

NEONATAL SCREENING PROGRAM IN THAILAND

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Abstract. The Neonatal Screening Program for congenital hypothyroidism (CHT) and phenylketonuria (PKU) commenced in 1996 with the objective of bringing better quality of life to people throughout the country, especially in the remote areas. This involved the implementation of routine services to the public health infrastructure all over the country. The plan of action has been designed so that by the year 2000 all public health service units throughout the country may provide screening services which can cover 1.2 million babies/annum. Implementation of the screening program has been performed through public health sectors all over the country. These involved: education of the health personnel and communities, implementation of routine specimens collection and delivery systems to the central laboratories, establishment of central laboratory screening services, routine follow up and case management. Local in-house reagents using ELISA and IRMA techniques have been developed and utilized as screening and confirmation tests for CHT. In addition, Guthrie's test has been used for PKU screening and the automated Fluorometry has been selected for PKU confirmation. All 724 community hospitals have provided newborn screening services as one of the basic requirements for newborns according to public health policy. Of 1,425,025 babies screened, 3,450 (0.24%) were above the first screening cut off for CHT (TSH > 25 mU/l) and 321 (0.02%) for PKU (PKU > 4mg/dl). With a 63.10% follow up rate, the incidences were 1:3,314 for CHT and 1:237,504 for PKU. Newborn screening has been implemented as routine practice for all public health sectors of the country for CHT and PKU. It is expected that by the year 2003, all Thai newborns will be provided with screening services resulting in a better quality of life for the next generation.

INTRODUCTION

The Neonatal Screening Program for congenital hypothyroidism and phenylketonuria (PKU) commenced in 1996 with the objective of bringing a better quality of life to people throughout the country, especially in the remote areas. This involved the implementation of routine services to the public health infrastructure all over the country. The plan of action (Charoensiriwatana *et al*, 1995) has been designed so that by the year 2000 all public health service units throughout the country provided services for the screening of neonates, which will cover 1.2 million babies/annum. The government has supported the program by allocating the five-year budget of approximately US\$15 million to support these activities. Furthermore, the program has received the human resource development grant and technical support from the International Atomic Energy Agency and the Centers for Disease Control and Prevention (CDC) in order to strengthen the technical proficiency and to support the self-sustainable policy. It is expected that by the year 2002, all newborn babies in Thailand should have received the screening services at least for the

detection of Congenital Hypothyroidism (CHT) and Phenylketonuria (PKU).

ORGANIZATION AND ADMINISTRATION

The Ministry of Public Health has developed a standardized pattern for delivery of rural services, in which health care is provided through a hierarchy of facilities. Each level of health care has been organized administratively to provide a distinct set of services to a defined population group. The key institution providing specialized medical care in each province is the provincial hospital, commonly located in the provincial capital itself. Each province is divided into districts and subdistrict levels where community hospitals are responsible for the community health services. In addition, health volunteers also exist in communities and villages in order to support the community health program. All of these facilities except the provincial hospital are considered part of the rural health network. They are administered by the provincial health officials in the province capitals. All 75 provincial public health offices are administered under the Office of the Permanent Secretary in the Ministry of Public Health. There are 8

departments and 2 semi-public sectors in the central administration whose duties are to solve the national public health problems. The transfer of know-how and protocols in public health from these 10 sectors can be processed to the provincial health offices and Regional Centers of those sectors without difficulty by the administration of the Office of the Permanent Secretary and their own internal cooperation through the framework of the Ministry of Public Health. The Central and Provincial Administration can be demonstrated in the following flow chart (Fig 1).

There are five central departments that play very important roles in technical transfers and support of the operation of the program to the provincial health offices:

- Permanent Secretariat Office administers and manages all hospitals and health care centers throughout the country.
- Department of Medical Sciences establishes and performs laboratory testing including implementation of the laboratory quality assurance processes.
- Department of Medical Services provides proper

