Adolescent Medicine

SUICIDE ATTEMPTS IN CHILDHOOD AND ADOLESCENCE DURING A PERIOD OF 6 MONTHS

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INTRODUCTION: Suicide attempts in childhood and adolescence are a crucial issue that society should make every possible effort to solve.
OBJECTIVE: The goal was to correlate the problem of suicide attempts by children and adolescents with epidemiologic data concerning the kind of toxic substance used, the gender of the patient, and the timing of the suicide attempts.
METHODS: In a period of 6 months (May through October 2006), 3060 suicide attempts from all over the country were reported to the Poison Information Center at Panagiotis and Aglaia Kyriakou Children's Hospital, 513 (16.76%) of which concerned children. The epidemiologic data, the patient's clinical state, the amount of the toxic substance used, and the outcome were evaluated.
RESULTS: Five hundred thirteen incidents were studied (89.1% girls, 10.9% boys). The children's ages ranged between 10 and 18 years. Two percent of the incidents concerned children aged 10 to 12, 32.8% concerned children aged 13 to 15, and 65.2% concerned children aged 16 to 18. The majority of the drugs consumed were those with no need for a doctor's prescription (paracetamol: 38.6%; nonsteroidal antiinflammatory drugs: 21.2%; salicylates: 19.1%), whereas psychotropic drugs were involved in 18.9% of the intentional intoxications. Of the 513 patients, 8.6% were under treatment with psychotropic medicines. In addition, 6.6% had at least 1 previous suicide attempt. Of the patients, 20.6% had taken a highly toxic dose of substances. No deaths were reported.
CONCLUSIONS: Suicide attempts during childhood and adolescence remain a great problem. Immediate steps should be taken to decrease this number of attempts. Society, families, and the medical community should also make every possible effort to face this serious problem, which has an important social cost.

HEALTH RISK BEHAVIORS OF STUDENTS IN AN ANATOLIAN UNIVERSITY

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INTRODUCTION: Adolescence is a period of rapid personal development in which health risk behaviors that contribute to the leading causes of social problems, morbidity, and mortality among youth and adults are often established.
OBJECTIVE: The purpose of this cross-sectional study was to investigate the health risk behaviors of Anatolian university students.
METHODS: Differences according to gender and socioeconomic status in risk behaviors regarding use of tobacco, alcohol, and illegal substances; sexual activity; and physical activity were analyzed. Students from Kirikkale University (1060) were enrolled. The students' privacy was protected by allowing for anonymous and voluntary participation.
RESULTS: Mean age of the 684 male (64.5%) and 376 female (35.5%) students was 20.3 years (minimum: 17; maximum: 30 years). of all the students, 876 (82.9%) had some kind of information about sexuality; however, this number dropped to 546 students (51.5%) within the context of adequacy. Also, 25.3% of all the students had had some kind of sexual intercourse, and only 53.9% used protection during intercourse. Tobacco usage was 35.1% among those in the group, and 8.7% of the male and 3.6% of the female students were using illegal substances. Thirty percent of all the students reported having weight problems. The majority of students had witnessed violence (eg, 32.7% from parents, 77.2% from their friends, and 76.2% at school).
CONCLUSIONS: Risk-taking behaviors are considerably common among Turkish university students, and family characteristics have significant effects.

INTERNET USE AND ABUSE IN AN ADOLESCENT POPULATION IN ATHENS: ASSOCIATIONS WITH PSYCHOLOGICAL PROFILE AND LIFESTYLE OF USERS

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INTRODUCTION: Use of the Internet has become very popular among youth, but phenomena of Web abuse

with negative physical and psychosocial consequences have emerged.
OBJECTIVE: The researchers' goal was to study Internet use and abuse by Greek adolescents and to identify the psychological profile and lifestyle of users. Intervention attempts will also be designed and discussed.
METHODS: An Athens adolescent population representative sample of 315 (164 boys, 151 girls) high school students (mean age: 15 years) were included in the study. For Internet-addiction diagnosis, an international tool (Young's Internet Addiction Test questionnaire) was used. The Strengths and Difficulties Questionnaire was applied to screen for emotional and behavioral problems. Physical activity and physical fitness were also assessed with appropriate questions. Correlation and χ^2 statistics were performed by using SPSS (SPSS Inc, Chicago, IL).
RESULTS: According to the results, 167 (53.4%) of 315 adolescents were using the Internet for >1 year, 82 (26%) of 315 reported daily use, and 25 (8%) of 315 reported >20 hours' use weekly. Boys were spending significantly more time using the Internet than girls ($P < .05$). According to Young's Questionnaire scoring, no youngster in our sample was addicted. However, in 28 (9.4%) of 315 adolescents, Young's Questionnaire scoring was suggestive of occasional or frequent problems of Internet overuse. The most frequent reason for using the Internet was games ($P < .05$), and 18 (5.8%) of 315 children in our sample were cyberbullying victims. There was a positive correlation of Internet use and hyperactivity according to the Strengths and Difficulties Questionnaire results ($P < .05$). Positive correlations were also noted for Internet use and delinquency ($P < .001$) as well as dysfunctional peer relationships ($P < .001$).
CONCLUSIONS: Use of the Internet is popular among Greek youth, and it can be related to psychosocial problems if overused.

SIESTA AND SLEEP HABITS OF ADOLESCENTS IN GREECE

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INTRODUCTION: The study of adolescents' sleep habits is of increasing scientific interest because of the variability of sleep patterns and the frequency of sleep disorders in those of this age group.
OBJECTIVE: The aim of our study was to investigate the sleep habits of adolescents living in Greece.
METHODS: We analyzed responses given to preconstructed questionnaires on sleep habits and disturbances from 1331 high school students (mean age: 15 years [range: 14–18 years]). The students were attending high schools of rural, semiurban, and urban areas of Thrace, Ipirus, and Crete (all in Greece).
RESULTS: The median nocturnal and total sleep duration was 7.75 hours (range: 2.5–12.3 hours) and 8.5 hours (range: 2.5–14.0 hours), respectively, and the average bedtime was 11:30 PM. Male students, older adolescents, and residents of towns were going to bed later than female students, younger adolescents, and residents of villages ($P = .039$, .0003, and .056, respectively). Siesta on a regular basis was reported by 43% and on an occasional basis by 46% of the students. Siesta median duration was 2 hours (range: 0.5–4.5 hours). Daytime sleepiness, difficulties in morning awakening, difficulties in falling asleep, and night awakenings were reported by 15.6%, 14%, 17.2%, and 8.11%, respectively. Students who practiced siesta reported less daytime sleepiness ($P < .0001$). Significant differences were observed between boys and girls regarding sleep disturbances.
CONCLUSIONS: Adolescents in provincial Greece present quite a different sleep pattern compared with their northern European peers, characterized by a late bedtime and midday siesta. Similar to their peers in other countries, considerable rates of sleep disturbances were reported.

PREVALENCE OF SEXUAL ABUSE AMONG ADOLESCENT MEDICAL AND NURSING STUDENTS IN A COLLEGE IN PUNJAB, INDIA

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OBJECTIVE: We sought to determine the prevalence of sexual abuse among adolescent medical and nursing students who were attending a college in Punjab, India.
METHODS: Five hundred thirty-two subjects (150 male medical students, 220 female medical students, and 162 female nursing students) between 17 and 26 years old filled out a detailed questionnaire, in absolute privacy, to gather demographic and sexual abuse information.
RESULTS: of the participating students, 28.2% were male and 71.8% were female. The overall prevalence rate of any form of sexual abuse was 32.1% (171 subjects). A severe form of sexual abuse (intercourse) was reported by 30 subjects (10 among males and 20 among females). The most common type of abuse reported was

in the form of showing pornographic material among male students (41 subjects [23%]) and touching of breasts (58 subjects [33.9%]) among females. The minimum age of victims at the time of the first incident was >16 years in 83 subjects (48.5%). The abuser was a friend in 32.1% (29 in males and 27 in females) of the cases. The perpetrators of sexual abuse were males for 132 subjects of both genders. In 56% (96 subjects), the time of abuse was between 2 and 10 PM. Forty-one subjects (23%) currently experience abuse memories in the form of unwanted scenes flashing in dreams, difficulty in maintaining relationships, feeling of guilt, fear, or nausea when touched, and disturbing sexual thoughts, alone or in combination.

CONCLUSIONS: These results provide baseline information on the prevalence and type of sexual abuse among adolescents. Abuse involved both genders, but the perpetrators were male. For nearly one fourth of the students the incident seems to have left a long-term psychological impact on the victim.

Allergology

CORRELATION BETWEEN ALLERGIC RHINITIS, ASTHMA, AND ATOPIC DERMATITIS IN CHILDREN

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INTRODUCTION: Allergic rhinitis, asthma, and atopic dermatitis are atopic diseases with the same pathogenic base with regard to the allergic reaction and the type of oversensitivity (facilitated by immunoglobulin E antibodies) with the release of numerous mediators causing allergic inflammation. The incidence of these diseases is increasing constantly. One precedes the others, or they often appear combined.

