# Jan-April 2011 Newborn Screening Articles of Interest

1. Acta Paediatr. 2011 May;100(5):636-7. Epub 2011 Jan 11.

**Pulse oximetry screening for detection of critical congenital heart disease in newborns: a survey of current practices in the United Kingdom.**

Shastri AT, Clarke P, Roy R.

2. J Pediatr. 2011 May;158(5):859.

**Universal newborn hearing screening improves quality of life for children with permanent hearing impairment.**

Kemper AR.

3. J Pediatr. 2011 May;158(5):A3.

**Hemoglobin H newborn screening: let's not**.

Welch TR.

4. Rev Panam Salud Publica. 2011 Mar;29(3):145-52.

**Overview of newborn hearing screening activities in Latin America.**

Garcia BG, Gaffney C, Chacon S, Gaffney M.

Abstract
OBJECTIVE: Ascertain the status of early hearing detection and intervention services in Latin America.
METHODS: Between June and November 2007, Gallaudet University, in collaboration with the U.S. Centers for Disease Control and Prevention Early Hearing Detection and Intervention Diversity Committee, disseminated a survey to 11 Latin American countries. It included questions about newborn hearing screening (NHS) procedures, the availability of intervention

services for infants with hearing loss, and challenges in identifying infants with hearing loss. In addition, a literature review was conducted to help identify the status of NHS efforts in Latin America.
RESULTS: Six countries (Chile, Costa Rica, Guatemala, Mexico, Panama, and Uruguay) and one U.S. territory (Puerto Rico) responded to the survey. Responses indicated that efforts to identify infants with hearing loss vary within and across countries in Latin America. In some countries, activities have been implemented at a national level; in others, activities have been implemented at a single hospital or region within a country. Common barriers to implementation of NHS programs include a lack of funding, screening and diagnostic equipment, public awareness, and personnel qualified to work with infants and young children.
CONCLUSIONS: In spite of several barriers, NHS programs have been implemented in at least some facilities and regions in Latin America. Additional efforts are needed to expand NHS activities in Latin America.

**5.** J Pediatr. 2011 May;158(5):780-3. Epub 2010 Dec 16.

**Weighing the evidence for newborn screening for hemoglobin h disease.**

Kemper AR, Knapp AA, Metterville DR, Comeau AM, Green NS, Perrin JM.

Abstract
OBJECTIVE: To conduct a systematic review to assist the United States Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) to determine whether Hemoglobin H screening should be included among the core recommended conditions for newborn screening.
STUDY DESIGN: We identified 21 articles in MEDLINE from 1989 to March 2010 that provided evidence regarding screening, treatment, and outcomes associated with Hemoglobin H disease.
RESULTS: In California, newborn screening has identified 9 cases per 100 000 of deletional hemoglobin H disease and 0.6 cases per 100 000 of nondeletional hemoglobin H disease. Five cases of hemoglobin Bart's hydrops fetalis syndrome were also identified in over ten years of

screening for Hemoglobin H disease. Although Hemoglobin H disease is associated with a wide range of morbidity, no studies were found that evaluated the benefits of early identification and treatment.
CONCLUSIONS: The SACHDNC found the data insufficient to recommend that states adopt newborn screening for Hemoglobin H disease.

**6.** Paediatr Perinat Epidemiol. 2011 May;25(3):298-305. Epub 2011 Jan 4.

**Age at diagnosis and disease progression of cystic fibrosis in an area without newborn screening.**

de Monestrol I, Klint A, Sparén P, Hjelte L.

Abstract
de Monestrol I, Klint Å, Sparén P, Hjelte L. Age at diagnosis and disease progression of cystic fibrosis in an area without newborn screening. Paediatric and Perinatal Epidemiology 2011; 25: 298-305. We studied age at diagnosis and disease progression of cystic fibrosis (CF) patients with a new study design, using data of 119 patients extracted from Stockholm CF Centre registry. Risk factors for overall morbidity and for lung, liver and nutritional morbidity were investigated separately using time to event methodology (Kaplan-Meier curves, proportional hazards regression). The patients were followed from: (i) healthy at diagnosis to morbidity, (ii) diagnosis with symptoms of morbidity to being free of morbidity, and (iii) free of morbidity to relapse of morbidity. Median age at diagnosis was 5.0 months. Of the patients with overall morbidity at diagnosis 50% became free of morbidity after 4.8 years; however, the patients above the age of 24 months at diagnosis had a reduced chance of becoming free of morbidity (crude hazard ratio 0.14 [95 % confidence interval 0.04, 0.45]) compared with those with diagnosis between the ages of 2 and 12 months ($P < 0.01$). Of the healthy at diagnosis, 50% experienced overall morbidity after 1.4 years. They had a slow decline to the endpoint of the specific morbidities; 50% experienced lung morbidity after 3.4 years and liver morbidity after 4.8 years, while 50% never reached nutritional morbidity during the 10 years follow-up. We

conclude that there was a disadvantage for the CF patients diagnosed after the age of 24 months with symptoms of overall morbidity at diagnosis in an area without newborn screening.

**7.** Ital J Pediatr. 2011 Apr 11;37(1):16. [Epub ahead of print]

**Universal neonatal audiological screening: experience of the University Hospital of Pisa.**

Ghirri P, Liumbruno A, Lunardi S, Forli F, Boldrini A, Baggiani A, Berrettini S.

Abstract
ABSTRACT: The early identification of pre-lingual deafness is necessary to minimize the consequences of hearing impairment on the future communication skills of a baby. According to the most recent international guidelines the deafness diagnosis must occur before the age of three months and the prosthetic-rehabilitative treatment with a traditional hearing aid should start within the first six months. When a Cochlear implant becomes necessary, the treatment should start between the age of 12 months and 18 months. The only way to diagnose the problem early is the implementation of universal neonatal audiological screening programs. Transient evoked otoacoustic emissions (TEOAE) is the most adequate test because it's accurate, economic and of simple execution. Automatic auditory brainstem response (AABR) is necessary to identify patients with auditory neuropathy but it is also important to reduce the number of false-positives.The 20-30% of infant hearing impairment is represented by progressive or late-onset hearing loss (HL) so it's also necessary to establish an audiological follow up program, especially in infants at risk. From November 2005 all neonates born in the University hospital of Pisa undergo newborn hearing screening. From 2008 the screening program follows the guidelines for the execution of the audiological screening in Tuscany which have been formulated by our group according to the 2007 JCIH Position Statement and adaptated to our regional reality by a multidisciplinary effort. From November 2005 to April 2009 8113 neonates born in the Neonatal Unit of Santa Chiara Hospital (Pisa) have undergone newborn hearing screening. 7621 neonates (93.9%) without risk factors executed only the TEOAE test. 492 (6.1%) neonates had audiological risk factors and thus underwent TEOAE and AABR. 84 patients (1,04%) failed both TEOAE and AABR tests. 78 of them underwent further investigations. 44 patients resulted

falsepositives (the 0,54% of the screened newborns). 34 neonates (4,2 per thousand) had a final diagnosis of hearing impairment. 8 patients (0.99 per thousand) had unilateral hearing loss (HL). 26 patients (3,2 per thousand) had bilateral hearing impairment. In our screening program the percentage of false-positives was quite low (0.54%)while the incidence of bilateral HL (3.2 per thousand) is a little higher than that found in literature reports. In most of our patients premature birth or neonatal suffering represent the main cause of HL.

**8.** Acta Otolaryngol. 2011 Apr 5. [Epub ahead of print]

**Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry.**

Berninger E, Westling B.

Abstract

Abstract Conclusion: This universal newborn hearing-screening (UNHS) programme revealed high efficacy. The proportion of congenital sensorineural hearing loss was higher in left ears and in males than in right ears and females, which was in line with the systematic ear asymmetries and sex differences in transient-evoked otoacoustic emission (TEOAE) pass percentage. Objectives: To study the long-term outcome of a UNHS programme based on multiple TEOAEs and clinical click-evoked auditory brainstem response (ABR). Method: The study included all the newborns that were screened during a 6-year period (n = 31 092). TEOAE pass/fail was analysed in detail. In an assessment performed 10 years after the start of the 6-year UNHS, prevalence, degree and type of congenital hearing loss were studied. Results: The proportion of screened newborns was high, i.e. 98%. Multiple TEOAE recordings minimized the need for clinical ABR. Fifty-seven (0.18%) subjects showed bilateral hearing loss (exceeding ≈ 30 dB HL); median ABR threshold = 60 dB nHL (at 2.5 months of age). Bilateral and unilateral sensorineural hearing loss was found in 0.17% (n = 52; 56% males) and 0.06% (n = 18; 61% left ears, 56% males) of the screened newborns, respectively. Higher TEOAE pass percentages ($p < 0.01$) were demonstrated in right ears and in females than in left ears and males.

**9.** Curr Pharm Biotechnol. 2011 Apr 5. [Epub ahead of print]

**Altered Metabolism and Newborn Screening using Tandem Mass Spectrometry: Lessons Learned from the Bench to Bedside.**

Chace DH, Spitzer AR.

Abstract

The use of tandem mass spectrometry (MS/MS) for screening of inherited metabolic disease in newborns has afforded many unique opportunities in the understanding of the benefits early their early detection, diagnosis and treatment. From the standpoint of the laboratory and modern analytical methods, the use of MS based analysis demonstrated that a multiple metabolite-multiple disease screen-one method approach expanded screening significantly. MS/MS and newborn screening has served as a model of one type of approach in preventative health care that has shown proven benefits. It has been nearly 20 years since the introduction of MS/MS analysis of dried blood spots from newborns. There have been many lessons learned in both the analytical approach as well as follow-up at the bedside. These lessons can be applied to future applications of MS/MS in newborn screening as well as other areas of metabolism and metabolic profiles such as that from acquired disease, environmental disease and other factors such as nutrition and age. The use of a highly specific, sensitive and multiplex platform such as MS/MS will continue to grow and experience in the newborn screening application will insure this outcome.

**10.** Clin Chim Acta. 2011 Apr 2. [Epub ahead of print]

**The screening of inborn errors of metabolism in sick Chinese infants by tandem mass spectrometry and gas chromatography/mass spectrometry.**

Sun W, Wang Y, Yang Y, Wang J, Cao Y, Luo F, Lu W, Peng Y, Yao H, Qiu P.

Abstract

BACKGROUND: Analyses of amino acid/acylcarnitines in dried blood spots (DBS) and organic acids in urine are the primary tests for inborn errors of metabolism (IEMs). Automated tandem

mass spectrometry (MS/MS) and gas chromatography/mass spectrometry (GC/MS) can rapidly and simultaneously detect numerous metabolic compounds with high precision and sensitivity. METHODS: Three thousand four hundred and twenty-nine DBSs and 2781 urine samples were collected from our hospital patients with suspected IEMs, and analyzed for amino acid/acylcarnitines and organic acids by MS/MS and GC/MS, respectively. The results were used in a coincidental survey to determine the efficacy of these methods for the diagnosis of IEMs. RESULTS: Nineteen different types of IEMs were detected in 121 affected cases (1.95% of 6210 samples). There were 66.12% amino acid disorders, 29.75% organic acid disorders and 4.13% with fatty acid oxidation disorders. Conclusions: the sick infants tested in this study had high prevalence rates of neonatal intrahepatic cholestasis, methylmalonic acidemia, hyperphenylalaninemia, tyrosinemia type I, and urea cycle disorders.
CONCLUSION: The combined use of MS/MS and GC/MS is an appropriate tool for screening of IEMs in sick infants.

**11.** Anal Bioanal Chem. 2011 Apr;400(1):237-44. Epub 2011 Feb 18.

**Direct analysis of dried blood spots by in-line desorption combined with high-resolution chromatography and mass spectrometry for quantification of maple syrup urine disease biomarkers leucine and isoleucine.**

Miller JH 4th, Poston PA, Karnes HT.

