratory quality control program has been established and provides oversight for a newborn screening system from blood collection through treatment of patients. The goal is to ensure that patients with the disorders of interest can be identified from within the normal newborn population with an acceptable minimum number of false positives while attempting to eliminate false negatives. External proficiency testing materials are provided quarterly by the CDC, repackaged by the Center for Newborn Screening Quality Control of Shandong (CNQCS), and distributed to the testing laboratories. Analytical results are reported within a specified period of time and then compared to CDC reported results. Laboratories unable to analyze the samples correctly are provided technical assistance. Additionally, the CNQCS oversees and provides educational assistance in training phlebotomists and other health workers associated with newborn screening. Brochures, posters, videotapes and parent support groups are also developed as a function of the CNQCS. Ultimately, control materials will be prepared for distribution with linkages to CDC for international comparability.

INTRODUCTION

Shandong is a large province located in northeastern China with a population of over 80 million. There are about 800 thousand babies born each year. Newborn Screening (NBS) begun in Qingdao and Jinan in 1996 and was developed and implemented in other Shandong locations in the late 1990s. Currently, there are 15 laboratories in local cities testing for CH and PKU. The other two are preparing for testing. Since 1996, the number of newborns screened has steadily increased until the number screened annually now exceeds 600,000 (over 70%). In some cities like Qingdao, Jining and Linyi, the screening rate exceeds 95%. From August 1, 1996 – December 31, 2000, there were 97 cases of classical PKU and 399 cases of congenital hypothyroidism confirmed from screening giving respective incidences of 1:11,644 and 1:2,831 within the province.

Ideally, each newborn should receive identical newborn screening services and the screening laboratories should have equal abilities. The large number of newborns being screened and the relatively large number of screening laboratories performing the testing presents a quality control challenge. The Center for NBS Quality Control of Shandong (CNQCS) was established by the Shandong Health Department in 1999. Its functions are: (1) to assure NBS laboratory quality throughout the province; (2) to assist individual screening centers in NBS program planning; and (3) to provide technical consultation and guidance for NBS program operations. With assistance from the US Centers for Disease Control and Prevention (CDC), the CNQCS has established a provincial laboratory quality control program. A complete newborn screening system has been defined, and has provided oversight from blood collection through patient treatment. Samples were collected in village hospitals,

transported to the town hospitals and then carried to the testing center weekly. The city testing center analyzed samples 1-3 days per week. This system's goal is to ensure that patients with the disorders of interest can be identified from within the normal newborn population with an acceptably low number of false positives while attempting to completely eliminate false negatives.

NEWBORN SCREENING POLICY

On Dec 31, 1999, a Newborn Screening Program statement was issued by the Shandong Department of Health. It stated that only one Newborn Screening Center should be set up in every city (in China, the word city refers to a defined political jurisdiction). Newborn screening occurring in local towns and villages would feed into city centers. The criteria for blood collection, sample transportation, test analysis, and diagnosis for the two diseases - CH and PKU were included in the Statement. Written rules of sample acceptability were also published.

MATERIALS AND METHODS

In Shandong, dried blood spots (DBS) are collected from the newborn's heel at day 3 of life by nurses or midwives in the village hospital or local maternity and childcare center and transported weekly to the town hospital (maternity and child health care hospital). There, sample quality is checked for volume, uniformity, and saturation by an assigned newborn screening coordinator. If the sample is acceptable, it is sent to the city center for testing. If it is unacceptable, it is returned to the sender who is requested to collect another if the baby is still there, or to inform the baby's parents to return to the hospital for repeat testing if the baby has been discharged. The CNQCS or testing centers train all newborn screening coordinators and blood collectors to distinguish unacceptable samples before transportation to the city center and to communicate quickly with the sample sender or family when the sample is unacceptable so that retesting can be rapidly performed. If the sample is positive, the testing center could inform the family by mail or phone so that the test could be repeated as soon as possible. For those babies discharged early from hospitals, or in intensive care institutions, the coordinators are responsible for informing the collector or parent of the need for sample collection. All sample collectors and coordinators meet regularly to discuss problems and solutions with sample collection and recall procedures. The city center manager in the local region convenes these meetings.