OBJECTIVE: The goal of this research was to establish the correlation between allergic rhinitis, asthma, and atopic dermatitis in children treated at our health center.

METHODS: In preparation for the research, 3638 medical charts of children aged 3 to 18 years were studied.

RESULTS: Processed were the cases of 142 children with allergic rhinitis (105 boys [73.9%] and 37 girls [26.1%]) who were diagnosed to have allergic rhinitis, asthma, or atopic dermatitis over the previous 4 years. The diagnosis was made on the basis of anamnesis, clinical record, skin-prick test, and consultation with the otolaryngologist. Of all the patients, 25 (17.6%) boys and 18 (12.6%) girls had atopic dermatitis, and 105 (73.9%) boys and 36 (25.3%) girls had asthma. The total number of children with atopic dermatitis was 43 (30.3%), and there were 141 (99.3%) with asthma.

CONCLUSIONS: In 30.3% of the cases, the children with allergic rhinitis also had atopic dermatitis; in 99.3% of the cases, the children with allergic rhinitis also had asthma. The degree of correlation between allergic rhinitis and asthma was higher than that between allergic rhinitis and atopic dermatitis. The boys suffered more often from allergic rhinitis, and its correlation with asthma was greater than that in girls, with whom it was combined with atopic dermatitis to a larger degree.

CYTOKINE PROFILE IN LONG-TERM USE OF INHALED CORTICOSTEROID IN ASTHMATIC CHILDREN RECEIVING SPECIFIC IMMUNOTHERAPY

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INTRODUCTION: Inhaled corticosteroids are widely used for the management of persistent asthma, including by those who receive specific immunotherapy.

OBJECTIVE: Our goal was to elucidate the cytokine profile in long-term use of corticosteroid inhalation in asthmatic children who were receiving specific immunotherapy.

METHODS: We performed a randomized, paralleled, comparative study of asthmatic children allocated into 3 groups: those in group A received inhaled budesonide, those in group B received specific immunotherapy, and those in group C received both specific immunotherapy and inhaled budesonide. The primary outcomes were interleukin 4 (IL-4), IL-5, interferon γ (IFN-γ), and IL-2 levels and forced expiratory volume in 1 second (FEV_1) reversibility.

RESULTS: Significant differences were observed before and after treatment in all groups ($P < .05$). Patients who received inhaled budesonide showed attenuation of IL-4, IL-5, IFN-γ, and IL-2 and 29% failure of FEV_1 reversibility. Patients who received immunotherapy showed attenuation of IL-4 and IL-5, elevation of IFN-γ and IL-2, and 24% failure of improvement of FEV_1 reversibility. Patients who received inhaled corticosteroids and immunotherapy showed attenuation of IL-4 and IL-5, elevation of IFN-γ and IL-2, and 100% improvement of FEV_1 reversibility. Analysis of the discriminator yielded IL-2 as the primary discriminator, which correlated with the decrease of IL-5.

CONCLUSIONS: Long-term use of inhaled corticosteroids by children with asthma who received immunotherapy resulted in elevation of IFN-γ and IL-2 and a decrease of IL-4 and IL-5. Addition of inhaled corticosteroids to immunotherapy resulted in marked attenuation of IL-5 and correlated with greater elevation of IL-2.

ANTIBIOTIC SKIN TESTING FOR CHILDREN LABELED WITH TYPE 1 HYPERSENSITIVITY: A USEFUL CLINICAL TOOL

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INTRODUCTION: Children are often unnecessarily labeled as being allergic to antibiotics that may potentially be life saving. Aside from penicillin, good diagnostic testing has not been available in pediatrics to differentiate between type 1 hypersensitivity and other causes of adverse reactions to antibiotics.
OBJECTIVE: We sought to determine the safety of antibiotic skin testing of children and to describe its potential clinical impact.
METHODS: A retrospective chart review was performed of patients between 0 and 18 years of age who were seen in our clinic over a 2-year period with a history of a possible immunoglobulin E–mediated reaction to various antibiotics other than penicillin. We included patients with either extremely limited antibiotic options or complex medical issues that require antibiotics. We did not perform testing if there was a history of a convincing immunoglobulin E–mediated or serum sickness–like reaction. Skin testing was performed by using nonirritating concentrations of the antibiotic in question that have been used in adults. If skin-prick testing results were negative, we performed intradermal testing. A provocative challenge was offered if all skin-testing results were negative.
RESULTS: of 28 visits, 23 met our inclusion criteria; 4 (17%) of 23 could not be skin-tested. Of those who were skin-prick–tested, all 19 (100%) had a negative result, and 17 (89%) of 19 also had a negative intradermal test. Of those 17 (88%), 15 patients agreed to undergo provocative challenge, 14 (93%) of whom were then unlabeled as allergic to the respective antibiotic.
CONCLUSIONS: Skin-prick testing is a novel tool in pediatrics that may have an important clinical impact in the accurate diagnosis of antibiotic allergies by guiding provocative challenges.

MILK-SPECIFIC IMMUNOGLOBULIN E/TOTAL IMMUNOGLOBULIN E RATIO AS A PREDICTOR OF POSITIVE ORAL FOOD CHALLENGES IN CHILDREN WITH ALLERGY TO COW'S MILK

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INTRODUCTION: Skin-prick test wheal size and serum-specific immunoglobulin E (IgE) levels are able to predict, to an extent, the presence of allergy to certain foods. Nevertheless, the predictive value of these markers is not enough to substitute for oral food challenges, which suggests the need for improvement.
OBJECTIVE: The goal was to determine the prognostic value of specific IgE/total IgE (tIgE) ratio in patients with allergy to cow's milk by using receiver operating characteristic (ROC) analysis.
METHODS: Thirty-four open challenges were performed in children with a mean age of 18.4 months (range: 10.3–69.2 months) who had a previously diagnosed IgE-mediated allergy to cow's milk to reintroduce milk into their diet. Specific IgE levels, assessed by ImmunoCAP fluorescence enzyme immunoassay (Pharmacia Corp, Bridgewater, NJ), were obtained, and skin-prick tests were performed just before the challenge. The specific IgE (f2)/tIgE ratio was evaluated as a potential predictor of a positive challenge and compared with f2 alone by using ROC analysis.
RESULTS: Of 34 challenges, 6 (17.6%) results were positive. Prechallenge milk-specific IgE levels and the f2/tIgE ratio were significant predictors ($P_{f2} = .007$; $P_{ratio} = .008$) of a positive challenge outcome. After ROC analysis, f2 provided a discrimination (between positive and negative provocations) of 0.8601 (ROC area under the curve); however, the f2/tIgE ratio provided a significantly greater discrimination of 0.9464. Values of the f2/tIgE ratio that are >0.1121 provide a 100% diagnostic accuracy (probability of a positive provocation result).
CONCLUSIONS: The f2/tIgE ratio may be a novel, promising predictor of positive oral food-challenge results and should be evaluated prospectively in a larger sample.

BREASTFEEDING AND ATOPIC DISEASE IN CHILDHOOD: THE GENESIS STUDY

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INTRODUCTION: The prevalence of asthma and atopic disease in childhood is increasing yearly. A pro-

tective connection between breastfeeding and development of atopy has been suggested in several studies.

OBJECTIVE: Our goal was to investigate the correlation between breastfeeding and atopy.

METHODS: We screened 1525 children aged 2 to 5 years. Information on the outcome variables "ever wheezing," "recurrent wheezing," "diagnosed asthma," "itchy rash," "recurrent rash," and "diagnosed atopic dermatitis" was obtained. Multiple logistic regression analysis was used to estimate the association of outcome variables with the independent variable (breastfeeding) after adjustment for gender and parental history of allergy.

RESULTS: Median duration of exclusive breastfeeding was 1 month (range: 0–2 months). Children who were breastfed exclusively for >3 months had 28% (95% confidence interval [CI]: 0.53%–0.98%) and 29% (95% CI: 0.51%–1.00%) lower likelihood of ever developing wheezing and recurrent wheezing, respectively. Partial breastfeeding seemed to place the children at significantly greater risk for ever and recurrent wheezing when compared with exclusive breastfeeding. There was no significant difference between exclusive breastfeeding versus formula feeding. Of the ever-breastfed children, 15.2% developed itchy rash versus 10.9% of those who never breastfed. Girls had a significant lower odds ratio (OR) for ever wheezing (OR: 0.76 [95% CI: 0.62–0.94]) and "diagnosed asthma" (OR: 0.60 [95% CI: 0.43–0.85]). Of the children studied, 3.7% had a positive parental background for allergy. Parental history of allergy comprised a significant factor that indicated a greater OR for all outcome variables apart from "diagnosed asthma."