Abstract
A in-line desorption device was developed, which allows for direct analysis of dried blood spots eliminating the need for punching disks from the filter paper cards. Using this device, we have validated a method to quantify biomarkers related to maple syrup urine disease (MSUD), a metabolism disorder that often requires a second-tier test for confirmation. Direct analysis of newborn screening cards is conducted in-line with a high-resolution chromatographic separation with mass spectrometry using electrospray ionization and multiple-reaction monitoring. Quantification of leucine and isoleucine using an isotopically labeled internal standard encompasses a range suitable for MSUD assessment. Precision and accuracy of the technique

was acceptable with relative standard deviations within 10% at three fortified concentrations and an unfortified level. A post-column infusion test shows minimum matrix suppression was observed using this direct sampling technique.

**12.** Anal Biochem. 2011 Apr 1;411(1):32-42. Epub 2010 Dec 13.

**High-throughput determination of urinary hexosamines for diagnosis of mucopolysaccharidoses by capillary electrophoresis and high-performance liquid chromatography.**

Coppa GV, Galeotti F, Zampini L, Maccari F, Galeazzi T, Padelia L, Santoro L, Gabrielli O, Volpi N.

Abstract

Mucopolysaccharidoses (MPS) diagnosis is often delayed and irreversible organ damage can occur, making possible therapies less effective. This highlights the importance of early and accurate diagnosis. A high-throughput procedure for the simultaneous determination of glucosamine and galactosamine produced from urinary galactosaminoglycans and glucosaminoglycans by capillary electrophoresis (CE) and HPLC has been performed and validated in subjects affected by various MPS including their mild and severe forms, Hurler and Hurler-Scheie, Hunter, Sanfilippo, Morquio, and Maroteaux-Lamy. Contrary to other analytical approaches, the present single analytical procedure, which is able to measure total abnormal amounts of urinary GAGs, high molecular mass, and related fragments, as well as specific hexosamines belonging to a group of GAGs, would be useful for possible application in their early diagnosis. After a rapid urine pretreatment, free hexosamines are generated by acidic hydrolysis, derivatized with 2-aminobenzoic acid and separated by CE/UV in ∼10min and reverse-phase (RP)-HPLC in fluorescence in ∼21min. The total content of hexosamines was found to be indicative of abnormal urinary excretion of GAGs in patients compared to the controls, and the galactosamine/glucosamine ratio was observed to be related to specific MPS syndromes in regard to both their mild and severe forms. As a consequence, important correlations between analytical response and clinical diagnosis and the severity of the disorders

were observed. Furthermore, we can assume that the severity of the syndrome may be ascribed to the quantity of total GAGs, as high-molecular-mass polymers and fragments, accumulated in cells and directly excreted in the urine. Finally, due to the high-throughput nature of this approach and to the equipment commonly available in laboratories, this method is suitable for newborn screening in preventive public health programs for early detection of MPS disorders, diagnosis, and their treatment.

**13.** Arch Dis Child. 2011 Apr;96(4):374-9. Epub 2011 Jan 17.

**Prevention of intellectual disability through screening for congenital hypothyroidism: how much and at what level?**

Grosse SD, Van Vliet G.

Abstract

Objective Congenital hypothyroidism (CHT) is a common cause of preventable mental retardation, and the quantification of intellectual disability due to CHT is needed to assess the public health benefit of newborn screening. Design Review of published studies conducted among children born prior to the introduction of newborn screening for CHT and reporting cognitive test scores. Setting Population-based studies. Patients Children with clinically diagnosed CHT. Interventions Thyroid hormone substitution. Main outcome measures Intelligence quotient (IQ) (mean and distribution). Results The prevalence of recognised CHT rose from one in 6500 prior to screening to approximately one in 3000 with screening. In four population-based studies in high-income countries, among children with clinically diagnosed CHT 8-28% were classified as having intellectual disability (defined as an IQ <70) and the mean IQ was 85 (a leftward shift of 1 SD). Among children with subclinical CHT, the risk of overt intellectual disability was lower (zero in one study), but decreased intellectual potential and increased behavioural abnormalities were documented. Conclusions Although the prevalence of overt disability among children with CHT in the absence of screening may be less than previously estimated, the preventable burden of intellectual disability due to CHT is substantial and justifies newborn screening. However, changes in existing newborn screening protocols to

capture more cases are unlikely to prevent overt cases of disability and should therefore be justified instead by the documentation of other benefits of early detection.

**14.** Clin Biochem. 2011 Apr;44(5-6):406-11. Epub 2011 Jan 28.

**Thalassemia and hemoglobinopathies in Southeast Asian newborns: diagnostic assessment using capillary electrophoresis system.**

Srivorakun H, Fucharoen G, Changtrakul Y, Komwilaisak P, Fucharoen S.

Abstract
BACKGROUND: We have investigated the Capillarys 2 Hemoglobin testing system to assist in presumptive diagnosis of thalassemia and hemoglobinopathies commonly found in Southeast Asia.
METHODS: Study was conducted on 226 newborns. Hematological parameters were recorded and Hb profiles were examined on the Capillarys 2 Hemoglobin analyzer (SEBIA). DNA analyses were used to establish the final diagnoses.
RESULTS: Among 226 newborns examined, 122 had thalassemias with 17 different genotypes. The capillary electrophoresis system could provide useful data for presumptive diagnoses of cases, especially those with Hb E and α-thalassemia. Hb E was found to be 2.6-6.2% in heterozygote whereas Hb Bart's were clearly observed in cases with compound heterozygous or homozygous α(+)-thalassemia and heterozygous α(0)-thalassemia. Hb H disease and other forms of α-thalassemia could be differentiated based on the presence of Hb Bart's and its percentage.
CONCLUSION: The capillary electrophoresis system is applicable to newborn screening for common forms of thalassemia in Southeast Asia.

**15.** Clin Chem. 2011 Apr;57(4):623-6. Epub 2011 Feb 18.

**Newborn screening for isovaleric acidemia using tandem mass spectrometry: data from 1.6 million newborns.**

Ensenauer R, Fingerhut R, Maier EM, Polanetz R, Olgemöller B, Röschinger W, Muntau AC.

Abstract

BACKGROUND: Electrospray ionization-tandem mass spectrometry (ESI-MS/MS) has been used in the Bavarian newborn screening (NBS) program since 1999. The use of ESI-MS/MS has led to the inclusion of isovaleric acidemia (IVA) into NBS. We retrospectively evaluated data on more than 1.6 million newborns screened during 9.5 years.

METHODS: Acylcarnitines from whole blood spotted on filter paper were converted to their corresponding butyl esters, and the samples were analyzed by use of ESI-MS/MS with stable isotope labeled internal standards.

RESULTS: A total of 24 individuals with IVA were detected by use of a multiparametric threshold criteria panel including isovalerylcarnitine (C5) and the ratios of C5 to octanoyl-, butyryl-, and propionylcarnitine. A cutoff set at the 99.99th percentile for isolated C5 or at the 99th percentile for C5 plus at least 2 ratios resulted in a positive predictive value for IVA screening of 7.0% and an overall recall rate of 0.024%. Adjusted reference ranges for age and birth weight were applied, and the incidence of IVA in the study population was calculated to be 1 in 67 000. Missed cases were not brought to our attention. IVA was also detectable in cord blood and early postnatal blood samples.

CONCLUSIONS: IVA can be reliably detected in NBS through acylcarnitine analysis in dried blood spots by using multiparametric threshold criteria. Further improvement (positive predictive value 13.0%, recall rate 0.01%) can be achieved by using more stringent recall criteria. In view of the potentially life-threatening natural course of IVA in early life, presymptomatic diagnosis may thus prevent mortality and morbidity.

**16.** Eur Arch Otorhinolaryngol. 2011 Apr;268(4):501-5. Epub 2010 Nov 11.

**Incidence and clinical value of prolonged I-V interval in NICU infants after failing neonatal hearing screening.**

Coenraad S, Hoeve LJ, Goedegebure A.

Abstract

Infants admitted to neonatal intensive care units (NICUs) have a higher incidence of perinatal complications and delayed maturational processes. Parameters of the auditory brainstem response (ABR) were analyzed to study the prevalence of delayed auditory maturation or neural pathology. The prevalence of prolonged I-V interval as a measure of delayed maturation and the correlation with ABR thresholds were investigated. All infants admitted to the NICU Sophia Children's Hospital between 2004 and 2009 who had been referred for ABR measurement after failing neonatal hearing screening with automated auditory brainstem response (AABR) were included. The ABR parameters were retrospectively analyzed. Between 2004 and 2009, 103 infants were included: 46 girls and 57 boys. In 58.3% (60 infants) of our population, the I-V interval was recordable in at least one ear at first diagnostic ABR measurement. In 4.9%, the I-V interval was severely prolonged. The median ABR threshold of infants with a normal or mildly prolonged I-V interval was 50 dB. The median ABR threshold of infants with a severely prolonged I-V interval was 30 dB. In conclusion, in case both peak I and V were measurable, we found only a limited (4.9%) incidence of severely prolonged I-V interval (≥0.8 ms) in this high-risk NICU population. A mild delay in maturation is a more probable explanation than major audiologic or neural pathology, as ABR thresholds were near normal in these infants.

**17.** Evid Based Med. 2011 Apr;16(2):57-8. Epub 2011 Jan 12.

**Universal newborn hearing screening improves quality of life in children aged 3-5 years but does not show a clear relationship with spoken language skills.**

Fitzpatrick EM, Durieux-Smith A.

**18.** Genet Med. 2011 Apr;13(4):301-304.

**Secretary's Advisory Committee on Heritable Disorders in Newborns and Children response to the President's Council on Bioethics report: The changing moral focus of newborn screening.**

Trotter TL, Fleischman AR, Howell RR, Lloyd-Puryear M; for the Secretary s Advisory Committee on Heritable Disorders in Newborns and Children.

**19.** Genet Med. 2011 Apr;13(4):305-313.

**Research use of leftover newborn bloodspots: Attitudes of Canadian geneticists regarding storage and informed consent requirements.**

Richer J, Ghebremichael MS, Chudley AE, Robinson WM, Wilfond BS, Solomon MZ.

Abstract

PURPOSE: Leftover newborn spots can provide a powerful research tool as a population-wide DNA bank. Some provinces/states store them for more than 20 years; however, parents are usually not informed of the retention of leftover newborn spots. To examine the opinions of Canadian geneticists regarding permission for leftover newborn spots storage for research purposes and the associated risks, a web-based survey was distributed to all members of the Canadian College of Medical Geneticists with a valid e-mail address (n = 209) and completed by 78 respondents (37%).

RESULTS: The majority of respondents (73%) favored opt-out notification for retention of samples that would be held for longer than 2 years. For research on multifactorial conditions using leftover newborn spots originally banked without parental permission, geneticists favored different types of permission depending on the level of identifiable information attached to samples. Thirty-eight percent were concerned that information pamphlets that state that leftover newborn spots will be stored and may be "a source of DNA for research" would lead to a decreased participation in newborn screening. Twenty-eight percent believed that group stigma or family anxiety was likely to result from using nonidentified leftover newborn spots to study multifactorial conditions.

CONCLUSION: The concerns of this knowledgeable cohort supports the critical importance of public engagement about both the potential risks and societal benefits associated with the use of leftover newborn spots in research as policy for leftover newborn spots is developed.

**20.** Int J Pediatr Otorhinolaryngol. 2011 Apr;75(4):535-42. Epub 2011 Feb 17.

**Newborn hearing concurrent gene screening can improve care for hearing loss: A study on 14,913 Chinese newborns.**

Wang QJ, Zhao YL, Rao SQ, Guo YF, He Y, Lan L, Yang WY, Zheng QY, Ruben RJ, Han DY, Shen Y.

Abstract

OBJECTIVE: Newborn hearing screening has been widely adopted and made an achievement to some degree. Current screening protocols rely solely on detecting existing auditory disorders at the time of screening and are unable to identify individuals susceptible to auditory disorders in later life. Even if the hearing loss newborn is referred, most cases could not be diagnosed until 6-12 months old with no etiology being elucidated. This study reports the first effort to combine traditional hearing screening with genetic screening to improve the efficacy of newborn hearing screening.

