優生保健暨罕見疾病防治

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Taiwan Foundation for Rare Disorders

協辦單位：台灣罕見病病患權益促進會

Taiwan Organization for Rare disorders

台灣地區新生兒篩檢之回顧與展望

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摘要

有些先天代謝異常疾病在新生兒時期沒有明顯的臨床症狀，若不能早期發現診斷及治療，會產生一些嚴重的後遺症，例如腦部發展遲緩，或甚至死亡。這些疾病可考慮利用新生兒篩檢來早期發現診斷，及時提供正確的治療及預防措施，將疾病的後遺症降至最低。台灣於 1982 至 1983 年間研發建立新生兒篩檢的檢體採集作業、篩檢檢驗及確認診斷方法，並先行篩檢臺灣地區啓智班學童，共發現 3 名苯酮尿症及 7 名先天性甲狀腺低能症患者，由篩檢結果可看出臺灣地區智障之發生與這些先天代謝異常疾病是有關聯的。隨後在 1984 年 1 月以先期發展完成的新生兒篩檢作業爲架構，展開全國性的新生兒篩檢服務。篩檢項目爲先天性甲狀腺低能症 (CHT)、苯酮尿症 (PKU)、楓漿尿病 (MSUD)、高胱胺酸尿症 (HCU)、半乳糖血症 (GAL) 等，篩檢作業系統中包括了檢體採集機構、新生兒篩檢中心、公共衛生護士追蹤網及負責確認診斷與治療的轉介醫院。

葡萄糖六磷酸鹽去氫酶缺乏症 (G6PD) 的篩檢方法於 1985 年 7 月發展完成，併入執行中的全國新生兒篩檢作業進行先期篩檢，由兩年 (1985.7~1987.6) 的篩檢結果估算出台灣的 G6PD 缺乏症的發生率約爲 2% (男性 3%，女性 0.9%)。自 1984 年展開全國性新生兒篩檢開始，在約 20 萬位新生兒中未發現楓漿尿病個案，故於 1987 年 9 月以 G6PD 缺乏症取代 MSUD 成爲五項常規篩檢項目之一。台灣的新生兒篩檢率從最初的 6.7% (1984 年)，1990 年時達到 80%，在 1996 年以後就已超過 99%。從 1984 年 1 月至 2004 年 12 月的 21 年間，篩檢了 4,960,950 名新生兒。CHT, PKU, HCU, 以及 GAL 的發生率分別爲 1/2,600, 1/37,600, 1/236,000, 以及 1/620,000。大多數的罹病個案能在出生一個月內被發現並給予適當治療，至今發展正常。

從 2000 年 3 月開始，台灣 3 家新生兒篩檢中心開始提供先天性腎上腺增生症 (CAH) 篩檢服務，2001 年 8 月開始篩檢中心另外陸續提供利用串聯質譜儀分析法 (MS/MS) 篩檢其他的胺基酸 (amino acid) 及肉鹼 (acylcarnitines) 代謝異常，這兩種的篩檢服務目前是由民眾自行選擇並付費。從 2000 年 3 月至 2004 年 12 月共約 868,000 名新生兒參加了 CAH 篩檢，CAH 的發生率約爲 1/17,000。在 2001 年 8 月至 2004 年 12 月間，篩檢中心利用串聯質譜儀分析法篩檢了 452,800 名新生兒，共發現 36 名患者，分別爲 15 名 3-甲基巴豆醯輔酶 A 羧化酶缺乏症 (3MCC) / 3-羥基-3-甲基戊二酸尿症 (HMG)、6 名 MSUD、2 名酪胺酸血症、4 名瓜胺酸血症 (CIT)、4 名戊二酸血症第一型(GAI)、2 名中

鏈醯基輔酶 A 去氫酶缺乏症 (MCAD)、以及甲基丙二酸血症 (MMA)、丙酸血症 (PA) 、短鏈醯基輔酶 A 去氫酶缺乏症 (SCAD) 及非酮性高甘胺酸血症 (NKH) 各 1 名。

衛生署國民健康局於 2003 年委託評估探討「國內新生兒先天代謝異常疾病篩檢項目增減可行性」的計畫，依據 WHO 的篩檢指導方針及參考國內、外新生兒篩檢之相關經驗與文獻，透過專家會議討論決議出下列的結論: 1). 維持原有之五項常規篩檢項目，2). 建議將 CAH、MSUD、MCAD、GA I、異戊酸血症（IVA）及 MMA 等六項疾病爲納入常規篩檢項目， 3). 建議包含生物素酶缺乏症（BD）、精胺丁二酸酶缺乏症（ASA）， CIT 、PA 及所有 C5OH 可篩檢出之疾病，共十一項進行「先趨性全面篩檢」，4). 其他可利用串聯質譜儀篩檢之疾病項目，現階段只可考慮爲研究項目而不宜進行全面篩檢， 5). 在新增的新生兒常規篩檢項目及先趨性全面篩檢項目正式實施前，應將整體篩檢流程，自採血、寄送檢體、篩檢中心檢測，至轉介醫院確診、治療及後續的治療監偵系統皆完整規劃建立完善且測試完成後，再行全面正式提供篩檢服務，6). CAH、G6PD、GAL 及利用串聯質譜儀篩檢項目之篩檢陽性個案應於出生後「七天」以內接獲通知並轉介至轉介醫院，進行適當的確診及防治工作， 7). 國內所有新生兒均應接受新生兒「常規篩檢項目」檢測之服務 (不宜有選擇性的自費篩檢項目)， 8). 新生兒常規篩檢項目內容應定期檢討評估。