CONCLUSIONS: Breastfeeding seems to have a significant protective effect against the development of wheezing and asthma but not toward the development of skin atopy. A prospective randomized, controlled trial with longer follow-up time is required to confirm our findings.

ESSENTIAL FATTY ACID STATUS IN CORD-BLOOD ERYTHROCYTES AND POSSIBLE FETAL PRIMING OF ATOPY

Submitted by Georgia Skouli

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INTRODUCTION: Environmental factors, diet among them, that act during gestation may play an important role in determining subsequent atopy development. Studies conducted on adults and children have suggested that an imbalance of essential fatty acid (EFA) intake may predispose one to atopic diseases. Few data are available on the possible relation between EFAs and fetal priming of atopy.

OBJECTIVE: We sought to investigate the hypothesis that EFAs may play a role in the regulation of the fetal immune response.

METHODS: We collected umbilical cord-blood samples from 236 neonates with a gestational age of >34 weeks. Serum immunoglobulin E (IgE) levels and fatty acid composition of the erythrocyte membrane were determined by enzyme-linked immunosorbent assay and gas chromatography, respectively. Neonates were separated into 2 groups according to IgE value: the infants in group A had IgE levels of >0.35 IU/mL, and those in group B had IgE levels of ≤0.35 IU/mL.

RESULTS: Group A consisted of 30 neonates with increased IgE levels. Analysis of fatty acid composition revealed higher percentages of arachidic acid (20:0) (mean: 0.22 vs 0.19; $P < .05$) and docosahexaenoic acid (22:6*n*-3) (mean: 1.36 vs 1.04; $P < .05$) in the infants in group B.

CONCLUSIONS: Important differences were detected in cord-blood fatty acid composition in neonates with increased IgE levels. These differences suggest that EFAs may play a role in the development of atopy predisposition in utero life.

Cardiology

CLINICAL SIGNIFICANCE OF LINEAR SHADOWS INSIDE CORONARY ARTERIAL LESIONS ON TWO-DIMENSIONAL ECHOCARDIOGRAPHY IN PATIENTS WITH KAWASAKI DISEASE

Submitted by Akiko Hamaoka

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INTRODUCTION: In Kawasaki disease, we have detected linear shadows inside large- or moderate-sized coronary arterial lesions (CALs) on high-resolution two-dimensional echocardiography (2DE).

OBJECTIVE: For this study, we wanted to investigate the origin and clinical significance of these linear shad-

ows compared with findings on coronary angiography (CAG), MRI, and intravascular ultrasound.
RESULTS: Linear shadows were detected in 11 CALs on high-resolution 2DE in 9 patients with Kawasaki disease. The outer diameters of CALs on 2DE (7.0 ± 2.1 mm) were larger than those on CAG (4.4 ± 1.6 mm), whereas the inner diameters between linear shadows (3.9 ± 1.6 mm) were almost equal to the diameters of CALs on CAG. There was a statistically significant positive correlation ($y = 0.99x - 0.10$; $r^2 = 0.77$) between the diameters of CALs on CAG and the inner diameters between linear shadows on 2DE. A thickened intima was revealed in the same regions that showed linear shadows on 2DE, in 7 of 11 lesions on MRI, and in all 4 lesions on which intravascular ultrasound was performed. In 3 patients who had been followed up over 3 years, linear shadows inside CALs on 2DE persisted, and the diameter between linear shadows was almost consistent with the diameter of CALs on CAG.
CONCLUSIONS: These results suggest that linear shadows inside CALs on 2DE would reflect the existence of a thickened intima. We expected that following up the changes of linear shadows inside CALs was useful for noninvasive evaluation of coronary arterial remodeling such as intimal hypertrophy or stenotic change.

LONG-TERM FOLLOW-UP RESULTS OF PERCUTANEOUS CATHETER INTERVENTION FOR CORONARY ARTERY LESIONS AFTER KAWASAKI DISEASE: MULTICENTER COLLABORATIVE STUDY

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INTRODUCTION: The long-term prognosis in patients with Kawasaki disease (KD) after percutaneous coronary intervention (PCI) remains unclear.
OBJECTIVE: We sought to clarify the long-term results of PCI for KD.
METHODS: Patients who developed coronary stenotic lesions caused by KD and were treated with PCI were investigated. Restenosis or obstruction was diagnosed when the stenosis was ≥75% according to coronary angiography or ischemic change was observed by myocardial perfusion imaging.
RESULTS: A total of 55 stenotic lesions were reported in 49 patients in 5 institutions. The types of PCI included percutaneous transluminal coronary angioplasty (n = 22), stent implantation (n = 7), percutaneous transluminal coronary rotational ablation (PTCRA) (n = 22), and combination of PTCRA with stent implantation (n = 4). Median age at PCI was 14.5 years, and the median follow-up period in the PCI group was 6.3 years. of 55 stenotic lesions in the PCI group, 52 (95%) were dilated successfully by PCI. Immediate complications in the PCI group included neoaneurysm in 5 patients, transient bradycardia in 3 patients, and atrial fibrillation in 1 patient. Treatment for restenosis in the PCI group included re-PCI in 3 patients, coronary artery bypass grafting in 6 patients, and heart transplantation in 1 patient. No patient in the PCI group died. There was no difference in effectiveness among the 3 PCI devices (percutaneous transluminal coronary angioplasty versus stent implantation versus PTCRA: log-rank test, P = .3).
CONCLUSIONS: PCI for KD can be accomplished and can be effective in the long-term.

EXPOSURE TO TOBACCO SMOKE DECREASES ELASTICITY OF THE AORTA IN CHILDREN

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INTRODUCTION: Attenuated arterial elasticity is one of the earliest markers of atherosclerosis.
OBJECTIVE: Our aim was to investigate the relationship of passive smoking and elastic properties of the aorta.
METHODS: We studied 11-year-old healthy children (n = 386) from the randomized, prospective atherosclerosis prevention trial (STRIP). Aortic elasticity was analyzed by using M-mode ultrasound imaging on the basis of the measurement of blood pressure and arterial diameter changes during diastole and systole. Aortic compliance (AC) and aortic stiffness index (SI) were calculated. Exposure to tobacco smoke was measured by using serum cotinine concentration, which was analyzed with gas chromatography.
RESULTS: Cotinine concentrations ranged from nondetectable (detection limit: 0.16 ng/mL) to 6.8 ng/mL. Cotinine values and aortic elasticity measures were similar between genders. Children were classified into 3 groups according to their cotinine concentration: the top-decile cotinine group (n = 39), the nondetectable cotinine group (n = 220), and the low cotinine group (n = 127). Conventional atherosclerosis risk factors were similar between the 3 cotinine groups. A decreasing trend in AC (P = .041) and an increasing trend in SI (P = .006) was observed across the cotinine groups with an

increasing level of tobacco smoke exposure. In addition, systolic and diastolic blood pressure and BMI were independent predictors of the aortic elasticity indices. In multivariable models, cotinine level ($P = .020$) and systolic blood pressure ($P < .001$) were inversely associated with AC and directly related to SI (cotinine level, $P = .005$; systolic blood pressure, $P = .0003$).
CONCLUSIONS: These data suggest that passive smoking is associated with decreased aortic elasticity in children, indicating early arterial changes.

RHEUMATIC FEVER IN THE NEW MILLENNIUM

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INTRODUCTION: During the past 2 decades the presentation of rheumatic fever (RF) has changed markedly from that of an acute florid illness to a more subtle subacute form that is frequently missed.
OBJECTIVE: With this work we attempted to describe the changing face of RF with its different patterns and time of presentation, particularly subclinical carditis.
METHODS: This work included 1732 patients with RF followed up in the pediatric department and pediatric cardiology clinic at Pediatric Hospital, Ain Shams University. Every patient was subjected to a thorough clinical examination, measurement of erythrocyte sedimentation rate and antistreptolysin O titer and C-reactive protein levels, a chest radiograph, electrocardiography, and echocardiography Doppler. Echocardiography was performed at the time of admission and repeated after 2, 4, and 6 weeks and 1 year after the attack. Diagnosis of RF was based on the revised Jones criteria.
RESULTS: Age at the first attack was <5 years for 10% of the patients, 5 to 10 years for 51%, 11 to 15 for 36%, and >15 for 3%; the male/female ratio was 1:1.34. Major clinical RF manifestations were carditis (60%), polyarthritis (56%), chorea (15%), erythema marginatum (0.12%), and subcutaneous nodules (0.12%). Seventy-two percent had carditis, after we combined clinical and echocardiographic criteria of cardiac affection 6 weeks after the attack. Pure arthritis was present in 41% of the patients, arthritis and carditis in 29%, and arthritis and subclinical carditis in 30%. One year after the initial attack the number of patients with echocardiographic features of valve affection remained the same. Pure chorea was present in 55% of the patients, chorea and carditis in 30%, and chorea and subclinical carditis in 25%. One year after the initial attack, 70% of the patients with chorea had echocardiographic features of valve affection. Chronicity of chorea is common with multiple relapses.
CONCLUSIONS: RF is not uncommon in children <5 years of age. Subclinical carditis should be anticipated and looked for at the right time in susceptible patients, particularly those with rheumatic arthritis and chorea. Multicenter studies should be carried out for the addition of the echocardiographic features of carditis to Jones' minor criteria for the diagnosis of RF. Diagnosis of carditis requires a high index of suspicion in at least 1 of 3 cases.