METHODS: This study was undertaken in 12 regional hospitals located in 11 provinces of China. 14,913 newborn babies received hearing concurrent genetic screening. The hearing screening was performed with OAE or AABR. Blood sample was collected with a universal newborn genetic screening card. And three common gene, mtDNA 12S rRNA, GJB2 and SLC26A4 were screened with standard protocol.

RESULTS: Among all the 14,913 newborns, 86.1% (12,837/14,913) individuals passed the first-step hearing screening, 7.8% (1168/14,913) babies passed only one side, and the other 6.1% (908/14,913) were bilaterally referred. Gene screening found 306 individuals had one or two mutant alleles, the carrier rate is 2.05% (306/14,913) among the entire newborn population. The risk for hearing loss was 100% (7/7) for those newborns carrying causative GJB2 or SLC26A4 mutations (homozygotes or compound heterozygotes), 14.4% (23/160) for GJB2 heterozygote carriers, 12.3% (15/122) for SLC26A2 heterozygous carriers, and the total prevalence of referral hearing screening was approximately 14.7% (45/306). However, 85.3% (261/306) newborns passed hearing screening among these carriers including 18 newborns with 12S rRNA

mt.1555A>G pathogenic mutation, who would suffer from sudden hearing loss once applying aminoglycoside drugs.
CONCLUSION: The cohort studies provided the essential population parameters for developing effective programs for hearing care of newborns in China. Hearing concurrent gene screening in newborns may confirm the abnormal results from hearing screening tests, help to find the etiologic of the hearing loss, and better recognize infants at risk for late-onset hearing loss occurring prior to speech and language development. In conclusion, a survey on 14,913 Chinese newborns proved that concurrent genetic screening could improve newborn hearing screening for hearing defects.

**21.** Int J Pediatr Otorhinolaryngol. 2011 Apr;75(4):513-7. Epub 2011 Feb 2.

**Anxiety of the mothers with referred baby during Universal Newborn Hearing Screening.**

Mohd Khairi MD, Noor Rafidah K, Affizal A, Normastura AR, Suzana M, Mohamad Normani Z.

Abstract
OBJECTIVE: To investigate the anxiety among mothers whom their babies have failed test results in the first stage of Universal Neonatal Hearing Screening Program.
PATIENTS AND METHODS: A cross-sectional study was carried out on mothers whom their baby have positive test results in the first stage of Universal Neonatal Hearing Screening Program. Face to face interview was conducted to obtain data on sociodemographic profiles, knowledge about hearing loss and past medical history. Symptoms experienced by the mothers due to positive hearing test results and level of anxiety were measured by using the Malay translation Beck Anxiety Inventory questionnaire. These mothers were then given an appointment to come for the second screening six weeks after the first screening. The same questionnaire was given to them before the start of the second screening. SPSS version 11.5 was used for data entry and analysis. Wilcoxon signed Rank Test was used to compare the level of anxiety between the first and second screening.

RESULTS: From a total of 78 mothers who were participated during the first screening, 50 of them have completed the study at the second screening (response rate=64%). Fifty-two percent of them knew about the hearing screening before hand. Ninety-six percent of the mothers became alert about their child response towards sounds after they knew that their child had failed the first hearing screening. During the first screening, 74% of the mothers felt mild anxiety which was decreased to 68% before the mothers undergone the second screening. Moderate anxiety was felt by 10% of the mothers during both the first and second screening. There were 8% of the mothers having severe anxiety during the first screening but have reduced to half (4%) before the mothers undergone the second screening. The anxiety level was significantly less before the second screening with the median score of 5 (IQR: 13.0) compared to after the first screening (8, IQR=14.25); p=0.001.
CONCLUSIONS: There are considerable portion of the mothers of false-positive test result during Universal Neonatal Hearing Screening Program experienced unacceptable anxiety. This group of mothers needs to be identified and given a necessary help.

**22.** J Biomed Inform. 2011 Apr;44(2):319-25. Epub 2010 Dec 15.

**Data mining methods for classification of Medium-Chain Acyl-CoA dehydrogenase deficiency (MCADD) using non-derivatized tandem MS neonatal screening data.**

Van den Bulcke T, Broucke PV, Hoof VV, Wouters K, Broucke SV, Smits G, Smits E, Proesmans S, Genechten TV, Eyskens F.

Abstract
Newborn screening programs for severe metabolic disorders using tandem mass spectrometry are widely used. Medium-Chain Acyl-CoA dehydrogenase deficiency (MCADD) is the most prevalent mitochondrial fatty acid oxidation defect (1:15,000 newborns) and it has been proven that early detection of this metabolic disease decreases mortality and improves the outcome. In previous studies, data mining methods on derivatized tandem MS datasets have shown high classification accuracies. However, no machine learning methods currently have been applied to datasets based on non-derivatized screening methods. A dataset with 44,159 blood samples was

collected using a non-derivatized screening method as part of a systematic newborn screening by the PCMA screening center (Belgium). Twelve MCADD cases were present in this partially MCADD-enriched dataset. We extended three data mining methods, namely C4.5 decision trees, logistic regression and ridge logistic regression, with a parameter and threshold optimization method and evaluated their applicability as a diagnostic support tool. Within a stratified cross-validation setting, a grid search was performed for each model for a wide range of model parameters, included variables and classification thresholds. The best performing model used ridge logistic regression and achieved a sensitivity of 100%, a specificity of 99.987% and a positive predictive value of 32% (recalibrated for a real population), obtained in a stratified cross-validation setting. These results were further validated on an independent test set. Using a method that combines ridge logistic regression with variable selection and threshold optimization, a significantly improved performance was achieved compared to the current state-of-the-art for derivatized data, while retaining more interpretability and requiring less variables. The results indicate the potential value of data mining methods as a diagnostic support tool.

**23.** J Biomol Tech. 2011 Apr;22(1):5-9.

**Comparison of DNA Extraction Methods from Small Samples of Newborn Screening Cards Suitable for Retrospective Perinatal Viral Research.**

McMichael GL, Highet AR, Gibson CS, Goldwater PN, O'Callaghan ME, Alvino ER, Maclennan AH; for the South Australian Cerebral Palsy Research Group.

Abstract

Reliable detection of viral DNA in stored newborn screening cards (NSC) would give important insight into possible silent infection during pregnancy and around birth. We sought a DNA extraction method with sufficient sensitivity to detect low copy numbers of viral DNA from small punch samples of NSC. Blank NSC were spotted with seronegative EDTA-blood and seropositive EBV EDTA-blood. DNA was extracted with commercial and noncommercial DNA extraction methods and quantified on a spectrofluorometer using a PicoGreen dsDNA quantification kit. Serial dilutions of purified viral DNA controls determined the sensitivity of

the amplification protocol, and seropositive EBV EDTA-blood amplified by nested PCR (nPCR) validated the DNA extraction methods. There were considerable differences between the commercial and noncommercial DNA extraction methods (P=0.014; P=0.016). Commercial kits compared favorably, but the QIamp DNA micro kit with an added forensic filter step was marginally more sensitive. The mean DNA yield from this method was 3 ng/µl. The limit of detection was 10 viral genome copies in a 50-µl reaction. EBV nPCR detection in neat and 1:10 diluted DNA extracts could be replicated reliably. We conclude that the QIamp Micro DNA extraction method with the added forensic spin-filter step was suitable for retrospective DNA viral assays from NSC

**24.** J Genet Couns. 2011 Apr;20(2):115-28. Epub 2010 Oct 9.

**A tailored approach to family-centered genetic counseling for cystic fibrosis newborn screening: the Wisconsin model.**

Tluczek A, Zaleski C, Stachiw-Hietpas D, Modaff P, Adamski CR, Nelson MR, Reiser CA, Ghate S, Josephson KD.

Abstract

This article describes the development of a tailored family-centered approach to genetic counseling following abnormal newborn screening (NBS) for cystic fibrosis (CF). A genetic counseling consortium reviewed research literature, selected theoretical frameworks, and incorporated counseling psychology micro skills. This innovative intervention integrated theories and empirically validated techniques. Pilot testing and parent feedback confirmed satisfaction with and feasibility of the approach designed to (a) minimize parents' distress, (b) facilitate parents' understanding, (c) increase parents' capacities to use genetic information, and (d) enhance parents' experiences with genetic counseling. Counselors engage in a highly interactive process of evaluating parents' needs and tailoring assessments and interventions that include a therapeutic environment, the family's emotional needs, parents' informational needs, and a follow-up plan. This promising new model is the first to establish a theory-driven, evidence-

based standard for genetic counseling in the context of NBS for CF. Additional research will evaluate the model's efficacy in clinical practice.

**25.** J Inherit Metab Dis. 2011 Apr;34(2):409-14. Epub 2011 Feb 22.

**Newborn screening for galactosemia by a second-tier multiplex enzyme assay using UPLC-MS/MS in dried blood spots.**

Ko DH, Jun SH, Park KU, Song SH, Kim JQ, Song J.

Abstract

Galactosemia is one of the most important inherited metabolic disorders detected by newborn screening tests. Abnormal results during screening should be confirmed by enzyme activity assays. Recently, we developed a multiplex enzyme assay for galactosemia in erythrocytes using ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). In this study, we proposed a second-tier multiplex enzyme assay for galactosemia that can be directly applied to dried blood spots (DBSs). Supernatants from two rehydrated-punched 3.2-mm DBSs were incubated with a reaction mixture containing [(13)C6]galactose, [(13)C2]galactose-1-phosphate, and UDP-glucose as substrates for three galactose-metabolizing enzymes. After a 4-hour incubation, the end products from the combined reaction mixture, [(13)C6]galactose-1-phosphate, UDP-[(13)C2]galactose, and UDP-galactose, were simultaneously measured using UPLC-MS/MS. Substrates, products, and internal standards from the mixture of the three enzyme reactions were clearly separated in the UPLC-MS/MS system, with an injection cycle time of 10 min. Intra- and inter-assay imprecisions of the UPLC-MS/MS were 8.4-14.8% and 13.2-15.7% CV, respectively. Enzyme activities in DBSs from 37 normal individuals and 10 patients with enzyme deficiencies were analyzed. DBSs from galactosemia patients showed consistently lower enzyme activities as compared to those of normal individuals. In conclusion, multiplex enzyme assays using UPLC-MS/MS can be successfully applied to DBS analysis. This method allows a fast and effective second-tier test for newborns showing abnormal screening results.

**26.** J Inherit Metab Dis. 2011 Apr;34(2):399-407. Epub 2011 Feb 3.

**Features and outcome of galactokinase deficiency in children diagnosed by newborn screening.**

Hennermann JB, Schadewaldt P, Vetter B, Shin YS, Mönch E, Klein J.

Abstract

Galactokinase deficiency (GALK-D), an autosomal recessive disorder in the Leloir pathway, results in accumulation of galactose, galactitol, and galactonate and leads to early onset of juvenile bilateral cataract. Highest incidence of GALK-D is found in Romani populations. The migration wave due to the Yugoslavian civil war has changed the spectrum of inborn errors of metabolism within Europe. Hence, newborn screening (NBS) in the Berlin region, performed from 1991 until 2010 in 683,675 neonates, revealed an increased incidence of GALK-D of 1:40,000, comparable to that of galactose-1-phosphate-uridyltransferase deficiency. A total of 44% of GALK-D patients were of Romani origin. All patients of Bosnian or Serbian origin were homozygous for the Romani founder mutation p.P28T. Detection of GALK-D by NBS and early start of galactose-restricted diet resulted in regression or prevention of cataracts. Slight cataracts without visual impairment occurred in 50% of the patients, 56% of whom were noncompliant. Further clinical symptoms, e.g., hypoglycemia, mental retardation, microcephaly, and failure to thrive, were associated with noncompliance. With treatment, galactose in blood decreased from 8,892 ± 5,243 to 36.5 ± 49.3 μmol/l, galactose in urine from 31,820 ± 32,103 to 30.0 ± 36.1 μmol/mmol creatinine, galactitol in RBC from 1,584 ± 584 to 12.3 ± 9.4 μmol/l, and galactitol in urine from 11,724 ± 4,496 to 236 ± 116 μmol/mmol creatinine. This is the first presentation of outcome and clinical features in GALK-D patients diagnosed by NBS. As our data suggest, GALK-D should be considered for inclusion in NBS in populations expected to have substantial numbers of GALK-D carriers, e.g., Yugoslavian immigrants.