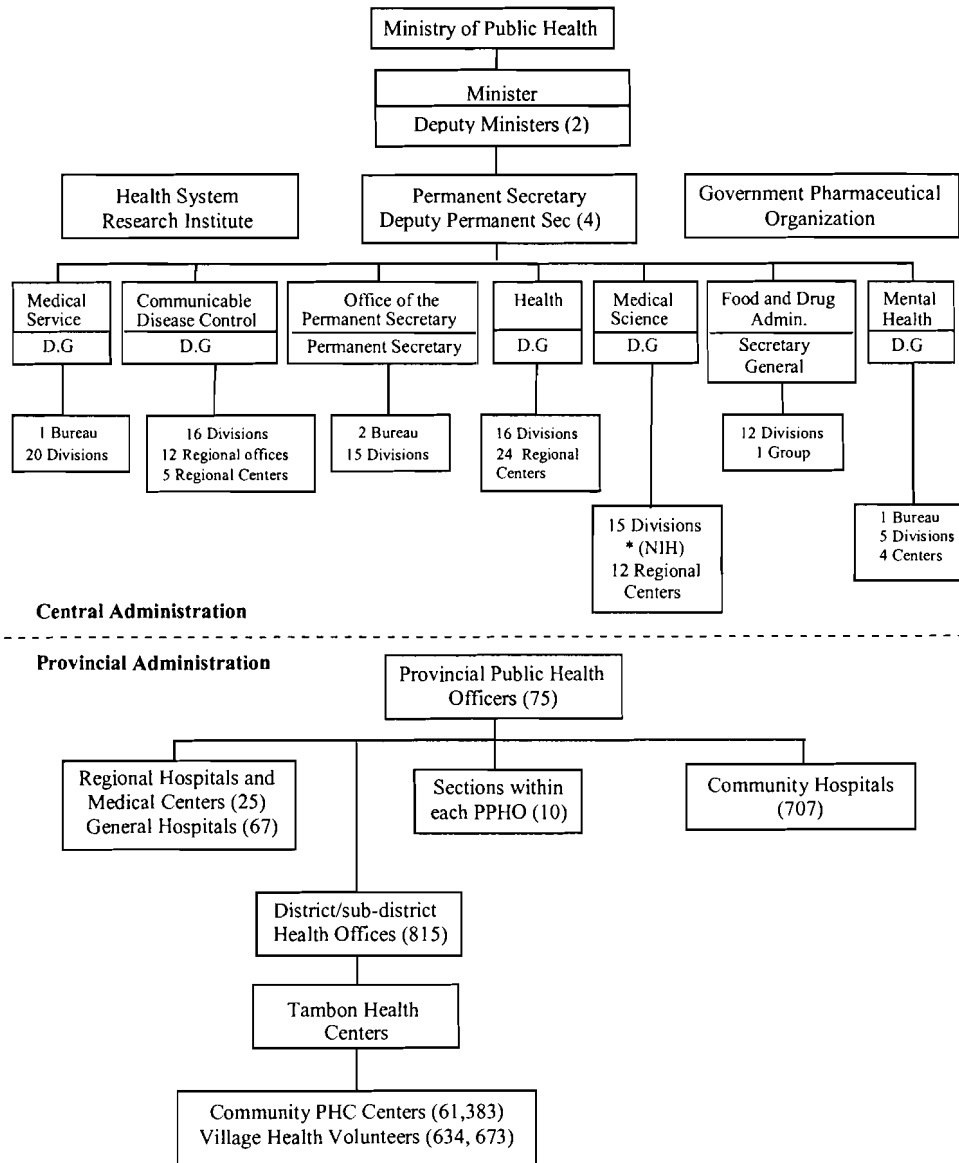


Fig 1. Organizational structure of the Thai Ministry of Public Health in the central and provincial areas.

treatment to the detected patients.

- Department of Health provides health care services for the mother and the child.
- Department of Mental Health provides and promotes mental health development.

A pilot survey for neonatal screening was conducted in 1992. The survey showed a high incidence rate of CHT especially in iodine deficient areas. These data resulted in the establishing nationwide neonatal screening services to improve quality of life. In 1995, a Public Health Policy was issued emphasizing Neonatal Screening for Congenital Hypothyroidism and PKU. Fig 2 demonstrates the newborn screening program

operation in Thailand. The country is divided into 4 regions, ie North, East, Central and South. Four screening laboratories have been established for these regions to cope with 300,000 specimens/center/year. Specimens are obtained from hospitals and health care centers throughout the country as filter paper-blood spots and mailed to the central laboratory at the National Institute of Health (NIH) or to the other three Regional Medical Sciences Centers in their respective areas. Besides the routine operation, the central laboratory at the NIH is also responsible for newborn screening quality assurance and reagents for the affiliated laboratories.