EXPERIMENTAL RESEARCH OF SIMVASTATIN IN REVERSING PULMONARY VASCULAR REMODELING IN VIVO AND IN VITRO

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INTRODUCTION: Simvastatin was predicted to be a potential inhibitor to pulmonary vascular remodeling. This novel reversion induced by simvastatin has remained an uncertain mechanism.
OBJECTIVE: Our goal was to explore the role of simvastatin as a potential inhibitor of pulmonary vascular remodeling.
METHODS: We established a neointimal pulmonary hypertensive rat model receiving monocrotaline after pneumonectomy. Simvastatin was administered after the operation. Hemodynamic and vascular remodeling corresponding indices were detected. *GATA-6*, a gene transcription factor, was evaluated in vivo. Proliferation and the cellular cycle were assessed in cultured vascular smooth muscle cells (VSMCs). α-SM-actin, F-actin, and paxillin were detected to evaluate the phenotype changes.
RESULTS: Neointimal changes developed in 88.5% of right lung intraacinar arteries after pneumonectomy and monocrotaline administration. Mean pulmonary artery pressure, the right ventricle/(left ventricle + S) ratio, and media wall thickness significantly increased in rats that had pneumonectomy and were treated with monocrotaline but decreased significantly in simvastatin-treated rats. The expression of *GATA-6* markedly decreased in these rats and was significantly upregulated after receiving simvastatin. In vitro, the proliferation was significantly downregulated in VSMCs with simvastatin compared to that with platelet-derived growth factor. α-SM-actin increased significantly, and F-actin or paxillin was downregulated in simvastatin-treated rats.
CONCLUSIONS: Our data indicate that simvastatin is most likely a pulmonary vascular remodeling inhibitor, which may reverse the proliferation of VSMCs and phenotype changes. Simvastatin can also upregulate *GATA-6* expression in lung tissue.

LEFT-VENTRICULAR MASS INDEX IN HYPERTENSIVE CHILDREN AND ADOLESCENTS

Submitted by Stella Stabouli
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OBJECTIVE: Our aim was to investigate differences in left-ventricular mass corrected for height$^{2.7}$ (LVMI) in children and adolescents according to 24-hour ambulatory blood pressure (BP) levels.
METHODS: A total of 67 consecutive children and adolescents aged 5 to 20 years were analyzed. Patients underwent 24-hour ambulatory BP monitoring and echocardiography. LVMI was calculated by using the Devereux equation. All subjects underwent 24-hour ambulatory blood pressure monitoring on a usual school day. Ambulatory hypertension was defined as mean daytime systolic BP and/or diastolic BP at ≥95th percentile for gender and height (n = 22). Prehypertension was defined as mean daytime systolic BP and/or diastolic BP at ≥90th percentile and <95th percentile for gender and height (n = 13). Normotension was defined as mean daytime systolic BP and/or diastolic BP at <90th percentile for gender and height (n = 32).
RESULTS: LVMI was 28.3 ± 9.4 g/m$^{2.7}$ (mean ± SD) in the normotensive subjects (n = 32), whereas it was 35.1 ± 8.7 g/m$^{2.7}$ in the hypertensive subjects (n = 22), a difference that was significantly higher ($P < .001$, Mann-Whitney test). LVMI was 32.4 ± 5.4 g/m$^{2.7}$ in prehypertensive subjects (n = 13), values that tended to be lower than the values of hypertensive subjects ($P = .275$) and significantly higher than the values of normotensive subjects ($P < .05$, Mann-Whitney test).
CONCLUSIONS: Children and adolescents characterized as hypertensive or prehypertensive using the ambulatory blood pressure criteria exhibited significantly higher LVMI than normotensive subjects. Prehypertensive children may be at a similar risk for cardiovascular target-organ damage as that established for hypertensive children.

STRATEGY FOR HIGH-DOSE IMMUNOGLOBULIN THERAPY–RESISTANT KAWASAKI DISEASE: CURRENT STATUS IN JAPAN

Submitted by Hirotaro Ogino
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INTRODUCTION: High-dose intravenous immunoglobulin (IVIg) therapy has decreased the risk for development of coronary arterial lesions (CALs) in Kawasaki disease (KD), whereas patients who show resistance to IVIg have a higher risk for CALs.
OBJECTIVE: The purpose of this study was to determine the risk for CALs in patients with IVIg-resistant KD and to investigate whether an additional therapy might affect its risk, based on the nationwide survey (2003–2004) in Japan.
METHODS: Information from 11 510 children with KD treated with IVIg with the first 9 days of illness was available. The incidence of CALs was compared among 4 groups: group 1 (G1), children who responded to initial IVIg; group 2 (G2), IVIg-resistant patients who received additional IVIg; group 3 (G3), IVIg-resistant patients who received additional prednisolone (PSL); and group 4 (G4), IVIg-resistant patients who received additional IVIg plus PSL. CALs were assessed on the 30th day of illness.
RESULTS: Among 11510 cases, 2229 patients (19.4%) were resistant to initial IVIg treatment and received additional therapy. The incidence of CALs was significantly lower in children who responded to IVIg (G1, n = 9281) than in those with IVIg resistance (1.87% and 11.03%, respectively). In each of the additional therapy groups, the incidences of CALs were as follows: G2 (n = 1108), 6.68%; G3 (n = 93), 9.68%; and G4 (n = 135), 22.22%. Thus, the risk for development of CALs was significantly higher for patients in G4 than those in G1 and G2.
CONCLUSIONS: Additional therapy including PSL may increase the risk for CALs; however, several selection biases, such as more severe cases in G3 and G4, might have affected the results.

Community Pediatrics

THE AMERICAN ACADEMY OF PEDIATRICS I-CATCH PROGRAM: IMPROVING CHILDREN'S ACCESS TO COMMUNITY-BASED CARE IN RESOURCE-LIMITED SETTINGS

Submitted by Anna Mandalakas
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INTRODUCTION: The great disparities in children's access to health care depend on many factors. Expanding the availability of community-based services through programs designed to decrease these disparities is imperative.
METHODS: In 2006, the American Academy of Pediatrics Section on International Child Health implemented a new program to address these disparities, the International Community Access to Child Health (I-CATCH) program, which offers mentorship in grant preparation and project execution and provides 3-year funding to support project development and implementation. Projects are community-based initiatives that increase children's access to health care or services not otherwise available. Project initiatives will decrease health disparities and will develop sustainable community-based child health programs that may be replicated in other communities.
RESULTS: During the first grant cycle, innovative proposals were received from colleagues in 16 countries. A great variety of opportunities were described to improve children's access to health. Four projects were funded, each of which focused on community education and development: (1) improve children's nutrition and decrease gastrointestinal and respiratory disease (El Salvador); (2) train community health care workers (Pakistan); (3) identify and serve high-risk pregnancies and neonates (Philippines); and (4) promote essential newborn care (Uganda).
CONCLUSIONS: The first grant cycle illuminated the impressive creativity of colleagues, who outlined many opportunities to improve children's access to care through community-based programs with the expectation of decreasing health disparities. The tremendous potential of the I-CATCH program was validated. Although assessment of the long-term impact of the I-CATCH program is needed, the initial year showed great promise.

THE EUROPEAN ASSOCIATION FOR CHILDREN IN HOSPITAL (EACH) CHARTER

Submitted by Giulianna Brandazzi Filippazzi
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The European Association for Children in Hospital (EACH) Charter, adopted in 1988 in Leiden, Netherlands, is a list of the rights of all children before, during, and after a hospital stay. The rights mentioned in the charter apply to all sick children regardless of their illness, age, or disability, their origin or social or cultural background, or any possible reason for treatment, whether as inpatients or outpatients.

All rights mentioned in the charter and all measures derived from it must, in the first place, be in the best interests of children and enhance their well-being.

The rights/needs of children in hospital include accommodation for parents, support for parents and children, informed participation in the decision-making process, and care in pediatric units by staff who are adequately trained.

The EACH Charter is in line with corresponding and binding rights stipulated at the United Nations Convention on the Rights of the Child and refers to children as being aged 0 to 18 years.

Some of the goals of the EACH Charter are still unachieved, such as:

- the right of children to have their parents with them in the hospital;
- painless medical treatment;
- to receive information they can understand;
- the possibility for children to have their own say in the care plan;
- opportunities for play and education in the ward;
- to have contact with peers; and
- a healing environment.