**27.** J Pediatr. 2011 Apr;158(4):538-42. Epub 2011 Jan 13.

**Congenital hypothyroidism with a delayed thyroid-stimulating hormone elevation in very premature infants: incidence and growth and developmental outcomes.**

Woo HC, Lizarda A, Tucker R, Mitchell ML, Vohr B, Oh W, Phornphutkul C.

Abstract

OBJECTIVE: To test the hypothesis that very low birth weight (VLBW) and extremely low birth weight (ELBW) infants have an increased incidence of congenital hypothyroidism (CH) with a delayed thyroid-stimulating hormone (TSH) elevation and that the outcomes of these infants are similar to control infants.

STUDY DESIGN: Retrospective analysis of newborn thyroid screening data for 92 800 live births in Rhode Island to identify CH with a delayed TSH elevation. Developmental, growth, and endocrine outcomes of the index cases were assessed at 18 months corrected age.

RESULTS: CH with a delayed TSH elevation occurred in 1 in 58 ELBW, 1 in 95 VLBW, and 1 in 30 329 infants weighing ≥1500 grams ($P < .0001$). The incidence of head circumference <10(th) percentile was higher in VLBW infants with CH associated with a delayed TSH elevation ($P < .05$), and the mean head circumferences, weights, lengths, and developmental scores were similar to matched control infants. Three infants received short-term levothyroxine replacement.

CONCLUSIONS: The incidence of CH with a delayed TSH elevation was higher in ELBW and VLBW infants compared with infants weighing ≥1500 grams. The outcomes of these infants were comparable with matched control infants.

**28.** Mol Genet Metab. 2011 Apr;102(4):399-406. Epub 2010 Dec 14.

**Retrospective review of Japanese sudden unexpected death in infancy: The importance of metabolic autopsy and expanded newborn screening.**

Yamamoto T, Tanaka H, Kobayashi H, Okamura K, Tanaka T, Emoto Y, Sugimoto K, Nakatome M, Sakai N, Kuroki H, Yamaguchi S, Matoba R.

Abstract

Sudden unexpected death in infancy is defined as sudden unexpected death occurring before 12months of age. The common causes of sudden unexpected death in infancy are infection,

cardiovascular anomaly, child abuse, and metabolic disorders. However, the many potential inherited metabolic disorders are difficult to diagnose at autopsy and may therefore be underdiagnosed as a cause of sudden unexpected death in infancy. In the present study we retrospectively reviewed 30 Japanese sudden unexpected death in infancy cases encountered between 2006 and 2009 at our institute. With postmortem blood acylcarnitine analysis and histological examination of the liver, we found two cases of long-chain fatty acid oxidation defects. Molecular analysis revealed that the one patient had a compound heterozygote for a novel mutation (p.L644S) and a disease-causing mutation (p.F383Y) in the carnitine palmitoyltransferase 2 gene. Furthermore, retrospective acylcarnitine analysis of the newborn screening card of this patient was consistent with carnitine palmitoyltransferase II deficiency. Metabolic autopsy and expanded newborn screening would be helpful for forensic scientists and pediatricians to diagnose fatty acid oxidation disorders and prevent sudden unexpected death in infancy.

**29.** Pediatrics. 2011 Apr;127(4):703-12. Epub 2011 Mar 28.

**State laws regarding the retention and use of residual newborn screening blood samples.**

Lewis MH, Goldenberg A, Anderson R, Rothwell E, Botkin J.

Abstract
BACKGROUND: After newborn screening has been completed, many states retain residual newborn screening dried blood samples for various purposes, including program evaluation, quality assurance, and biomedical research. The extent to which states possess legal authority to retain residual dried blood samples (DBS) and use them for purposes unrelated to newborn screening is unclear.
OBJECTIVE: The purpose of this study was to evaluate state laws regarding the retention and use of DBS.
METHODS: State statutes and regulations related to newborn screening of all 50 states plus the District of Columbia were accessed online between November 2008 and December 2009 and

reviewed by 2 independent reviewers to determine the extent to which the retention and use of DBS were addressed.
RESULTS: The retention or use of DBS has not been addressed in 18 states. In 4 states, DBS becomes state property. Eight states require that parents be provided information regarding the retention of DBS. Parents in 5 states may request the destruction of their child's residual sample. Parental consent is required under certain circumstances to release DBS for research in 6 states. One state prohibits DBS from being used for research purposes.
CONCLUSIONS: States have wide variability in their policies regarding the retention and use of DBS. Many states have not addressed key issues, and some states that retain DBS may be acting outside the scope of their legal authority. The lack of transparency on the part of states in retaining DBS may undermine public trust in state newborn screening programs and the research enterprise.

**30.** Pediatrics. 2011 Apr;127(4):e940-7. Epub 2011 Mar 14.

**Effect of liposomal lidocaine and sucrose alone and in combination for venipuncture pain in newborns.**

Taddio A, Shah V, Stephens D, Parvez E, Hogan ME, Kikuta A, Koren G, Katz J.

Abstract
OBJECTIVE: To determine the relative effectiveness of liposomal lidocaine, sucrose, and their combination for reducing pain in term newborns.
METHODS: Ours was a double-blind, randomized, controlled, double-dummy trial of 330 healthy term newborns. Before venipuncture for the newborn screening test, neonates received (1) 1 g of liposomal lidocaine cream topically, (2) 2 mL of 24% sucrose solution orally, or (3) sucrose and liposomal lidocaine. The facial grimacing score (0-100) was used to assess pain. Adverse events and lidocaine levels were used to assess safety.
RESULTS: Infant characteristics did not differ among groups. Facial grimacing scores were lower in the sucrose group compared with those in the liposomal lidocaine group (mean difference: -27 [95% confidence interval (CI): -36 to -19; P < .001) and for the sucrose plus

liposomal lidocaine group compared with those in the liposomal lidocaine group (mean difference: -23 [95% CI: -31 to -14]; P < .001). The sucrose and sucrose plus liposomal lidocaine groups did not differ (mean difference: -5 [95% CI: -13 to 4]; P = .3). Local skin reactions were not observed, and the incidence of spitting up did not differ between sucrose-exposed and non-sucrose-exposed infants (1.4% vs 2.7%, respectively; P = .22). The mean (SD) plasma lidocaine level was 44.6 (55.3) ng/mL.
CONCLUSIONS: Sucrose was more effective than liposomal lidocaine for reducing pain during venipuncture in newborns. The addition of liposomal lidocaine to sucrose did not confer any additional benefit to sucrose alone. There was no evidence of harm from liposomal lidocaine or sucrose

**31.** JAMA. 2011 Mar 23;305(12):1198-200.

**Expanded newborn screening for detection of vitamin B12 deficiency.**

Sarafoglou K, Rodgers J, Hietala A, Matern D, Bentler K.

**32.** J Pediatr. 2011 Mar 21. [Epub ahead of print]

**Positive Newborn Screen in a Normal Infant of a Mother with Asymptomatic Very Long-Chain Acyl-CoA Dehydrogenase Deficiency.**

McGoey RR, Marble M.

**33.** Med J Aust. 2011 Mar 21;194(6):319-22.

**Newborn screening cards: a legal quagmire.**

Bowman DM, Studdert DM.

Abstract

Newborn screening (NBS) programs are a well established and cost-effective method for early identification of genetic disorders. However, a raft of legal questions surrounds the collection, storage, ownership and secondary use of NBS cards. The absence of clear legal rules governing NBS programs in Australia means that there are few straightforward answers to these questions. A series of controversial incidents have exposed this uncertainty in Australia, and remarkably similar controversies have occurred in the United States and European Union. We review the situation, using Victoria as a case study. We also make the case for a dedicated regulatory regime for NBS programs, arguing that the lack of such a regime threatens public trust and the robust operation of NBS programs in Australia. New rules would likely introduce stricter requirements for informed consent at the point of blood collection than has been the norm to date. However, the scope for use of cards in research could expand rather than contract, and it may be possible to reduce the risk that vast card archives will need to be destroyed in response to future public outcries.

**34.** Blood. 2011 Mar 17;117(11):3243-6. Epub 2011 Jan 27.

**Neonatal diagnosis of severe combined immunodeficiency leads to significantly improved survival outcome: the case for newborn screening.**

Brown L, Xu-Bayford J, Allwood Z, Slatter M, Cant A, Davies EG, Veys P, Gennery AR, Gaspar HB.

Abstract
Severe combined immunodeficiency (SCID) carries a poor prognosis without definitive treatment by hematopoietic stem cell transplantation. The outcome for transplantation varies and is dependent on donor status and the condition of the child at the time of transplantation. Diagnosis at birth may allow for better protection of SCID babies from infection and improve transplantation outcome. In this comparative study conducted at the 2 designated SCID transplantation centers in the United Kingdom, we show that SCID babies diagnosed at birth because of a positive family history have a significantly improved outcome compared with the first presenting family member. The overall improved survival of more than 90% is related to a

reduced rate of infection and significantly improved transplantation outcome irrespective of donor choice, conditioning regimen used, and underlying genetic diagnosis. Neonatal screening for SCID would significantly improve the outcome in this otherwise potentially devastating condition

**35.** Indian J Pediatr. 2011 Mar 17. [Epub ahead of print]

**Neonatal Screening for Inborn Errors of Metabolism Using Tandem Mass Spectrometry: Experience of the Pilot Study in Andhra Pradesh, India.**

Sahai I, Zytkowicz T, Rao Kotthuri S, Lakshmi Kotthuri A, Eaton RB, Akella RR.

Abstract

OBJECTIVE: To estimate the prevalence of the Inborn Errors of Metabolism (IEM), evaluate biomarker distributions and determine benefits of screening for the inborn errors of metabolism in Andhra Pradesh, India, using Tandem Mass Spectrometry (MS/MS).

METHODS: The 4,946 newborns born during the period 2006-2008 in four major Government Maternity Hospitals in a rural district in Andhra Pradesh, India, were screened at an established newborn screening laboratory in the US using their previously established norms.

RESULTS: Forty-seven neonates had out-of-range results (5 high probability; 28 low probability; 14 indeterminate). Two infants with disorders (carnitine uptake disorder and isovaleric aciduria) identified by screening are currently doing well. One infant with presumed glutaric aciduria type II, was deceased at the time of reporting. Another infant, with glutaric aciduria type I, became symptomatic and died at the age of 1 year despite early detection and treatment. A comparison of the concentrations of biomarkers among babies born in India and those born in Massachusetts, US, was also undertaken and significant differences were noted.

CONCLUSIONS: A high prevalence of disorders was observed, but to estimate the true extent of the IEM in India larger studies are required. This study also illustrates challenges encountered in disease management highlighting the importance of considering the access to confirmatory testing and continuing clinical care before implementing any large-scale NBS for conditions with resource-intensive health needs such as the IEM detected by MS/MS.

**36.** Anal Chem. 2011 Mar 15;83(6):2265-70. Epub 2011 Feb 22.

**Hemoglobin Variant Analysis via Direct Surface Sampling of Dried Blood Spots Coupled with High-Resolution Mass Spectrometry.**

Edwards RL, Creese AJ, Baumert M, Griffiths P, Bunch J, Cooper HJ.

Abstract

Hemoglobinopathies are the most common inherited disorders. Newborn blood screening for clinically significant hemoglobin variants, including sickle (HbS), HbC, and HbD, has been adopted in many countries as it is widely acknowledged that early detection improves the outcome. We present a method for determination of Hb variants by direct surface sampling of dried blood spots by use of an Advion Triversa Nanomate automated electrospray system coupled to a high-resolution mass spectrometer. The method involves no sample preparation. It is possible to unambiguously identify homozygous and heterozygous HbS, HbC, and HbD variants in <10 min without the need for additional confirmation. The method allows for repeated analysis of a single blood spot over a prolonged time period and is tolerant of blood spot storage conditions.

**37.** MCN Am J Matern Child Nurs. 2011 Mar 14. [Epub ahead of print]

**Ethical Implications of Newborn Screening, Life-Limiting Conditions, and Palliative Care.**

Sudia-Robinson T.