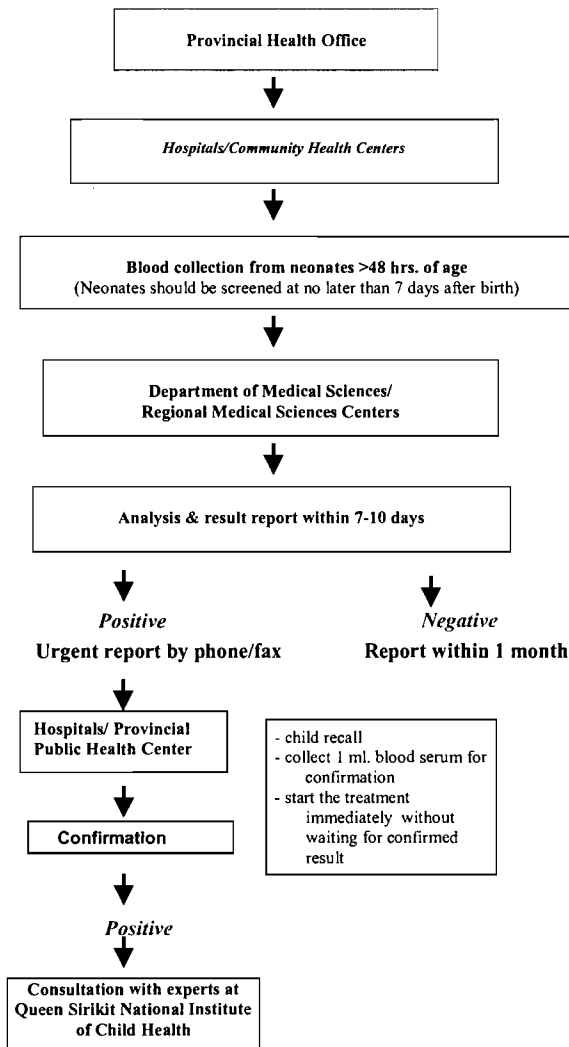


Fig 2. Overview of the Neonatal Screening Program in Thailand.

MATERIALS AND METHODS

Specimen collection

Blood specimens are collected from neonates at least 48 hours old by heel prick or by venipuncture from dorsal hand veins onto blood collection cards and dried horizontally at room temperature for at least 3 hours. The collection cards are then mailed to the screening laboratory in the region.

Laboratory methodology

For routine CHT screening (Dussault *et al*, 1976), all regional screening centers are equipped with fully automated ELISA processors and computerized punching machines for high throughput screening of approximately 2,000 specimens/day. In addition, the IRMA has also been used for confirmatory purposes.

Neonatal TSH ELISA reagents are produced in house at the National Institute of Health using the double monoclonal antibodies-sandwich technique. A monoclonal antibody is coated onto a microtiter plate and the other is conjugated with the horse radish peroxidase enzyme. TSH is extracted from the blood spot and is allowed to react with the monoclonal antibody on the microtiter plate, it then reacts with the antibody-enzyme conjugate at different epitopes. The color reaction is performed by using the TMB substrate. The optical density is determined at 450 nm.

TSH blood spot calibrators are prepared by spiking human pituitary TSH into 55% PCV human blood and spot onto Whatmann BFC 180 or S&S 903 blotting paper. These calibrator blood spots are calibrated against the WHO 2nd International reference preparation of hTSH no. 80/558 (NIBSC, UK).

For the PKU assay, Guthrie's bacterial inhibition assay (Guthrie and Susi, 1963) has been selected as a

screening test and the automated fluorometric method is used for confirmation of phenylalanine levels.

Internal Quality Control Specimens are also provided to all centers as a component in the ELISA kits. The External Quality Assurance Program for Neonatal TSH Screening is conducted by the Bureau of Laboratory Quality Standard (BLQS). In addition, the central laboratory participates with the CDC Newborn Screening Quality Assurance Program for TSH and PKU Blood spot assay, which is one of the main activities in the Neonatal Laboratory Quality Assurance Scheme to standardize the screening laboratories.

Follow up and treatment

For the provincial level, the health promotion section of the provincial health office has duties to implement health promotion activities according to the public health policy. The follow up of patients is normally done by the public welfare section of the provincial hospitals or by the health promotion official through the community healthcare network after being notified from the laboratories. Usually, babies will be brought to the nearby community hospitals for reinvestigation. Serum will be collected and sent for confirmatory tests by measuring T4 and TSH and thyroxine will be given after the serum was collected. Treatment will be performed according to the guideline provided by the Thai Pediatric Endocrinology Society as stated in the flow chart in Fig 3.

RESULTS

Since the commencement of the Neonatal Screening Program 1,425,025 neonates have been screened for Congenital Hypothyroidism (CHT) and Phenylketonuria (PKU). Four hundred thirty were confirmed to have CHT and 5 were confirmed to have PKU. The recall rate was 0.2% (Fig 4) and the follow up rate is 63.1% (Fig 5). The average time used to follow the babies back for treatment is 30 days due to transportation in the rural areas. The

Table 1. Summary of newborn screening output grouped by regions.