TRADITIONAL PRACTICES AFFECTING CHILD HEALTH: A SUB-SAHARAN AFRICAN EXPERIENCE

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INTRODUCTION: Culture includes the values of a people and affects nurturing of children as well as illness attribution. In spite of scientific discoveries, traditional practices that relate to health-seeking behaviors have persisted.
OBJECTIVE: The purpose of this work was to highlight the harmfulness and consequent negative effects of some of these practices on child health.
METHODS: A 1-year longitudinal study of children who attended the children's emergency and outpatient departments of a health institution in an urban area in Nigeria was carried out. Oral interviewing of the caregivers and physical inspection of the children was carried out for all patients. Treatment history, preferences for health care, and obvious traditional attempts at cure were evaluated.
RESULTS: There were 4484 hospital visits during which 2040 children were evaluated. The most common form of medical intervention at home before the visit was the use of herbal remedies (964 [47.25%]), scarifications that remained after blood-letting procedures

(867 [42.5%]), and pastes applied on the anterior fontanel (24 [1.18%]). Other less common but more traumatic therapies were foot roasting (18 [0.88%]), heat treatment of extremities (6 [0.29%]), and application of special preparations orifices (0.88%).
CONCLUSIONS: The high use of traditional methods of treatment and the harmfulness of some of them calls for health providers in any environment to evaluate these practices to use the information obtained as tools for health education, thereby discouraging harmful treatments and encouraging the practice of useful ones.

MEASURING QUALITY OF LIFE IN GREEK CHILDREN: FIRST PSYCHOMETRIC RESULTS OF THE GREEK VERSION OF THE PEDIATRIC QUALITY OF LIFE INVENTORY (PEDSQL) 4.0 GENERIC CORE SCALES

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INTRODUCTION: Health-related quality of life concerning children is a growing field of research. The Pediatric Quality of Life Inventory (PedsQL) is a promising instrument that is available in age-appropriate versions and parallel forms for both children and their parents.
OBJECTIVE: The purpose of this study was to evaluate the psychometric properties of the Greek translation of the PedsQL 4.0 generic core scales in a sample of healthy children.
METHODS: After a successful pilot test, the Greek PedsQL was used in a cross-sectional study of 645 healthy 8- to 12-year-old schoolchildren and 567 of their caregivers within the framework of the European project (KIDSCREEN). Reliability of the instrument was assessed by Cronbach's α. Construct validity was assessed by exploring the intercorrelations between the 4 PedsQL subscales and between self- and proxy-report subscales. Impact of gender, health status, and socioeconomic class was detected.
RESULTS: All PedsQL scales showed satisfactory reliability (>.70). Correlations among self-report subscales and between self- and proxy-report subscales were significant. Girls reported lower health-related quality of life than boys on the emotional-functioning subscale. There were significant differences in scores between low and high socioeconomic groups. Healthy children scored significantly higher on all self- and proxy-report scales.
CONCLUSIONS: The PedsQL Greek version for children 8 to 12 years old is a valid and reliable instrument, replicating some of the earlier findings of the original version. The Greek PedsQL 4.0 version will be a valuable tool that can be used effectively in quality-of-life measurement in Greek clinical trials and population-based exercises.

MANAGEMENT OF CHILDREN WITH OTITIS MEDIA: A SURVEY OF AUSTRALIAN ABORIGINAL MEDICAL SERVICES

Submitted by Hasantha Gunasekera
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INTRODUCTION: Otitis media remains one of the most common reasons for childhood primary health care presentations. Indigenous children are at the highest risk, but there are scarce data on how they are managed.
OBJECTIVE: We sought to determine how Australian primary health care medical practitioners diagnose and manage otitis media in Indigenous and non-Indigenous children.
METHODS: We contacted all of Australia's Aboriginal Medical Services by using the national government's register to identify their medical practitioners. We mailed a pilot 5-page clinical vignette questionnaire instrument to these primary health care practitioners (N = 257). Responses for Indigenous children were compared with those for non-Indigenous children.
RESULTS: Questionnaires were returned from 40.9% of medical practitioners (105 of 257) and 64.8% (57 of 88) of the nation's Aboriginal Medical Services. When examining children, practitioners used otoscopy (99.0% often/always) but not pneumatic otoscopy (67.0% never) or tympanometry (55.8% never). When practitioners diagnosed acute otitis media, they were more likely to use antibiotics (104 of 113 [92.0%]) when the child was Indigenous versus non-Indigenous (53 of 112 [47.3%]) (odds ratio: 12.9 [95% confidence interval: 5.9–27.9]). Amoxicillin was the most common antibiotic used (309 of 356 [86.8%]). The major factors that determined the practitioners' otitis media antibiotic use were Indigenous status (65.7%), wet perforations (63.7%), bulging tympanic membranes (58.3%), and fever (56.3%). The major factors for choosing no antibiotics were dry perforations (35.3%) and a well child (24.8%). Most practitioners were aware of the national

guidelines (97.1%) but not the guidelines for Indigenous children (47.0%).
CONCLUSIONS: Aboriginal Medical Service practitioners rely on otoscopy alone to diagnose otitis media and are more likely to use antibiotics for Indigenous children despite not knowing the guidelines.

HEALTH NEEDS OF CHILDREN LIVING IN OUT-OF-HOME CARE

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INTRODUCTION: Children in out-of-home care have high, unrecognized, and unmet health needs. The combination of exposure to abuse and neglect and a background of social disadvantage place them at significant risk for poor health, which affects their physical, developmental, and emotional health.
OBJECTIVE: The aim of this study was to screen children in out-of-home care for unidentified health problems and recommend appropriate health interventions.
METHODS: A health screening clinic for children in out-of-home care was established in a tertiary children's hospital in 2005 in collaboration with social services. Working within a multidisciplinary framework, the children had a comprehensive physical, developmental, and behavioral health screen. Recommendations were made to social services for appropriate health care.
RESULTS: Of the 122 children screened, 24% had incomplete immunizations, 20% had visual problems, 30% had dental problems, and 26% had hearing loss, 45% of the children under 5 years of age had speech delay, 60% failed the developmental screen, and 54% had significant behavioral and emotional problems.
CONCLUSIONS: Children in out-of-home care are a vulnerable group of the child population who experience unacceptable levels of poor health. Comprehensive health screens are important for identifying previously undetected health problems and recommending appropriate health interventions.

Critical Care

PREDICTION OF CAPILLARY LEAKAGE IN PATIENTS WITH DENGUE VIRUS INFECTION: WHAT ELSE BESIDES HEMATOCRIT AND PLATELET COUNTS?

Submitted by Apichai Khongphatthanayothin
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INTRODUCTION: Besides clinical examination, hematocrit and platelet counts are often used to predict if a patient with suspected dengue virus infection had dengue hemorrhagic fever.
OBJECTIVE: In this study, we investigated the role of Doppler study of the portal vein as a predictor for capillary leakage in these patients.
METHODS: Doppler studies of the right portal vein blood flow velocity were performed for 61 patients (aged 10.2 ± 2.9 years; 34 boys and 27 girls) with serologically confirmed dengue virus infection at defervescence. Presence of right pleural effusion was detected by ultrasound in 32 patients 24 to 48 hours later. Binary logistic regression analysis and receiver operating characteristic (ROC) curves were constructed for the following variables as predictors of pleural effusion 24 to 48 hours after defervescence: age, gender, maximum hematocrit level, lowest platelet count, and the velocity of blood flow in the right portal vein (PVDPL).
RESULTS: Hematocrit level and PVDPL were independent predictors of pleural effusion. The area under the ROC curve, sensitivity, and specificity for these variables as predictors for right pleural fluid 24 to 48 hours after defervescence are shown in Table 1.

TABLE 1. Variables as Predictors of Pleural Effusion

Variables	Area Under ROC Curve	Cutoff	Sensitivity, %	Specificity, %
Hematocrit, %	0.79	>43	72	83
PVDPL, cm/s	0.88	<15.3	72	79
Hematocrit/PVDPL, s/cm	0.93	>2.66	81	83

CONCLUSIONS: Doppler-derived portal venous blood flow velocity may be used to predict the clinical progression of patients with dengue virus infection.

A DOUBLE-BLIND RANDOMIZED, CONTROLLED TRIAL OF PROTEIN ENERGY–ENRICHED FORMULA ADMINISTERED TO CRITICALLY ILL INFANTS

Submitted by Dick Van Waardenburg
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INTRODUCTION: Nutritional support is an important aspect of clinical management of critically ill infants, but the nutritional requirements of these infants are not well defined.
OBJECTIVE: Our goal was to compare tolerance, nutritional, and metabolic effects of 2 different infant formulas in critically ill infants in a double-blind, randomized way.
METHODS: Eighteen ventilated infants with respiratory insufficiency caused by respiratory syncytial virus

infection were included and received an energy- and protein-enriched (PE) infant formula (Infatrini [Nutricia B.V. Zoetermeer, Zoetermeer, Netherlands]; $n = 8$) or standard infant formula (Nutrilon 1 [Nutricia B.V. Zoetermeer]; $n = 10$). Daily intake and tolerance (gastric retention, diarrhea) were recorded. Resting energy expenditure, respiratory quotient, L-amino acid concentrations, and metabolic parameters were measured, and cumulative energy balance, nitrogen balance, and substrate utilization were calculated.