Abstract

While the first few days of an infant's life usually involve incorporation into a joyous family, this period can also be fraught with conditions that affect and potentially threaten survival. This article explores the ethical components of neonatal conditions such as disorders of sex development and metabolic disorders. Ethical issues surrounding futility, requests for unwarranted care, palliative care, and neonatal hospice are also discussed. Helping parents

through the grief process and ensuring that they are provided opportunities to participate in important decisions for their neonate are key components of the nursing role. Implications for clinical practice are provided in the form of a case study and practical suggestions for assisting parents through these difficult situations.

**38.** J Clin Endocrinol Metab. 2011 Mar 9. [Epub ahead of print]

**Subtle Health Impairment and Socioeducational Attainment in Young Adult Patients with Congenital Hypothyroidism Diagnosed by Neonatal Screening: A Longitudinal Population-Based Cohort Study.**

Léger J, Ecosse E, Roussey M, Lanoë JL, Larroque B; the French Congenital Hypothyroidism Study Group.

Abstract

Context: Screening programs resulting in the early treatment of patients with congenital hypothyroidism (CH) have successfully improved neurodevelopmental outcome, but little is known about long-term health. Objectives: The aim of the study was to assess health status, and socioeconomic attainment, for a population-based registry of young adult patients. Design, Setting, and Participants: All 1748 eligible patients diagnosed during the first decade after the introduction of neonatal screening in France were invited to participate in this study at a median age of 23.4 yr. Completed questionnaires were obtained from 1202 of the selected patients. The comparison group included 5817 subjects from the last French Decennial Health Survey. Main Outcome Measures: Health indicators including medical conditions, hearing and visual status, sociodemographic characteristics, and quality of life were measured. Results: Patients with CH were significantly more likely than their peers to report associated chronic diseases (5.7 vs. 2.9%), hearing impairment (9.5 vs. 2.5%), visual problems (55.4 vs. 47.9%), and being overweight with a body mass index of at least 25 kg/m(2) (22.8 vs. 15.7%) ($P < 0.0001$). Furthermore, fewer patients attained the highest socioeconomic category (14.6 vs. 23.1%) and were in full-time employment (39.9 vs. 44.8%) ($P < 0.0001$). They were more likely to still be living with their parents and had a lower health-related quality of life than their healthy peers,

particularly for mental dimensions, with a mean difference for the mental summary component of 0.35 sd score ($P < 0.0001$). CH severity at diagnosis, treatment adequacy, and the presence of other chronic health conditions were the main determinants of educational achievement and health-related quality of life scores. Conclusion: These findings highlight the need for careful monitoring of neurosensory functioning, weight, and long-term treatment adequacy throughout childhood and adulthood

**39.** Clin Biochem. 2011 Mar 4. [Epub ahead of print]

**The preparation and storage of dried-blood spot quality control materials for lysosomal storage disease screening tests.**

Adam BW, Orsini JJ Jr, Martin M, Hall EM, Zobel SD, Caggana M, Hannon WH.

Abstract
OBJECTIVE: We aimed to prepare dried-blood spot (DBS) quality control (QC) materials for lysosomal storage disease (LSD) screening tests and to determine optimum blood and DBS storage conditions.
METHODS: We compared enzyme activities of five LSD markers in adult blood, umbilical-cord blood, and leukocyte-reduced blood. We measured activities in liquid blood and DBSs after predetermined intervals at controlled temperatures and humidities.
RESULTS: Lysosomal-enzyme activity levels in umbilical-cord blood mimicked those in newborn screening samples. Lysosomal-enzyme activities in leukocyte-reduced blood were lower than in LSD-positive patient samples. Enzyme activities were stable in refrigerated liquid blood for 32days and in frozen DBSs stored at low humidity for a year. Activity losses from DBSs after 34days at 37±1°C were 35%-66% in low humidity and 61%-100% in high humidity.
CONCLUSIONS: Umbilical-cord blood is the preferred matrix for LSD-normal DBS QC materials. Leukocyte-reduced blood is lysosomal enzyme-deficient. Failure to control humidity during DBS storage results in loss of lysosomal-enzyme activities

**40.** J Deaf Stud Deaf Educ. 2011 Mar 2. [Epub ahead of print]

**Congenitally Deaf Children's Care Trajectories in the Context of Universal Neonatal Hearing Screening: A Qualitative Study of the Parental Experiences.**

Hardonk S, Desnerck G, Loots G, Van Hove G, Van Kerschaver E, Sigurjónsdóttir HB, Vanroelen C, Louckx F.

Abstract

The objective of this study is to examine the early care trajectories of congenitally deaf children from a parental perspective, starting with universal neonatal hearing screenings. The analysis using a three-dimensional care trajectory concept is aimed at developing a basic typology of postscreening care trajectories. Children with severe/profound hearing loss, registered in the Flanders' (Belgium) universal neonatal hearing screening program, born between 1999 and 2001. Thematic content analysis of qualitative data collected retrospectively from participant's parents. Two basic types of care trajectories emerged; based on differences in care-use in the phase of further diagnosis and related parental experiences. Subtypes resulted from events related to cochlear implantation. Five trajectory phases were identified: screening, further diagnosis, care and technology, cochlear implantation, and reduction of care and were characterized by specific parental experiences such as confusion, disbelief, disappointment, and uncertainty. Those experiences relate to care professionals' acts and communication and the child's functional evolution. Early care interventions could benefit from coordinated transition between phases, parent support throughout the care trajectory, and a broad approach to deafness in professionals' communication.

**41.** J Inherit Metab Dis. 2011 Mar 2. [Epub ahead of print]

**Erratum to: Expanded newborn screening in Greece: 30 months of experience.**

Loukas YL, Soumelas GS, Dotsikas Y, Georgiou V, Molou E, Thodi G, Boutsini M, Biti S, Papadopoulos K.

**42.** Arch Otolaryngol Head Neck Surg. 2011 Mar;137(3):230-4.

**Limitations of universal newborn hearing screening in early identification of pediatric cochlear implant candidates.**

Young NM, Reilly BK, Burke L.

Abstract

OBJECTIVES: To determine whether implementation of universal newborn hearing screening (UNHS) in the state of Illinois has affected the ages at diagnosis of hearing loss and implantation in children receiving cochlear implants and to determine how often children undergoing implantation had UNHS results with no indication of hearing loss (pass).

DESIGN: Retrospective case review of 417 randomly selected pediatric implant recipients born before and after UNHS was mandated by law in Illinois. Data analyzed included hearing screening status, ages at initial diagnosis of sensorineural hearing loss (SNHL) and severe to profound SNHL, and age at implantation.

SETTING: Tertiary care medical center.

PATIENTS: Children receiving implants from 1991 through 2008.

MAIN OUTCOME MEASURES: Ages at diagnosis of SNHL and implantation.

RESULTS: Children born after legally mandated UNHS had significantly younger ages at diagnosis and implantation. However, a younger age at diagnosis of SNHL was not achieved in children who had passed UNHS or who were not screened. Approximately 30% of pediatric implant recipients passed UNHS, regardless of the cause of hearing loss or the presence or absence of known risk factors.

CONCLUSIONS: Almost one-third of our pediatric implant recipients pass UNHS and are older at the time of initial diagnosis and implantation than their peers who fail UNHS. Delayed onset of SNHL limits our ability to achieve early diagnosis and implantation of a significant number of deaf children. This problem will not be solved by the current design of universal hearing screening programs.

**43.** Clin Infect Dis. 2011 Mar;52(5):582-4.

**Dried blood spots and universal newborn screening for congenital cytomegalovirus infection.**

Pass RF.

Comment on:

- Clin Infect Dis. 2011 Mar;52(5):575-81.

**44.** Clin Infect Dis. 2011 Mar;52(5):575-81.

**Prospective identification of congenital cytomegalovirus infection in newborns using real-time polymerase chain reaction assays in dried blood spots.**

Leruez-Ville M, Vauloup-Fellous C, Couderc S, Parat S, Castel C, Avettand-Fenoel V, Guilleminot T, Grangeot-Keros L, Ville Y, Grabar S, Magny JF.

Comment in:

- Clin Infect Dis. 2011 Mar;52(5):582-4.

Abstract

BACKGROUND: Congenital cytomegalovirus (CMV) infection is a public health issue, and implementation of neonatal screening has been debated. Detection of CMV DNA by polymerase chain reaction (PCR) of dried blood spots (DBS) routinely collected for metabolic screening from all newborns has been proposed for congenital CMV infection screening. The goal of this study was to prospectively assess the performance of 2 CMV PCR assays of DBS for CMV neonatal screening in a selected population of neonates.

METHODS: We studied prospective congenital CMV screening in a population of neonates either born with symptoms compatible with congenital CMV or born to mothers with a history of primary infection during pregnancy. For each neonate, 2 CMV PCR assays of DBS were blindly performed in parallel with a gold standard technique (ie, CMV PCR of a urine sample).

RESULTS: Two hundred seventy-one neonates were studied, and CMV infection, defined by a positive urine sample in the first week of life, was confirmed in 64 (23.6%). Nineteen infected (29.7%) neonates were symptomatic, and 45 (70.3%) were asymptomatic. The ranges of

sensitivity, specificity, positive predictive value, and negative predictive value for the 2 CMV PCR assays of DBS were 95.0%-100%; 98.1%-99.0%; 94.1%-96.9%, and 98.5%-100%, respectively.
CONCLUSIONS: The sensitivity and specificity of both CMV PCR assays of DBS to identify congenital CMV were very high in this population of neonates with a high risk of sequelae. These new data should be considered in the ongoing debate on the appropriateness of the use of DBS as a sample to screen for congenital CMV infection.

**45.** Genet Med. 2011 Mar;13(3):230-54.

**Clinical validation of cutoff target ranges in newborn screening of metabolic disorders by tandem mass spectrometry: a worldwide collaborative project.**

Comment in:

- Genet Med. 2011 Mar;13(3):205.

Abstract
PURPOSE: To achieve clinical validation of cutoff values for newborn screening by tandem mass spectrometry through a worldwide collaborative effort.
METHODS: Cumulative percentiles of amino acids and acylcarnitines in dried blood spots of approximately 25–30 million normal newborns and 10,742 deidentified true positive cases are compared to assign clinical significance, which is achieved when the median of a disorder range is, and usually markedly outside, either the 99th or the 1st percentile of the normal population. The cutoff target ranges of analytes and ratios are then defined as the interval between selected percentiles of the two populations. When overlaps occur, adjustments are made to maximize sensitivity and specificity taking all available factors into consideration.
RESULTS: As of December 1, 2010, 130 sites in 45 countries have uploaded a total of 25,114 percentile data points, 565,232 analyte results of true positive cases with 64 conditions, and 5,341 cutoff values. The average rate of submission of true positive cases between December 1, 2008, and December 1, 2010, was 5.1 cases/day. This cumulative evidence generated 91 high

and 23 low cutoff target ranges. The overall proportion of cutoff values within the respective target range was 42% (2,269/5,341).
CONCLUSION: An unprecedented level of cooperation and collaboration has allowed the objective definition of cutoff target ranges for 114 markers to be applied to newborn screening of rare metabolic disorders.

**46.** Genet Med. 2011 Mar;13(3):205.

**Quality improvement of newborn screening in real time.**

Howell RR.

Miller School of Medicine, University of Miami, Miami, Florida, USA. rhowell@miami.edu

Comment on:

- Genet Med. 2011 Mar;13(3):230-54.

**47.** J Midwifery Womens Health. 2011 Mar;56(2):147-53.

**Midwives' knowledge, attitudes, and practices related to newborn hearing screening.**

Goedert MH, Moeller MP, White KR.