The S&S 903C (Schleicher and Schuell Inc, Keene, NH USA) filter-paper collection card is used for DBS specimens, QC materials, some calibrators and reference

materials. In addition to the acceptability criteria mentioned, samples that were not thoroughly air-dried or that may have been exposed to potentially interfering agents such as water, disinfectants, urine or other situations are also considered unsatisfactory. Samples are accepted up until 4 weeks after collection, although early delivery is recommended.

All specimens, acceptable or unacceptable, are documented in each laboratory. A computerized data management system is required to be used in all laboratories. Now in most centers, all information of the specimens are encoded into this management system. Every center is encouraged to implement a data management system. Some laboratories use ELISA (enzyme linked immunosorbent assay) for congenital hypothyroidism screening and BIA (bacterial inhibition assay) for phenylketonuria screening. Other laboratories use DELFIA (dissociation enhanced lanthanide fluoro-immuno assay) for CH and PKU testing. Laboratory equipment performance, maintenance and repair must be documented. Commercial reagents and other analytical materials are required to be labeled with the name, lot number, concentration, date received, date opened, expiration date, storage conditions and other relevant information as part of laboratory operations, and these instructions should be included in the laboratory procedural manual (Slazyk and Hannon, 1993). Laboratory personnel in each center are specially trained in testing procedures by CNQCS and must be aware of the importance of their work. Only those technicians who receive qualification certificates for screening may work in the program. The manner and format for documenting the information of specimen processing including provisions to document sample receipt, analytical procedures, result reporting and unacceptable samples, are required to be part of the laboratory's written procedural manual. Some laboratories are still seeking to comply with these requirements.

QUALITY CONTROL

The daily performance of screening methods is monitored by analyzing IQC materials in each analytical run of each laboratory. Laboratories are required to document concentrations of analytes in internal quality control materials and include 2-3 different concentration levels, including normal and abnormal values. One control must be targeted at the cutoff value of the assay. Laboratories are also required to determine the cutoff values from data obtained on a statistically appropriate large population (Slazyk and Hannon, 1993). Sometimes CNQCS help the laboratory to determine the cutoff values. External QA materials are analyzed in each

laboratory as part of their daily performance. QC materials are required to be treated in the same manner as the patient samples and randomly placed in each analytical run. Each laboratory determines the working QC ranges by calculating data obtained from a minimum of 20 successive and independent analytical runs. When plotted routine QC values fall outside of the established limits, problems or trends may be developing that call for corrective action (Slazyk and Hannon, 1993). Levy-Jennings control charts and Westgard multi-rule control procedures - $1_{2s}/1_{3s}/2_{2s}/R_{4s}/4_{1s}/10_x$ are used by all laboratories for judging when analytical runs are in or out of control.

With assistance from CDC, a Proficiency Testing (PT) program was established. External PT materials are provided quarterly by the CDC, repackaged by CNQCS, and distributed to the testing laboratories. PT samples are analyzed in the same way as patient samples. Analytical results are reported within a specified period of time and then compared to CDC reported results by CNQCS.

The test results and presumptive clinical classification for each unknown specimen are also evaluated. Summary reports including statistical data analyses and tables are distributed to all participating laboratories. Each participating laboratory evaluates its performance from these reports relative to other laboratories using the same methods. When analytical results differ significantly from expected values, the laboratory is alerted that its results may be suspect compared to other participating laboratories (Slazyk and Hannon, 1993). Likewise, when the clinical classification of a specimen differs from the expected classification,

the laboratory is also alerted that its presumptive clinical classification may be in error. Laboratories unable to analyze the samples correctly are provided technical assistance by CNQCS. Internal QC reports are sent to CNQCS quarterly. If a problem is detected, guidance and assistance is also provided to the laboratory by CNQCS. Other miscellaneous data from newborn screening are reported to CNQCS at the same time so that provincial data may be accumulated.

As previously mentioned, the CNQCS oversees and provides educational assistance in training phlebotomists and other health workers associated with newborn screening. All NBS health workers who get their qualification certificates for screening may work in the program. Picture posters in hospitals, announcements in streets, advertisements on TV, articles in magazines or newspapers, videos at Pregnancy Schools in hospitals, or parent support groups are also developed as an educational function of the CNQCS for the quality assurance program.

Ultimately, quality control materials will be prepared locally for distribution utilizing linkages with CDC for international comparability.

REFERENCE

Slazyk WE, Hannon WH. Quality assurance in the newborn screening laboratory. In: Therrell BL, ed. Laboratory methods for neonatal screening. Washington, DC: American Public Health Association, 1993: 23-46.