RESULTS: Baseline characteristics were similar in both groups. Both formulas were well tolerated with similar volumes of intake. Results from day 4 are presented in Table 1. Levels of several amino acids (His, Val, Met, Phe, Lys, and ornithine; $P < .05$) were significantly higher in the infants who received the PE-enriched formula.

TABLE 1. Results on Day 4 of Admission

Formula	Protein Intake, g/kg per day	Energy Intake, kcal/kg per day[a]	Resting Energy Expenditure, kcal/kg per day[a]	Respiratory Quotient	Cumulative Energy Balance, kcal/kg per day[a]	Cumulative Nitrogen Balance, mg/kg per day
PE-enriched ($n = 8$)	2.61 ± 0.24	111 ± 10	59 ± 5	0.98 ± 0.02	589 ± 115	162 ± 32
Standard ($n = 10$)	1.46 ± 0.11	78 ± 4	49 ± 4	0.91 ± 0.01	350 ± 50	68 ± 16
P	<.01	<.01	.26	<.01	<.05	.08

[a] 1 kcal = 4.2 kJ.

CONCLUSIONS: PE-enriched infant formula was well tolerated in critically ill infants and effective in achieving higher nutritional intakes in the first days of admission. PE-enriched formula improved energy balance and plasma amino acid profile, and a trend toward increased nitrogen balance was found.

Developmental and Behavioral Pediatrics

COGNITIVE AND BEHAVIORAL ABILITIES OF CHILDREN WITH HIV INFECTION IN GREECE

Submitted by Georgia Bertou
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OBJECTIVE: Our goal was to evaluate cognitive and behavioral abilities of HIV-positive children in Greece.

METHODS: The cognitive and behavioral abilities of 20 HIV-positive children (B and C status; 8 boys and 12 girls; aged 3–18 years [mean: 11.5 years]) who were vertically infected and were receiving antiretroviral treatment were assessed twice within a 7-year period. Clinical indices (CD4 lymphocyte and viral load counts) were monitored systematically. A detailed developmental assessment was performed for all children twice within a 7-year period. Cognitive abilities were assessed by using the Wechsler Intelligence Scale for Children III and Griffiths Mental Abilities Scales. Behavioral abilities were assessed by using the Strengths and Difficulties Questionnaire, which provides individual scores for anxiety, emotional tension, conduct, hyperactivity, and social relations with peers and provides an overall index of behavioral difficulties (IBD). Detailed neurologic examination and brain imaging were performed for all children.

RESULTS: HIV encephalopathy was evident in 3 children, and 5 of 20 children presented with coexisting diseases (2 neurofibromatosis encephalopathy, 1 brain aneurysm, and 2 autistic disorders). HIV-positive children with normal MRI findings and without signs of HIV encephalopathy scored within the normal range for their chronological age in all measures of general and specific domain cognitive abilities. Low IQ scores showed in 15 of 20 HIV-positive children in both assessments. Factors that were associated consistently with lower scores were positive MRI results, coexistence of an organic disease, maternal education, and gender. The IBD was raised in 7 children. In detail, 9 children had raised IBD scores in emotional tension, 6 seemed to have conduct disorders, 5 had hyperactivity, and 11 presented as having difficulties in social relations with their peers. Factors that were associated significantly and consistently with abnormal IBD scores were lower IQ, positive MRI findings, and coexistence of an organic disease.

CONCLUSIONS: Although the sample was small, the findings of our study support the idea that HIV infection places children at increased risk for poor cognitive and behavioral outcomes only if they experience a severe illness of advancing disease stage or a coexisting disease.

BEHAVIORAL PROBLEMS IN CHILDREN WITH LEARNING DIFFICULTIES ACCORDING TO THEIR PARENTS AND TEACHERS

Submitted by Panagiotis Diakakis
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INTRODUCTION: Learning difficulties (LDs) are associated with increased comorbidity, especially depression and anxiety. Studies have shown that 24% to 52% of children with LDs present with behavioral problems (BPs).

OBJECTIVE: The aim of our study was to evaluate whether parents' and teachers' opinions concerning BPs in children with LDs are identical.

METHODS: For this purpose, 658 students (aged 7–10 years) in elementary schools were evaluated by specialized questionnaires for parents and teachers. Of those students, 102 (15.5%) were identified as having LDs according to their teachers. The questions regarded symptoms of depression, anxiety/stress, irritability, and other BPs.

RESULTS: Our findings in children with LDs are summarized in Table 1.

TABLE 1. Behavioral Problems in Children With LDs

	Teachers and Parents Agree That There Are No BPs, %	Teachers and Parents Agree That There Are BPs, %	Only the Teachers Consider That There Is a BP, %	Only the Parents Consider That There Is a BP, %
Reduced self-confidence	24.6	26.3	42.1	7.0
Complains of headache/bellyache	19.4	28.4	37.3	14.9
Feeling tired frequently	13.6	24.2	56.1	6.1
Other children tease him/her	42.6	13.2	16.2	27.9
Being alone, without friends	37.1	11.3	35.5	16.1
Being unreliable	48.4	12.5	10.9	28.1
Often fights with other children	48.5	20.6	13.2	17.6
Increased irritability	36.8	20.6	11.8	30.9

CONCLUSIONS: BPs resulting from reduced self-confidence and anxiety/stress were observed at a higher rate by the teachers than by the parents, who more often acknowledged symptoms of social isolation and aggressive behavior. Stress was the BP about which parents and teachers gave identical replies.

QUALITY OF LIFE OF CHILDREN WITH MENTAL DISABILITIES AND THEIR FAMILIES IN CYPRUS

Submitted by Vassiliki Papavassiliou

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INTRODUCTION: Children with mental disabilities and their parents face challenging lives in an ever-changing social context.

OBJECTIVE: We sought to evaluate quality of life and daily habits of children with mental disabilities and their families in Cyprus.

METHODS: Sixty-three children (65.5% male) who were attending special schools were evaluated by questionnaires for parents and teachers, personal interviews, and local visits.

RESULTS: Mental disabilities were diagnosed in 45.8% of the children at birth and in 40.7% at 2.5 years, by which time most developmental milestones are normally achieved; 6.5% had not been diagnosed with a mental disability. For 18% of the children, another family member had also been diagnosed with mental disabilities. Pediatricians were considered most supportive (62.3%). Only 45% of the children were followed-up regularly, 30.5% rarely visited a doctor, and 66% had not been evaluated by electroencephalography after diagnosis. Children attended physiotherapy (39.2%), ergotherapy (51%), and arts therapy (45.3%), and 95.1% attended special education. Most of them went to school by bus (85.2%). They were somewhat accepted by their peers (49.1%), and 33.3% shared leisure time. They felt accepted by society (86.4%), but 16.9% reported problems with family members. The mother was mostly involved (61.8%), and in only 5.9% of the cases were both parents involved. Parents had little or no free time (67.1%), rarely went on holidays (55%), considered a big city favorable (61%), and were optimistic about their children's future (76.4%). Many parents needed assistance (60%), especially regarding free time (22.6%) and financial (20.8%) and medical (11.3%) issues. Most peers were informed and understanding (95%).

CONCLUSIONS: Quality of life is considered satisfactory; however, better medical follow-up and intensification of help provided to these families is needed. Children are quite well adapted in society, although there is room for improvement.

EVALUATION OF LEARNING DIFFICULTIES IN EPILEPTIC CHILDREN WITH IDIOPATHIC GENERALIZED EPILEPSY AND WELL-CONTROLLED SEIZURES

Submitted by Alexia Prassouli

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INTRODUCTION: Children with symptomatic epilepsy have more learning difficulties (LDs) than those with idiopathic or cryptogenic epilepsies. However, there is little information on the prevalence of LDs in well-defined pediatric epileptic populations.

OBJECTIVE: Our goal was to evaluate LDs in epileptic children.

METHODS: We evaluated LDs in 37 epileptic children (18 boys and 19 girls; mean age: 8.29 ± 1.00 years) who had idiopathic generalized epilepsy (IGE) and were being treated with sodium-valproate monotherapy (22 with generalized tonic-clonic seizures and 15 with absence epilepsy). The mean duration of epilepsy and treatment was 3.48 ± 1.88 and 2.96 ± 1.80 years, respectively. All children attended mainstream schools, and their seizures were well controlled (without seizures for at least 6 months). We used the Athina Test for the Diagnosis of Learning Difficulties, a test that is partly

based on the Illinois Test of Psycholinguistic Abilities, standardized in healthy Greek children.