Abstract
Introduction: Hearing loss is the most common congenital condition screened for at birth in the United States, and more than 95% of newborns are currently screened for hearing. Newborn hearing screening is most effective when infants receive timely and effective interventions. Unfortunately, follow-up rates for newborns not passing their initial hearing screenings are as low as 50% in some states. Midwives are well-positioned to encourage families to follow-up with their neonatal providers when newborns are referred for further testing. Newborn hearing screening is a relatively new practice in the United States and, to date, there has been no research

regarding the informational needs and practices of certified nurse-midwives or certified midwives related to hearing screening. This study examined the knowledge, attitudes, and follow-up practices of midwives related to newborn hearing screening and intervention. Methods: A survey instrument was developed and sent to 5255 American College of Nurse-Midwives members in 50 states and 2 territories. Results: Five hundred and eighteen surveys were returned, yielding a response rate of 9.9%. Only 68% of respondents said it was very important to screen all newborns for hearing loss. Respondents reported significant gaps in their knowledge about screening procedures, steps for referral, and the availability of resources when newborns did not pass the test. Midwives also reported the need for information about hearing loss conditions and genetics, screening guidelines, protocols for follow-up, referral networks, and therapies available. Discussion: Current practices in newborn hearing screening and intervention programs can be enhanced by strengthening the basic midwifery knowledge of and rationale for follow-up when newborns fail their hearing screenings. Midwives can play an integral role in optimizing hearing, speech, and family interaction by assuring that each newborn has access to the best hearing screening and referrals.

**48.** Mil Med. 2011 Mar;176(3):343-6.

**The use of newborn screening pulse oximetry to detect cyanotic congenital heart disease: a survey of current practice at Army, Navy, and Air Force hospitals.**

Smith AE, Vedder TG, Hunter PK, Carr MR, Studer MA.

Abstract

OBJECTIVE: To determine the prevalence of newborn screening pulse oximetry (+POx) among military hospitals, including barriers to instituting protocols.

METHODS: An internet-based questionnaire was forwarded to the senior pediatricians at military hospitals worldwide supporting newborn deliveries.

RESULTS: Forty seven of 53 hospitals (88%) supporting deliveries responded to the survey. Thirty percent of hospitals utilize a +POx protocol. Eight centers cited no problems with implementation. All hospitals screened at > or = 24 hours of life. The site of recording, positive

values, and follow-up for positive screens varied. Cardiology consult and echocardiogram were not mandated. Most hospitals (34/47) are unable to obtain a pediatric cardiology consult without transfer. Few hospitals (9/47) utilize a telemedicine system. Seventy-five percent (24/32) of hospitals not utilizing a protocol are interested in instituting one.
CONCLUSION: Though slightly less than one-third of military hospitals use a +POx, there is a greater interest in its use. More reliable consultative services and a robust telemedicine system may aid its implementation

**49.** Mol Genet Metab. 2011 Mar 1. [Epub ahead of print]

**Newborn screening for Tyr-I: Two years' experience of the New York State program.**

Morrissey MA, Sunny S, Fahim A, Lubowski C, Caggana M.

Abstract
In 2years, the New York newborn screening program has analyzed approximately 500,000 samples for succinylacetone (SUAC), the biomarker for Tyrosinemia, type I. There have been five screen-positive results. Two of these results were considered borderline, and a repeat specimen was requested. In three cases, an immediate referral was made to a specialty care center. Two of those three cases were confirmed for Tyr-I.

**50.** Mol Genet Metab. 2011 Mar;102(3):339-42. Epub 2010 Dec 13.

**Elevated concentrations of sedoheptulose in bloodspots of patients with cystinosis caused by the 57-kb deletion: implications for diagnostics and neonatal screening.**

Wamelink MM, Struys EA, Jansen EE, Blom HJ, Vilboux T, Gahl WA, Kömhoff M, Jakobs C, Levtchenko EN.

Abstract
Cystinosis is an autosomal recessive lysosomal storage disease caused by mutations in CTNS. The most prevalent CTNS mutation is a homozygous 57-kb deletion that also includes an

adjacent gene named SHPK (CARKL), encoding sedoheptulokinase. Patients with this deletion have elevated urinary concentrations of sedoheptulose. Using derivatisation with pentafluorobenzyl hydroxylamine and liquid chromatography-tandem mass spectrometry (LC-MS/MS), we developed a new sensitive method for the quantification of sedoheptulose in dried blood spots. This method can be utilized as a quick screening test to detect cystinosis patients homozygous for the 57-kb deletion in CTNS; which is the most common mutation of cystinosis. Sedoheptulose concentrations in the deleted patients were 6 to 23 times above the upper limit for controls. The assessment of sedoheptulose in a bloodspot from a known cystinosis patient homozygous for the 57-kb deletion retrieved from the Dutch neonatal screening program showed that sedoheptulose was already elevated in the neonatal period. There was no overlap in sedoheptulose levels between cystinosis patients homozygous for the 57-kb deletion and cystinosis patients not homozygous for this deletion. Our presented method can be used prior to mutation analysis to detect cystinosis patients homozygous for the 57-kb deletion. We feel that the presented method enables fast (pre)-symptomatic detection of cystinosis patients homozygous for the 57-kb deletion, allowing early treatment.

**51.** Obstet Gynecol. 2011 Mar;117(3):762-5.

**Committee Opinion No. 481: Newborn screening.**

American College of Obstetricians and Gynecologists Committee on Genetics.

Abstract

Newborn screening programs are mandatory, state-based public health programs. They provide newborns in the United States with presymptomatic testing and necessary follow-up care for a variety of medical conditions for which early intervention will improve neonatal and long-term health outcomes for the individual. Although current state requirements vary, the results of surveys and focus groups of expectant parents demonstrate that women and their families would like to receive information about newborn screening during their prenatal care. The Committee on Genetics recommends that obstetric care providers make resources regarding newborn

screening available to patients through informational brochures, electronic sources, or through discussion during prenatal visits.

**52.** Pediatr Pulmonol. 2011 Mar 1. doi: 10.1002/ppul.21434. [Epub ahead of print]

**Bronchoscopy in Cystic Fibrosis Infants Diagnosed by Newborn Screening**.

Stafler P, Davies JC, Balfour-Lynn IM, Rosenthal M, Bush A.

Abstract
BACKGROUND: There is evidence of early functional and structural changes in babies with cystic fibrosis (CF) diagnosed on newborn screening (NBS). The aim of the present study was to determine the yield of bronchoalveolar lavage (BAL) microbiology and cytology, and 24□hr pH monitoring in a group of CF infants diagnosed on NBS.
METHODS: Infants referred to a tertiary pediatric respiratory center between July 2007 and November 2009 underwent surveillance fiber-optic bronchoscopy (FOB), BAL, and insertion of a 24□hr dual pH probe under a single general anesthetic.
RESULTS: We studied 33 infants, median age of 100 days (47-215 days) at the time of FOB. In 9 of 33 (27%) bacterial organisms were identified. Seven of the nine patients (78%) were asymptomatic and only one had had a positive cough swab prior to FOB. Neutrophilia was identified in 18/27 (67%) cases with a median of 11% (6-73%). 13/31 (42%) had an abnormal pH study with a pH index >12%.
CONCLUSIONS: The high yield of microbiology, cytology, and pH probe investigations in NBS infants justifies invasive surveillance. Longitudinal studies to determine if early aggressive treatment results in improved outcome are awaited.

**53.** N Engl J Med. 2011 Feb 24;364(8):770-1.

**Newborn screening for α-thalassemia--keeping up with globalization.**

Benz EJ Jr.

Comment on:

- N Engl J Med. 2011 Feb 24;364(8):710-8.

**54.** Arch Dis Child Fetal Neonatal Ed. 2011 Feb 19. [Epub ahead of print]

**Neonatal pulse oximetry screening: a national survey.**

Kang SL, Tobin S, Kelsall W.

**55.** J Inherit Metab Dis. 2011 Feb 19. [Epub ahead of print]

**Newborn screening for congenital hypothyroidism in very-low-birth-weight babies: the need for a second test.**

Bijarnia S, Wilcken B, Wiley VC.

Abstract

BACKGROUND: Very-low-birth-weight babies (VLBW) with hypothyroidism may show a delayed postnatal rise in thyroid stimulating hormone (TSH), mainly due to immaturity of the hypothalamic-pituitary-thyroid axis. Transient hypothyroidism is prevalent in VLBW babies and some affected babies are considered to need treatment. There is disagreement about whether a second screening test is needed in VLBW babies to detect all cases that need treatment.

METHODS: We included in the study all babies with a birth weight ≤ 1,500 g born in New South Wales and the Australian Capital Territory between January 2006 and December 2008. Newborn screening samples for TSH measurement were taken in the first days of life and again at 1 month. During week 1, a blood-spot TSH level of ≥20 mIU/L was considered positive, and at 1 month a positive level was ≥7 mIU/L, and triggered full investigation.

RESULTS: In the cohort of 301,000 babies, 2,313 VLBW babies survived for testing, and 2,117 repeat screening samples were received. Forty-three babies had transient hypothyroidism, with thyroid function normalising before 2 months of age, usually without treatment. Eighteen babies

required treatment beyond 2 months of age (1:128 of surviving babies), 16 having had normal TSH results on initial testing, and 12 having levels below 6 mIU/L.
CONCLUSION: Significant hypothyroidism, transient or permanent, but persisting beyond 2 months of age is common in VLBW babies. There is a delayed rise in TSH in some, and secondary screening at 1 month of age detects babies deemed by local paediatric endocrinologists as needing treatment.

**56.** Am J Public Health. 2011 Feb 17. [Epub ahead of print]

**Concerns of Newborn Blood Screening Advisory Committee Members Regarding Storage and Use of Residual Newborn Screening Blood Spots.**

Rothwell EW, Anderson RA, Burbank MJ, Goldenberg AJ, Lewis MH, Stark LA, Wong B, Botkin JR.

Abstract
Objectives. We assessed attitudes and opinions of members of newborn blood screening (NBS) advisory committees regarding the storage and secondary research use of residual specimens from NBS. Methods. We conducted focus groups in 2008 and 2009 with NBS advisory committees (4 focus groups; n=39 participants) in the Mountain States region (i.e., Arizona, Colorado, Utah, New Mexico, Nevada, Texas, Montana, and Wyoming). Results. Participants identified several challenges to implementing policies for storage of and research on residual newborn blood specimens. Themes that emerged from the data were public health relevancy; improvement of parental knowledge; impact of enhanced parental involvement; concerns over ownership, privacy, and confidentiality; identification of secondary research uses; and role of advisory committees. Conclusions. Participants indicated that secondary uses of residual specimens entailed opportunities for improvements in NBS programs but also carried significant risks for their programs. Addressing concerns from stakeholders will be necessary for state-level adoption of national recommendations. (Am J Public Health. Published online ahead of print February 17, 2011: e1-e6. doi:10.2105/ AJPH.2010.200485).

**57.** Acta Paediatr. 2011 Feb 15. [Epub ahead of print]

**Neonatal Pulse oximetry screening: A National Survey.**

Kang S, Tobin S, Kelsall W.

Abstract

Aim: Studies suggest that universal pulse oximetry (PO) screening of all neonates before hospital discharge improves the detection rate of congenital heart disease (CHD). The aim is to survey the use of Pulse Oximetry (PO) screening in UK. Methods: A telephone interview was conducted between late 2009 to mid-2010 of all maternity units using a standardised questionnaire. Results: 209(93%) of 224 responding units did not routinely use PO. Among the 15 that performed PO, 5 measured pre and post ductal saturations, 9 measured only post-ductal saturations, and 1 measured only pre-ductal saturations. There were differences in the values used to trigger further investigation, ranging from <94% to <96% and/or difference of > 2-3% between pre and post-ductal saturations. When saturations were abnormal, 13 units performed echocardiography locally. In addition to an echocardiogram, 2 units performed chest x-ray (CXR); 2 units performed electrocardiogram (ECG) and 2 units performed both CXR and ECG. Conclusion: Only a minority of hospitals across the UK use PO to supplement the postnatal examination with inconsistent practice. National guidelines should be developed if PO screening is implemented with an agreed management plan if abnormal results are obtained.

**58.** Am J Med Genet C Semin Med Genet. 2011 Feb 15;157(1):1-2. Epub 2011 Feb 10.

**Newborn screening and inborn errors of metabolism.**

Pasquali M, Longo N.