Regions	Number of babies	NTSH >5mU/l	%Recall	%FollowUp	% IDD	No. of CHT
North	103,545	-	0.24	48.35	-	35 (1:2,958)
Central	1,101,013	142,360	0.18	72.77	12.93	284 (1:3,876)
Eastern	151,680	24,963	0.67	51.38	16.46	60 (1:2,528)
South	68,787	7,604	0.31	47.22	11.05	51 (1:1,349)

Remark : % IDD = $\frac{\text{no. of Neonates TSH} > 5\text{mU/l}}{\text{Total no. of neonates screened}} \times 100$

Total no. of neonates screened

TSH > 25 mU/l
 Confirmation by determining T4 and TSH levels in serum
 Physical examination:
 • X-ray: bone-age (knee)
 • Thyroid scan (technitium), if available
 Start treatment with Na-L-T4, 10-12 µg/kg/day

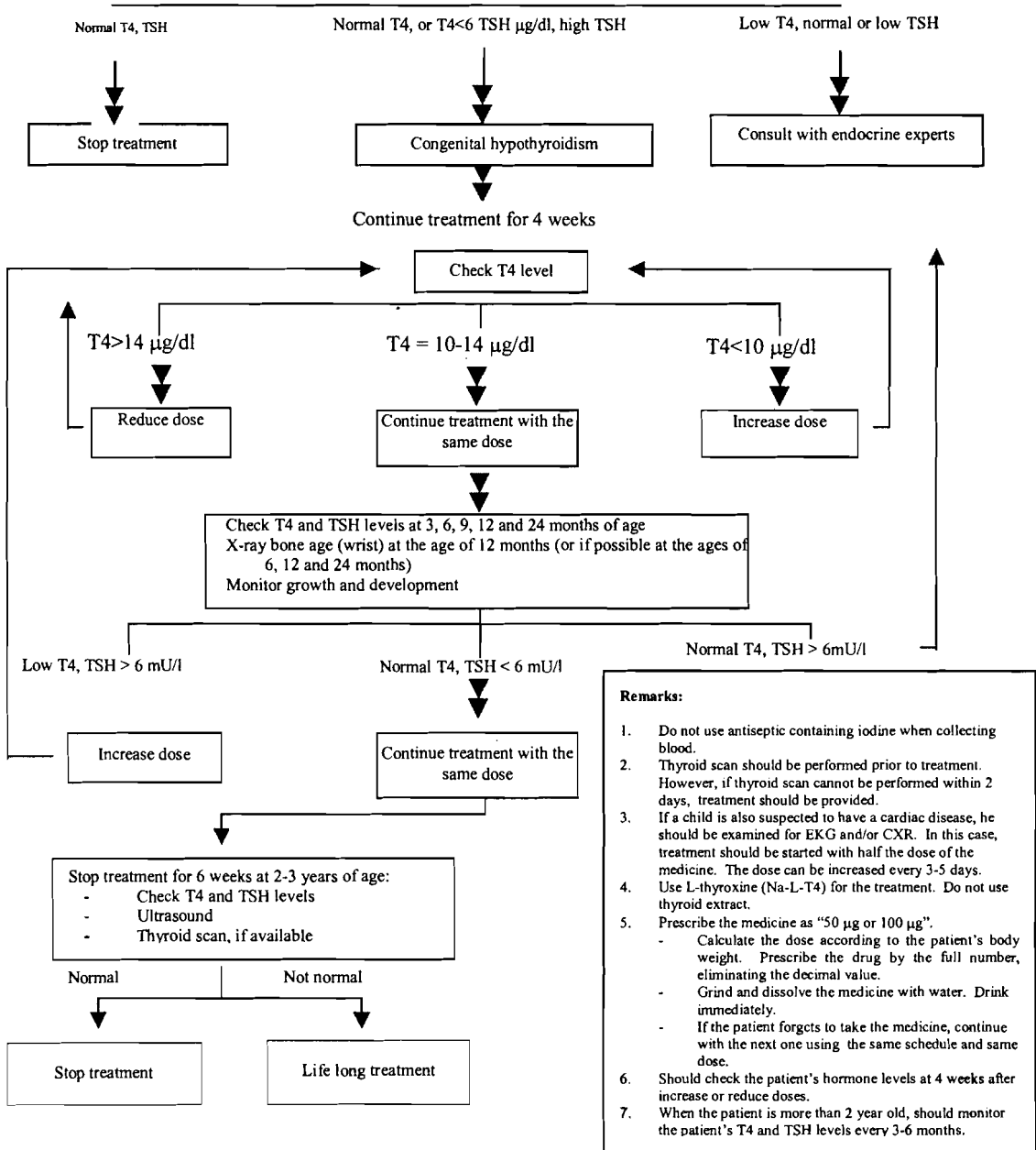


Fig 3. Guidelines for monitoring and control of congenital hypothyroidism.