RESULTS: Children with IGE performed significantly poorer in all subtests except the auditory closure subtest (Table 1). No significant difference was found between the 2 subgroups. A negative correlation was found between disease duration and the score in auditory memory ($r = -0.368$; $P = .025$).

TABLE 1. Athina Test for the Diagnosis of LDs

	Subjects With Inadequate Performance, %		*P*
	Children With IGE	Healthy Children	
Auditory memory	64.9	9.0	.000
Visual memory	43.2	9.0	.000
Grammatic closure	43.2	9.0	.000
Auditory closure	16.2	9.0	.125
Graphophonological awareness	32.4	9.0	.000
Visual-motor coordination	43.2	25.0	.010

CONCLUSIONS: Our results suggest an increased risk of LDs in children with IGE and well-controlled seizures. Early detection of the cognitive impact of IGE and subsequent intervention are needed to prevent educational underachievement.

MULTIDISCIPLINARY MEDICAL EVALUATION OF CHILDREN YOUNGER THAN 7.5 YEARS BORN AFTER PREIMPLANTATION GENETIC DIAGNOSIS FOR MONOGENIC DISEASES

Submitted by Loretta Thomaidis

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INTRODUCTION: The growing cohort of children conceived after preimplantation genetic diagnosis (PGD) techniques underlines the importance of evaluating potential risks for their developmental outcome. There are some data concerning the incidence of congenital anomalies, medical status, and cognitive development of children conceived after PGD techniques, based mainly on reports and not on objective medical evaluation.

OBJECTIVE: We sought to perform multidisciplinary evaluation (physical, genetic, and developmental) of 31 children conceived after PGD techniques (aged 30 days to 7.5 years) and the stress level of parents who used PGD regarding their parental role.

METHODS: Among 24 couples at risk for transmitting monogenic diseases and with an unsuccessful reproductive history, 31 children conceived after PGD techniques were examined. Genetic examination was performed by 2 independent geneticists, and developmental assessment included formal testing of cognitive and motor skills (Bayley scales, Griffiths scales, Athina test). Parental stress was measured by using the Parent Stress Index-Short Form (PSI-SF), a self-report questionnaire that assesses parental stress. The PSI-SF was also completed by 35 parents of naturally conceived, healthy children matched for age, gender, and socioeconomic level.

RESULTS: A high rate of cesarean deliveries were reported, but no higher risk was found for perinatal complications. The increased incidence of prematurity and low birth weight among children conceived after PGD techniques did not seem to affect their growth development later in life. Major malformations (cardiac, gastrointestinal, urogenital, skeletal) were present in 4 (12.9%) of 31 children, with a discrepancy between singletons and multiples. A significant number of children conceived after PGD techniques (6 of 31 [19%]), mostly multiple, premature, and small-for-gestational-age infants, experienced low levels of cognitive, verbal, and perceptual abilities (Global Development Quotient scores of <85). Parents who used PGD experienced lower levels of parenting stress compared with controls ($P < .05$).

CONCLUSIONS: Children conceived after PGD techniques seem to be at greater risk for exhibiting congenital malformations and lower cognitive skills. Whether these observations are linked to the PGD procedure itself, rather than to subfertility, multiplicity, or prematurity, is a question that is difficult to answer. An unexpected finding was that once parents who used PGD finally had what they struggled for (a healthy infant), the stresses of parenthood may have been offset by a broader sense of fulfillment.

LINGUISTIC DEVELOPMENT OF CHILDREN WITH WILLIAMS SYNDROME: A CONTROL STUDY

Submitted by Loretta Thomaidis

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INTRODUCTION: Williams Syndrome (WS; Online Mendelian Inheritance in Man No. 194050) is a rare

syndrome that has attracted a great deal of attention because of an uneven neurolinguistic profile characterized by relative strengths in language, facial processing, and social cognition in the context of poorer spatial cognition, planning, and problem solving. WS has also been used as evidence for the existence of dissociations within subsystems of the language module itself. It has been reported that individuals with WS perform better on grammatical versus lexical tasks and on regular versus irregular forms.

OBJECTIVE: This study addressed 2 main questions: (1) Do individuals with WS show differences between language and cognition? (2) Do individuals with WS perform differently across tasks that tap different aspects of language?

METHODS: We investigated nonverbal and verbal abilities of 20 Greek-speaking children with WS (aged 6–18 years with molecular definition of chromosome 7 deletions) and compared their performance to a group of 20 normal children aged 4 to 10 years. The 2 groups were matched on language ability (comprehension and expression) through the Diagnostic Verbal IQ Test. Verbal ability was measured by 3 experimental linguistic measures that assessed comprehension of pronouns and production of verbs and nouns.

RESULTS: Nonverbal IQ was low and ranged from 40 to 68 points. Those in the WS group, as a whole, showed unimpaired performance on pronouns but faced difficulties in using verbs and nouns. Great variation in performance was evident, which highlights the heterogeneity of the group. A subgroup of individuals with WS showed clear dissociations between language and cognition and within language.

CONCLUSIONS: Our results indicate that (1) there is a clear dissociation between language and cognition and (2) children with WS show strengths on some aspects of their linguistic development.

A NORMAL LIFE WITH AN UNHEALTHY BODY: SELF-IDENTITY IN ADOLESCENTS GROWING UP WITH CHRONIC ILLNESS

Submitted by AnneLoes Van Staa

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INTRODUCTION: Chronic illness is often described in terms of biographic disruption. However, for those growing up with congenital disorders, an unhealthy body is the norm. An important developmental task in adolescence is the formation of self-identity. How does a chronic disorder influence the development of self-identity in adolescents?

OBJECTIVE: Our aim was to investigate attitudes and preferences of adolescents living with chronic disorders.

METHODS: A qualitative study was conducted by using semistructured interviews that focused on daily life issues. The sample consisted of 31 adolescents (aged 12–19 years) with various chronic disorders who were randomly selected from the patient database of Erasmus Medical Center-Agia Sophia Children's Hospital. Data analysis was performed by using a qualitative analysis computer program (ATLAS.ti, Berlin, Germany).

RESULTS: For most adolescents with chronic disorders, living with illness is "normal." By comparing themselves with healthy peers, they recurrently stress their own normality. They strongly agreed with the statement, "I am like everyone else, my illness is something extra." Therefore, disclosure of health problems remains a sensitive issue, and contact with fellow patients is not often sought. Most held optimistic views about their futures, and only a minority told problematic accounts of the acceptance of their dysfunctional bodies.

CONCLUSIONS: Normalization of an unhealthy childhood seems to be an important strategy in identity-forming in adolescents. It may be interpreted as denial, but adolescents consider denial to be "dangerous" and "stupid." We view normalization as a strategy to accept reality while preventing illness to dominate their life: "I try not to think about it, not because it scares me, but because it's there."

Endocrinology

LYMPHOCYTES IN PERIPHERAL BLOOD AND THYROID TISSUE IN CHILDREN WITH GRAVES' DISEASE

Submitted by Iwona Ben-Skowronek

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OBJECTIVE: Our goal was to analyze interactions of lymphocytes in peripheral blood and thyroid tissue in children with Graves' disease (GD).

METHODS: The prospective study concerned 15 children affected with GD and 15 healthy children. The levels of autoantibodies against thyrotropin receptor, thyroid peroxidase, and thyroglobulin were assayed. Monoclonal antibodies (Ortho Diagnostic Systems, Raritan, NJ) were used to define peripheral blood lymphocyte subsets and analyzed by using a flow cytometer. After thyroidectomy, thyroid specimens were stained

with hematoxylin/eosin. T cells were detected by $CD3^+$, $CD4^+$, and $CD8^+$ antibodies and the antigen-presenting dendritic cells with $CD1a^+$ and $CD35^+$ antibodies (DakoCytomation, Glostrup, Denmark).
RESULTS: Before treatment, all children with GD had increased thyroid autoantibody levels, an increased percentage of $CD4^+$ helper cells, and decreased levels of $CD8^+$ suppressor/cytotoxic T cells, which resulted in an elevated CD4/CD8 ratio. The percentage of $CD19^+Cd5^+$ B cells was increased, although the total population of $CD19^+$ B cells did not differ from that of the control group. The number of lymphocytes in the thyroid was decreased in 10 patients after long-term thiamazole treatment. In 5 patients with short-term therapy (<6 months after relapse of GD), the lymphocytes had formed lymphatic follicles: antigen-presenting dendritic cells $CD1a^+CD35^+$ in the germinal center and T-helper $CD4^+$, T-suppressor $CD8^+$, and B cells $CD79^+$ on the edges.
CONCLUSIONS: The primary defect of immunoregulation in GD consists of an increase of T-helper lymphocytes with a simultaneous decrease in the number of T-cytotoxic/suppressor cells. Thiamazole therapy probably leads to reduction of the lymphocyte amount in the thyroid.