**59.** Am J Med Genet C Semin Med Genet. 2011 Feb 15;157(1):63-71. Epub 2011 Feb 10.

**Newborn screening for lysosomal storage disorders.**

Nakamura K, Hattori K, Endo F.

Abstract

Lysosomes are intracellular organelles containing acid hydrolases that degrade biological macromolecules. Lysosomal storage disorders (LSDs) are caused by absent activity of one or more of these enzymes due to mutations of genes encoding lysosomal hydrolases or enzymes that process, target, and transport these enzymes. The specific signs and symptoms of each LSD derive from the type of material accumulated within the lysosome, the site (organ) of accumulation and the response of the body (sometimes in the form of an inflammatory or immune response) to the accumulated material. Interest for inclusion of these disorders in newborn screening programs derives from the availability of effective therapy in the form of enzyme replacement or substrate reduction therapy and bone marrow transplant that may improve long-term outcome especially if started prior to irreversible organ damage. Based on the availability of therapy and suitable screening methods, Gaucher disease, Fabry disease, Pompe disease, mucopolysaccharidosis I and II, Niemann-Pick disease, and Krabbe disease are candidates for newborn screening. Pilot newborn screening projects have been performed for some of these conditions that indicate the feasibility of this approach. This review will provide insight into these screening strategies and discuss their advantages and limitations. 

**60.** Indian Pediatr. 2011 Feb 7;48(2):154-5.

**Neonatal screening for hemoglobinopathies.**

Bose M, Viswanathan R, Dasgupta S, Singh AK.

Abstract

A pilot study was undertaken to develop a feasible neonatal screening strategy for hemoglobinopathies. Isoelectric focusing using dried blood spots samples as a primary screening technique was standardized for the first time in India. The screened positives were confirmed by

high performance liquid chromatography followed by parental screening, confirmation, and education.

**61.** J Trop Pediatr. 2011 Feb 4. [Epub ahead of print]

**Long-term Consequences of the Early Treatment of Children with Congenital Hypothyroidism Detected by Neonatal Screening in Nanjing, China: a 12-year Follow-up Study.**

Sun Q, Chen YL, Yu ZB, Han SP, Dong XY, Qiu YF, Sha L, Guo XR.

Abstract

This study was performed to investigate the prevalence of congenital hypothyroidism (CH) in neonates in Nanjing, China and the long-term consequences of early treatment. A total of 442□454 neonates were screened for CH and 183 neonates were confirmed, with a prevalence of 1 in 2418. Of these, 163 neonates completed the follow-up process and 163 healthy children were recruited as the control group. The height, weight and body mass index (BMI) of the children with CH from 0.5 to 6 years were not significantly different from the control group (p□>□0.05). The children with CH had a significantly increased risk for being overweight or obese between 0.5 and 6 years (p□<□0.05). The children with CH showed a significantly lower developmental quotient (DQ) than the control group in all four areas of the Gesell test (p□<□0.05). The results suggest that children with CH that has been identified by newborn screening and early treatment have normal growth and neuromotor development.

**62.** J Cyst Fibros. 2011 Feb 3. [Epub ahead of print]

**Distribution of CFTR mutations in Eastern Hungarians: Relevance to genetic testing and to the introduction of newborn screening for cystic fibrosis.**

Ivady G, Madar L, Nagy B, Gonczi F, Ajzner E, Dzsudzsak E, Dvořáková L, Gombos E, Kappelmayer J, Macek M Jr, Balogh I.

Abstract

BACKGROUND: The aim of this study was characterization of an updated distribution of CFTR mutations in a representative cohort of 40 CF patients with the classical form of the disease drawn from Eastern Hungary. Due to the homogeneity of the Hungarian population our data are generally applicable to other regions of the country, including the sizeable diaspora.
METHODS: We utilized the recommended "cascade" CFTR mutation screening approach, initially using a commercial assay, followed by examination of the common "Slavic" deletion CFTRdele2,3(21kb). Subsequently, the entire CFTR coding region of the CFTR gene was sequenced in patients with yet unidentified mutations.
RESULTS: The Elucigene CF29(Tm) v2 assay detected 81.25% of all CF causing mutations. An addition of the CFTRdele2,3(21kb) increased the mutation detection rate to 86.25%. DNA sequencing enabled us to identify mutations on 79/80 CF alleles. Mutations [CFTRdele2,3(21kb), p.Gln685ThrfsX4 (2184insA) were found at an unusually high frequency, each comprising 5.00% of all CF alleles.
CONCLUSION: We have identified common CF causing mutations in the Hungarian population with the most common mutations (p.Phe508del, p.Asn1303Lys, CFTRdele2,3(21kb), 2184insA, p.Gly542X, and p.Leu101X), comprising over 93.75% of all CF alleles. Obtained data are applicable to the improvement of DNA diagnostics in Hungary and beyond, and are the necessary prerequisite for the introduction of a nationwide "two tier" CF newborn screening program.

**63.** Arch Dis Child. 2011 Feb;96(2):121-2. Epub 2010 Jul 6.

**Treating patients not numbers: the benefit and burden of lowering TSH newborn screening cut-offs.**

Krude H, Blankenstein O.

Comment in:

- Arch Dis Child. 2011 Feb;96(2):205.

Comment on:

- Arch Dis Child. 2010 Mar;95(3):169-73.

**64.** Eur J Endocrinol. 2011 Feb;164(2):269-76. Epub 2010 Nov 23.

**Psychological and behavioural aspects in children and adolescents with congenital hypothyroidism diagnosed by neonatal screening: comparison between parents' and children's perceptions.**

Bisacchi N, Bal MO, Nardi L, Bettocchi I, D'Addabbo G, Conti V, Monti S, D'Alberton F, Cicognani A, Cassio A.

Abstract

OBJECTIVE: To compare the psychological adjustment and behaviour of congenital hypothyroidism (CH) children and their parents with a control group.

STUDY DESIGN: A cross-sectional study was carried out with 84 CH subjects diagnosed by neonatal screening (range 2.7-18.6 years), subdivided into four age groups: group 1 (2-5 years); group 2 (6-10 years); group 3 (11-13 years); and group 4 (14-18 years) and was compared with an age-matched control group. Patients were assessed using two questionnaires: Child Behaviour Checklist for parents and Youth Self-Report for children over 11 years of age.

RESULTS: In groups 1, 3 and 4, total score (TS), internalising score (IS=problems within the self) and externalising score (ES=conflicts with other people) as reported by parents were not significantly different in CH patients and in controls. In group 2, parents of CH children showed values of TS ($P<0.05$), IS ($P<0.05$), ES ($P<0.05$) and scores on other scales significantly higher than controls. In self-reports of groups 3 and 4, the behavioural scales were not significantly different in CH patients and in controls.

CONCLUSIONS: Paediatricians should be informed about the increased risk of the development of behavioural problems at primary school age in CH patients. At this age special attention should be paid to parental worries and anxiety. However, it can be reassuring for the patients and parents to know that the problems may be related to CH, and that they may spontaneously disappear.

**65.** Int J Pediatr Otorhinolaryngol. 2011 Feb;75(2):159-62. Epub 2010 Nov 12.

**An initial overestimation of sensorineural hearing loss in NICU infants after failure on neonatal hearing screening.**

Coenraad S, Goedegebure A, Hoeve LJ.

Abstract

OBJECTIVE: Infants admitted to neonatal intensive care units have a higher incidence of significant congenital hearing loss. We classified audiologic diagnoses and follow-up in infants who had been admitted to our neonatal intensive care unit.

METHODS: We included all infants admitted to the neonatal intensive care unit at Sophia Children's Hospital between 2004 and 2009 who had been referred for auditory brainstem response measurement after failing neonatal hearing screening with automated auditory brainstem response. We retrospectively analyzed the results of auditory brainstem response measurement.

RESULTS: Between 2004 and 2009 3316 infants admitted to our neonatal intensive care unit had neonatal hearing screening. 103 infants failed neonatal hearing screening: 46 girls and 57 boys. After first auditory brainstem response measurement we found 18% had normal hearing or a minimal hearing loss. The remainder had a type of hearing loss, distributed as follows: 15% conductive, 32% symmetric sensorineural, 14% asymmetric sensorineural, and 21% absent auditory brainstem responses. Repeated auditory brainstem response measurement showed a shift in hearing outcome. The main difference was an improvement from symmetric sensorineural hearing loss to normal hearing. However, in a small percentage of children, the hearing deteriorated.

CONCLUSIONS: As many as 58% of infants in this high-risk population who failed the neonatal hearing screening were diagnosed with sensorineural hearing loss or absent auditory brainstem responses. An initial overestimation of sensorineural hearing loss of about 10% was seen at first auditory brainstem response measurement. This may be partially explained by a conductive component that has resolved. Finally, in a small percentage of children the hearing deteriorated.

**66.** J Inherit Metab Dis. 2011 Feb;34(1):185-95. Epub 2010 Nov 20.

**Urgent metabolic service improves survival in long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency detected by symptomatic identification and pilot newborn screening.**

Sykut-Cegielska J, Gradowska W, Piekutowska-Abramczuk D, Andresen BS, Olsen RK, Ołtarzewski M, Pronicki M, Pajdowska M, Bogdańska A, Jabłońska E, Radomyska B, Kuśmierska K, Krajewska-Walasek M, Gregersen N, Pronicka E.

Abstract

Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD) is a fatty acid oxidation disorder with especially high mortality and uncertain long-term outcome. The aim of the study was to analyze the influence of diagnostic approach on survival in 59 affected children. Referral to a metabolic center was replaced over time by urine/blood testing in centralized metabolic laboratory (selective screening) and by pilot tandem mass spectrometry newborn screening (NBS). Molecular analysis revealed the prevalent mutation in the HADHA gene in all 58 examined cases. Twenty patients died. The number of detections and number of deaths were respectively 9 and 4 (44%) in the patients recognized by differential diagnosis, 28 and 9 (32%) - by selective screening, and 11 and 1 (9%) - by NBS. In 80% of cases the death occurred before or within 3 weeks from the identification. Urgent and active metabolic service remarkably influenced the surviving. The current age of 39 survivors is 0.5 to 23 yrs (mean 7.2 yrs). The disease frequency estimated on the patients number was 1: 115 450, whereas in the pilot NBS - 1: 109 750 (658 492 neonates tested). Interestingly, the phenylalanine level in asymptomatic neonates frequently exceeded the cut-off values. Conclusions: 1) Urgent metabolic intervention decreases mortality of LCHAD-deficient patients, but the prognosis is still uncertain. 2) Emergent metabolic reporting and service are crucial also for the survival of neonates detected by NBS. 3) The nationwide selective screening appeared efficient in LCHADD detection in the country. 4) Transient mild hyperphenylalaninaemia may occur in LCHAD-deficient newborns.

**67.** J Perinatol. 2011 Feb;31(2):112-7. Epub 2010 Jun 10.

**Implementation and analysis of a pilot in-hospital newborn screening program for glucose-6-phosphate dehydrogenase deficiency in the United States.**

Nock ML, Johnson EM, Krugman RR, Di Fiore JM, Fitzgerald S, Sandhaus LM, Walsh MC.

Abstract

OBJECTIVE: The purpose of this study was to analyze a targeted screening program for glucose-6-phosphate dehydrogenase (G6PD) deficiency (G6PDdef) and clinical outcomes of G6PD-deficient vs G6PD normal newborns.

STUDY DESIGN: Retrospective chart review for 1578 male newborns was performed. The study group was those screened for G6PDdef. Comparisons between G6PD-deficient and normal infants were made with $\chi$ (2)-test and unpaired t-test.

RESULT: A total of 1095 male newborns were screened, 11.1% had G6PDdef. 97.8% of screen results were reported by 48 h. Total bilirubin (TB) levels in deficient infants were significantly higher than in normal infants throughout birth hospitalization and they were more likely to receive phototherapy. Nineteen screened newborns were rehospitalized for hyperbilirubinemia, 47% had G6PDdef.

CONCLUSION: In-hospital newborn screening for G6PDdef with rapid turnaround time is possible. G6PDdef is a risk factor for hyperbilirubinemia in American newborns. US centers with large at-risk populations can identify newborns at risk for severe hyperbilirubinemia with similar screening.