Developments of Neonatal Screening in Taiwan

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Abstract

Some of the congenital metabolic disorders have no specific clinical symptoms during neonatal period, if not treated early irreversible damages such as mental retardation will occur. The permanent damages can be avoided if these diseases are able to be detected biochemically by neonatal screening in the early stage of life, and treated immediately with appropriate therapy and intervention. Method development pilot programs (including dried blood sample collecting, screening tests, confirmatory diagnostic procedures and treatments) were carried out in mental retarded children between 1982 and 1983 in Taiwan. Based on the methods developed, the nationwide project to set up neonatal screening for congenital hypothyroidism (CHT), phenylketonuria (PKU), maple syrup urine disease (MSUD), homocystinuria (HCU), and galactosemia (GAL) was started in January 1984. The nationwide neonatal screening system consisted of sample collection institutes, newborn screening centers, public health nurse follow-up network, and referral hospitals for confirmatory diagnosis and treatment. After the nationwide neonatal screening system was established in July 1985, the method for screening of glucose-6-phosphate dehydrogenase (G6PD) deficiency was developed. The incidence of G6PD deficiency was estimated to be about 2% (male 3%, female 0.9%) in Taiwan based on the screening program. Since no MSUD was found from 200,000 newborns screened, after a two year (1985.7-1987.6) pilot study on G6PD screening, MSUD was replaced by G6PD in the routine nationwide neonatal screening program. The screening coverage rate in Taiwan has reached 80% in 1990 and over 99% since 1996. From 1984.1 to 2004.12, 4,960,950 newborns have been screened. The incidences of CHT, PKU, HCU, and GAL were reported to be about 1/2,600, 1/37,600, 1/236,000, and 1/620,000, respectively. Most of the affected cases were detected and treated accordingly within one month of birth and are developing normally at the present time.

Each of the three neonatal screening centers in Taiwan has started individual voluntary program paid by the parents for selective screening of congenital adrenal hyperplasia (CAH) and defects in other amino acids and acylcarnitines metabolisms, which were detected by tandem mass spectrometry (MS/MS), since 2000.3 and 2001.8, respectively. The incidence of CAH was estimated around 1/17,000 from 868,000 newborns screened between 2000.3 and 2004.12. Fifteen cases of 3-methylcrotonyl-CoA carboxylase deficiency (3MCC) / 3-hydroxy-3-methylglutaric aciduria (HMG), 6 cases of MSUD, 2 cases of tyrosinemia, 4 cases of citrullinemia (CIT), 4 cases of glutaric aciduria type I (GAI), 2 case of medium chain acyl-CoA dehydrogenase deficiency (MCAD), and 1 case each of methylmalonic aciduria (MMA), propionic acidemia (PA), short chain acyl-CoA dehydrogenase deficiency (SCAD) and nonketotic hyperglycinemia were detected from 452,800 newborns by the MS/MS screening between 2001.8 and 2004.12.

Recently, a technological assessment research supported by the Bureau of Health Promotion, Department of Health has reached following consent recommendation about the adjustment of the items for neonatal screening in Taiwan: 1). the 5 current routine items should be kept, 2). CAH, MSUD, medium chain acyl-CoA dehydrogenase deficiency (MCAD), glutaric aciduria Type I (GAI), methylmalonic aciduria (MMA), and isovaleric acidemia (IVA) should be included as routine items, 3). biotinidase deficiency, argininosuccinase deficiency, citrullinemia (CIT), propionic academia (PA), and C5OH-carnitine should be consider to be included as a pilot project, 4). any other disease which could be detected by MS/MS should be considered as a research item only at the present time, 5). any disease incorporated into the routine services, including pilot project items, should have confirmatory diagnosis and follow up treatment system prepared in place before its screening program starts, 6). the positive results of CAH, G6PD, GAL, and MS/MS tests should be referred for follow-up no later than 7 days after birth, 7). the routine screening items should be available to all the newborns non-selectively (e.g. should not be selected by voluntary payments), 8). the routine screening items should be reviewed periodically.