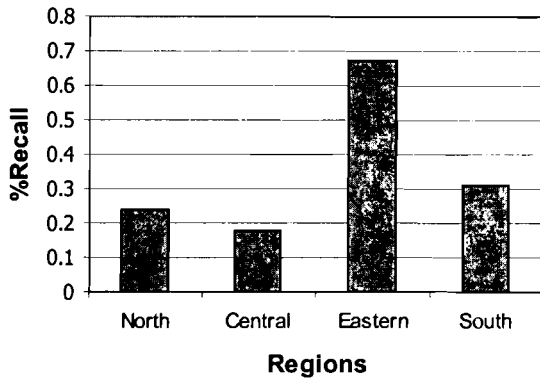


Fig 4. Percentage recall in various regions.

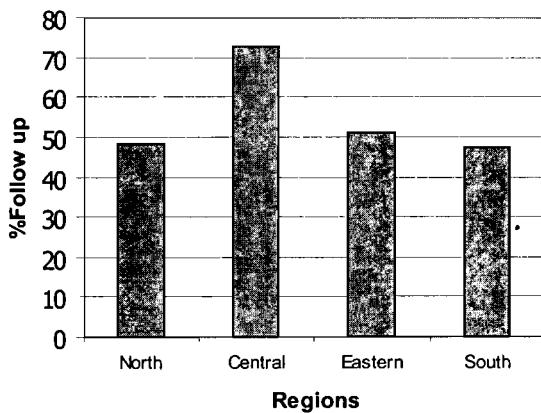


Fig 5. Percentage follow up in various regions.

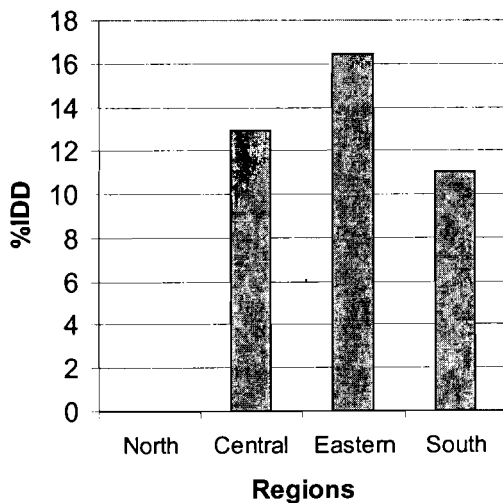


Fig 6. Percentage IDD in various regions.

failure to follow up patients is mostly due to the changes of address without proper notification and the migration of hill tribe people.

Table 1 and Fig 4 show the highest recall rate of 0.67% in the Eastern part of the country whereas in other regions the recall rate is much lower ie between 0.18-0.31%. The number of CHT cases found in the eastern region is 1: 2,528 which demonstrated that there are a lot of cases that have a temporary high level of TSH, or transient hypothyroidism, which may be caused by iodine deficiency. In addition, the higher % of IDD according to the ICCIDD criteria (Charoensiriwatana *et al*, 1995) ie 16.46 found in these eastern regions also support the hypothesis of transient hypothyroidism due to iodine deficiency. The incidence of CHT in the southern Region is the highest ie 1:1,349 whereas the % of IDD is 11.05% which is the lowest among the three regions (Fig 6). This might be from other risk factors that may affect the genetic variation of the southern population that should be further studied in detail.

DISCUSSION

The Neonatal Screening Program for CHT and PKU is well established and integrated into the national public health service infrastructure throughout the country. To further achieve success for the program, an increase in coverage of the babies by providing more educational materials to housewives and pregnant mothers is required. In addition, the campaign of the screening program through mass media communication is also needed. At the moment, a national website has been constructed for the National Neonatal Screening Program and can be accessed at: www.neoscreen.in.th. Computerized reporting of laboratory results through the website is being developed. For Thailand, it is expected that by the year 2002, all newborn babies delivered in hospitals will be screened for CHT and PKU.

It is obvious that the Neonatal Screening Program especially for CHT is one of the important public health service programs that should be established in developing countries to ensure a better Quality of Life for the people. The program should be developed in the direction of self-reliance in the long term with sustainability within the infrastructure of the public health system of those countries.

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