**68.** Nurs Womens Health. 2011 Feb-Mar;15(1):86-7.

**Newborn screening.**

Association of Women's Health, Obstetric & Neonatal Nursing.

**69.** Pediatrics. 2011 Feb;127(2):276-83. Epub 2011 Jan 10.

**Parental understanding of newborn screening for cystic fibrosis after a negative sweat-test.**

Lang CW, McColley SA, Lester LA, Ross LF.

Abstract

BACKGROUND: Newborn screening for cystic fibrosis (CF) in Illinois uses an immunoreactive trypsinogen/DNA methodology; most false-positive results identify unaffected carriers.

METHODS: Parents whose child received a negative result from the sweat test after a positive newborn screening for CF were surveyed ≥ 6 weeks later by telephone. All parents received genetic counseling while waiting for the sweat-test results.

RESULTS: A total of 90 parents participated. Overall knowledge of CF was high (78%), but the ability to understand the CF screening results was mixed. Although 94% of the parents understood that their child did not have CF, only 79% (62 of 78) of participants whose child had a mutation knew their child was definitely a carrier, and only 1 of 12 parents whose child had no mutation understood that the child may be a carrier. Respondents stated that most relatives were not interested in genetic testing. Both parents had been tested in only 13 couples. Fewer than half (36 of 77 [47%]) of the untested couples expressed interest in genetic testing. Although most participants were satisfied with the process, parents expressed frustration because of the lack of prospective newborn screening discussions by prenatal and pediatric providers and lack of knowledge and sensitivity by those who initially notified them of the abnormal newborn screening results. Speaking to a genetic counselor when scheduling the sweat test decreased anxiety for many parents (53 of 73 [73%] were "very worried" at notification versus 18 of 73 [25%] after scheduling; $P < .001$).

CONCLUSIONS: Parental knowledge about CF is high, but confusion about the child's carrier status and the concept of residual risk persist despite genetic counseling. Relatives express low interest in carrier testing.

**70.** Mol Genet Metab. 2011 Jan 27. [Epub ahead of print]

**Maternal medium-chain acyl-CoA dehydrogenase deficiency identified by newborn screening.**

Leydiker KB, Neidich JA, Lorey F, Barr EM, Puckett RL, Lobo RM, Abdenur JE.

Abstract

Prior to the advent of expanded newborn screening, sudden and unexplained death was often the first and only symptom of medium-chain acyl-CoA dehydrogenase deficiency (MCADD). With the use of tandem mass spectrometry, infants can now be identified and treated before a life threatening metabolic decompensation occurs. Newborn screening has also been shown to detect previously undiagnosed maternal inborn errors of metabolism. We have now diagnosed two women with MCADD following the identification of low free carnitine in their newborns. While one of the women reported prior symptoms of fasting intolerance, neither had a history of metabolic decompensation or other symptoms consistent with a fatty acid oxidation disorder. These cases illustrate the importance of including urine organic acid analysis and an acylcarnitine profile as part of the confirmatory testing algorithm for mothers when low free carnitine is identified in their infants.

**71.** J Med Ethics. 2011 Jan 25. [Epub ahead of print]

**Parents' experiences of newborn screening for genetic susceptibility to type 1 diabetes.**

Kerruish NJ.

Abstract

Advances in genomic medicine have lead to debate about the potential inclusion of genetic tests for susceptibility to common complex disorders in newborn screening programmes. Empirical evidence concerning psychosocial reactions to genetic testing is a crucial component of both ethical debate and policy development, but while there has been much speculation concerning the possible psychosocial impact of screening newborns for genetic susceptibilities, there remains a paucity of data. The aim of the study reported here is to provide some of this missing empirical evidence, using type 1 diabetes as an example of a common disorder with multiple significant genetic contributors to its aetiology. Semi-structured interviews were conducted with 11 parents of babies who had received increased risk results in a study that involved newborn screening for genetic susceptibility to type 1 diabetes. Interpretative phenomenological analysis was used to evaluate the data. The interview data suggest that the probabilistic nature of results

of genetic susceptibility tests impacts upon all aspects of parents' psychosocial reactions, resulting in a complex and dynamic process quite different to that described in relation to current newborn screening programmes. While parents generally reported fairly minor levels of concern in response to news of their child's increased genetic risk, these worries frequently recurred, and perception of risk also varied and fluctuated over time. Both individual and contextual factors appeared to interact with the inherent uncertainty of the test result to contribute to the dynamic nature of parental reactions, and their behavioural responses. The implications of these findings for future research and for the debate concerning potential expansion of newborn screening are discussed.

**72.** Mol Genet Metab. 2011 Jan 22. [Epub ahead of print]

**Improved assay for differential diagnosis between Pompe disease and acid α-glucosidase pseudodeficiency on dried blood spots.**

Shigeto S, Katafuchi T, Okada Y, Nakamura K, Endo F, Okuyama T, Takeuchi H, Kroos MA, Verheijen FW, Reuser AJ, Okumiya T.

Abstract

The high frequency (3.3-3.9%) of acid α-glucosidase pseudodeficiency, c.[1726G>A; 2065G>A] homozygote (AA homozygote), in Asian populations complicates newborn screening for Pompe disease (glycogen storage disease type II or acid maltase deficiency) on dried blood spots, since AA homozygotes have a considerably low enzyme activity. We observed that hemoglobin in the enzyme reaction solution strongly interferes with the fluorescence of 4-methylumbelliferone released from 4-methylumbelliferyl α-d-glucopyranoside (4MU-αGlc) by acid α-glucosidase. Therefore, we have searched for a method to effectively eliminate hemoglobin in the reaction solution. Hemoglobin precipitation with barium hydroxide and zinc sulfate (Ba/Zn method) carried out after the enzyme reaction considerably enhances the fluorescence intensity while it does not reduce the intensity to any extent as can occur with conventional deproteinization agents like trichloroacetic acid. The Ba/Zn method greatly improved the separation between 18 Japanese patients with Pompe disease and 70 unaffected AA homozygotes in a population of

Japanese newborns in the assay with 4MU-αGlc on dried blood spots. No overlap was observed between both groups. We further examined acid α-glucosidase activity in fibroblasts from 11 Japanese patients and 57 Japanese unaffected individuals including 31 c.[1726G; 2065G] homozygotes, 18 c.[1726G; 2065G]/[1726A; 2065A] heterozygotes and 8 AA homozygotes to confirm that fibroblasts can be used for definitive diagnosis. The patients were reliably distinguished from three control groups. These data provide advanced information for the development of a simple and reliable newborn screening program with dried blood spots for Pompe disease in Asian populations.

**73.** J Pediatr. 2011 Jan 11. [Epub ahead of print]

**Later-Onset Pompe Disease: Early Detection and Early Treatment Initiation Enabled by Newborn Screening.**

Chien YH, Lee NC, Huang HJ, Thurberg BL, Tsai FJ, Hwu WL.

Abstract
OBJECTIVE: To determine whether newborn screening facilitates early detection and thereby early treatment initiation for later-onset Pompe disease.
STUDY DESIGN: We have conducted a newborn screening program since 2005. Newborns with deficient skin fibroblast acid α-glucosidase activity and two acid α-glucosidase gene mutations but no cardiomyopathy were defined as having later-onset Pompe disease, and their motor development and serum creatine kinase levels were monitored every 3 to 6 months.
RESULTS: Among 344 056 newborns, 13 (1 in 26 466) were found to have later-onset Pompe disease. During a follow-up period of up to 4 years, four patients were treated because of hypotonia, muscle weakness, delayed developmental milestones/motor skills, or elevated creatine kinase levels starting at the ages of 1.5, 14, 34, and 36 months, respectively. Muscle biopsy specimens obtained from the treated patients revealed increased storage of glycogen and lipids.

CONCLUSION: Newborn screening was found to facilitate the early detection of later-onset Pompe disease. A subsequent symptomatic approach then identifies patients who need early treatment initiation.

**74.** Indian Pediatr. 2011 Jan 7;48(1):25-30. Epub 2010 Aug 1.

**Clinical screening for Congenital heart disease at birth: a prospective study in a community hospital in Kerala.**

Vaidyanathan B, Sathish G, Mohanan ST, Sundaram KR, Warrier KK, Kumar RK.

Comment in:

- Indian Pediatr. 2011 Jan 7;48(1):17-8.

Abstract
OBJECTIVE: To develop a clinical strategy for detection of Congenital heart disease (CHD) in the newborn through a combination of clinical signs and pulse oximetry.
DESIGN: Prospective longitudinal study.
SETTING: Community level hospital in the city of Kochi, Kerala. Participants and interventions: All consecutive newborns between June 2006 and February 2009 were prospectively screened for CHD, 48 hours after birth. The on-site pediatrician performed clinical screening. A study nurse recorded pulse oximetry in a lower extremity; value of <94% was defined as abnormal. Echocardiography was performed on site by a trained research officer. A 6-week clinical follow-up evaluation was done for all.
MAIN OUTCOME MEASURE: Detection of CHD by echocardiography.
RESULTS: Of 5487 babies screened, 425 (7.75%) had CHD. 17 (0.31%) had major CHD, two of whom (one ALCAPA and one large VSD) were missed during the initial evaluation. The rest were minor CHD (408 patients, 7.44%), most of which normalized by 6 weeks. On multivariate analysis, murmur, central cyanosis, abnormal precordial pulsations and abnormal pulse oximetry emerged as significant predictors of CHD. The sensitivity of clinical evaluation and pulse oximetry combined was 19% for all CHDs and 20% for major CHD; specificity was 88%.

CONCLUSIONS: In the community setting of a developing country, clinical evaluation and pulse oximetry after birth had a very low sensitivity for detection of CHD. Though an abnormal screening warrants prompt echocardiography, a 6 week clinical evaluation is recommended to ensure that major CHD is not missed.

**75.** Am J Med Genet A. 2011 Jan;155:fmvii-fmviii.

**Should 22q11 deletion be added to newborn screening panels?**

Levenson D.

**76.** Clin Immunol. 2011 Jan;138(1):3-8. Epub 2010 Oct 28.

**Early vs. delayed diagnosis of severe combined immunodeficiency: a family perspective survey.**

Chan A, Scalchunes C, Boyle M, Puck JM.

Abstract
Infants affected with severe combined immunodeficiency (SCID) are susceptible to severe and recurrent infections and do not survive unless provided with immune reconstituting treatments. In the absence of population-based newborn screening, infants with SCID who do not have an affected older relative are ascertained only after they have developed infections. However, only limited data are available from the perspective of patients and families to indicate what proportion of SCID cases might benefit from earlier detection by pre-symptomatic screening, whether adequate treatment facilities are available, and how screening could improve SCID treatment outcomes. A survey of parents of children with SCID evaluated family history, pre- and post-diagnosis events, outcomes, and impact of SCID on families. Affected infants diagnosed with SCID as neonates had better survival, demonstrating the potential benefit of universal newborn screening.

**77.** Dtsch Arztebl Int. 2011 Jan;108(1-2):11-21; quiz 22. Epub 2011 Jan 10.

**Neonatal screening for metabolic and endocrine disorders.**

Harms E, Olgemöller B.

Abstract

BACKGROUND: Neonatal screening for treatable endocrinopathies and inborn errors of metabolism is an important preventive measure. Advances in the diagnosis and treatment of these diseases have made it necessary to expand the screening program.

METHODS: This article is based on a selective literature review and our clinical experience.

RESULTS: In 2005, neonatal screening in Germany was expanded from 3 to 14 diseases, as mandated by the responsible governmental authority (the Gemeinsamer Bundesausschuss, i.e., Joint Federal Committee). From 2005 to 2008, screening revealed diseases requiring treatment in 1932 out of a total of 2,758,633 newborns (prevalence, 1 in 1428). The expansion of the screening program resulted in a 57% increase in the overall number of cases detected and a 92% increase for metabolic diseases alone.

CONCLUSION: The German neonatal screening program for treatable endocrinopathies and inborn errors of metabolism is a complex and integrated preventive measure that has become markedly more effective as a result of its expansion in 2005.