*HLA-DQB1*05* ASSOCIATION WITH HASHIMOTO THYROIDITIS IN CHILDREN OF NORTHERN GREEK ORIGIN

Submitted by Styliani Giza
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INTRODUCTION: Hashimoto thyroiditis (HT), an organ-specific autoimmune disorder of the thyroid gland, is considered to be associated with the major histocompatibility complex. Association studies of human leukocyte antigens (HLAs) with HT concern adults and have not revealed consistent results.
OBJECTIVE: We sought to investigate *HLA-DRB1* and *HLA-DQB1* gene polymorphisms in Greek children and adolescents with HT.
METHODS: We analyzed the distribution of *HLA-DRB1* and *HLA-DQB1* alleles in 17 Greek children and adolescents with HT and in 181 randomly chosen healthy subjects from northern Greece. The typing of *HLA-DRB1* and *HLA-DQB1* genes was performed by using polymerase chain reaction with sequence-specific primers. Differences of frequencies for HLA alleles were tested by the χ^2 test.
RESULTS: There was no significant association detected between HT and *HLA-DRB1* or *HLA-DQB1* alleles. However, *HLA-DRB1*16* was slightly significantly increased in patients with HT (41.2%) compared with that in controls (19.3%) ($P = .057$; relative risk: 2.92), and *HLA-DQB1*05* was significantly increased in patients with an age of diagnosis of >10 years (87.5%) as compared with those with an age of diagnosis of ≤10 years (33.3%) ($P = .05$; relative risk: 14).
CONCLUSIONS: This is the first study to examine children and adolescents from northern Greece with HT and analyze the distribution of *HLA-DRB1* and *HLA-DQB1* alleles according to the age of onset of HT. However, this study needs to include a greater number of patients to ascertain the possibility of an association and avoid the result of a chance event or random variation.

IMPAIRED DIURNAL BLOOD PRESSURE AND HEART RATE VARIATION AND THEIR RELATIONSHIP WITH LEFT-VENTRICULAR FUNCTION IN ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS

Submitted by Kyriaki Karavanaki
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INTRODUCTION: Diabetic cardiomyopathy is a well-defined complication of diabetes that occurs in the absence of ischemic heart disease or hypertension and has been associated with autonomic dysfunction.
OBJECTIVE: Our aim was to evaluate diurnal blood pressure (BP) fluctuations and autonomic function and their possible association with left-ventricular function in adolescents with type 1 diabetes mellitus.
METHODS: In 48 normotensive, normoalbuminuric diabetic adolescents, with a mean (±SD) age of 17.3 (±4.1) years and diabetes duration of 8.5 (±3.3) years, 24-hour ambulatory BP and heart rate (HR) monitoring was performed. Left-ventricular end-diastolic and end-systolic diameters were estimated by echocardiography, and left-ventricular mass index (LVMI) was calculated.
RESULTS: The patients were divided into 2 groups according to the absence of decrease (nondippers) or the decrease (dippers) of nocturnal diastolic BP. The nondippers presented, in comparison with the dippers, reduced mean HR during 24 hours (79.6 vs 84.0 beats/minute; $P = .05$) and also during daytime (81.3 vs 86.0

beats/minute; $P = .05$). The nondippers also presented greater end-systolic diameter (28.7 vs 25.9 mm; $P = .001$) and left-ventricular end-diastolic diameter (47.8 vs 45.1 mm; $P = .040$) and greater LVMI (90.2 vs 78.3 g/m^2; $P = .044$) compared with the dippers. During stepwise multiple regression, the most important factors affecting LVMI were mean HR (day) ($b = -0.40$; $P = .001$), high-frequency variable of heart rate variability ($b = 0.38$; $P = .016$), and hemoglobin A1c: ($b = 0.67$; $P = .001$).

CONCLUSIONS: A group of normotensive diabetic adolescents with abnormal nocturnal BP reduction and impaired heart rate variation also had impaired left-ventricular function. Our findings suggest that an altered diurnal BP profile, as a result of autonomic dysfunction, may contribute to the development of left-ventricular hypertrophy in patients with type 1 diabetes mellitus.

ADIPONECTIN AND PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR γ EXPRESSION IN SUBCUTANEOUS AND OMENTAL ADIPOSE TISSUE IN CHILDREN

Submitted by Xiaonan Li
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INTRODUCTION: Adiponectin is an adipocyte-specific protein with insulin-sensitizing properties. Peroxisome proliferator-activated receptor γ (PPARγ) may be involved in its gene transcription.

OBJECTIVE: The aim of this study was to compare the expression levels of the genes that encode adiponectin and PPARγ in subcutaneous and omental adipose tissue in children in relation to age and anthropometric variables.

METHODS: Paired biopsies (from subcutaneous and omental adipose tissue) were obtained from 53 children (age: 0.2–14.0 years; BMI: 12.5–25.8 kg/m^2). Messenger RNA (mRNA) levels of adiponectin and PPARγ were measured by using reverse-transcription and quantitative real-time polymerase chain reaction.

RESULTS: Adiponectin mRNA levels in adipose tissue were positively associated with PPARγ mRNA levels in children (subcutaneous adipose: $r = 0.73$, $P < .001$; omental adipose: $r = 0.78$, $P < .001$). In overweight children, the median adiponectin mRNA level was lower in omental adipose tissue (odds ratio: 0.51 [95% confidence interval: 0.1–2.17]) compared with subcutaneous adipose tissue (odds ratio: 1.29 [95% confidence interval: 0.16–5.08]) ($P = .032$) but not in normal-weight children ($P = .54$), and the difference remained significant after adjustment for age ($P = .045$).

CONCLUSIONS: The close association between adiponectin and PPARγ expression supports the hypothesis that PPARγ is involved in adiponectin gene regulation. The fact that adiponectin expression was decreased in omental adipose tissue relative to subcutaneous adipose tissue in overweight children suggests that a risk of insulin resistance may be present in childhood, which allows such resistance to develop after a relatively short duration of overweight.

EFFECT OF BODY WEIGHT ON BONE AGE AND HORMONAL PARAMETERS IN CHILDREN WITH PREMATURE ADRENARCHE

Submitted by Asteroula Papathanasiou
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OBJECTIVE: Our goal was to investigate the effect of body weight on bone age (BA) and hormonal features in children with benign premature adrenarche.

METHODS: We studied 221 children (175 girls, 46 boys) with premature adrenarche (pubic and/or axillary hair at <8 years of age in girls and <9 years of age in boys) and mean chronological age (CA) at presentation of 7.0 years (girls) and 7.8 years (boys). Anthropometric features and laboratory data (dehydroepiandrosterone sulfate [DHEA-S], 17-hydroxyprogesterone, Δ^4-androstenedione [Δ^4-A], testosterone, estradiol, insulin-like growth factor I [IGF-I], cholesterol, triglycerides, high- and low-density lipoprotein cholesterol, and BA) were recorded. The population was divided into 3 groups according to BMI: (1) normal weight, (2) overweight (BMI: 85th–95th percentile), and (3) obese (BMI: >95th percentile). Children with late-onset congenital adrenal hyperplasia were excluded from study.

RESULTS: Mean CA of adrenarche was 6.3 years (girls) and 7.1 years (boys). The percentages of overweight and obese children was significantly higher than those reported in the general population of children in Greece. Obese children had significantly more advanced BA compared with overweight and normal-weight children. Higher levels of DHEA-S and Δ^4-A were observed in overweight and obese girls compared with normal-weight girls, whereas higher levels of DHEA-S, testosterone, and IFG-I were observed in overweight and obese boys (Table 1). No statistically significant difference was observed between the 3 groups in the levels of 17-hydroxyprogesterone, estradiol, cholesterol, triglycerides, or high- and low-density lipoprotein cholesterol.

TABLE 1. Levels of Adrenal Androgens in Normal-Weight and Obese Children

	Normal Weight Mean (Range)	Overweight Mean (Range)	Obese Mean (Range)	P[a]
Girls				
Testosterone, ng/mL	0.11 (0.06–0.20)	0.14 (0.10–0.21)	0.16 (0.09–0.24)	.112
DHEAS, μg/mL	0.71 (0.41–1.10)	0.85 (0.61–1.15)	0.88 (0.57–1.21)[b]	.081
Δ^4-A, ng/mL	0.4 (0.2–0.8)[b]	0.6 (0.4–1.1)[b]	0.6 (0.4–0.8)[b]	<.05[b]
IGF-1, ng/mL	199 (140–318)	236 (180–283)	200 (190–266)	.681
Boys				
Testosterone, ng/mL	0.08 (0.04–0.15)[b]	0.17 (0.06–0.26)[b]	0.28 (0.09–0.39)[b]	<.05[b]
DHEAS, μg/mL	0.51 (0.21–0.92)	1.10 (0.82–1.24)[b]	1.12 (0.20–2.12)	.056
Δ^4-A, ng/mL	0.4 (0.2–0.7)	0.5 (0.3–0.6)	0.6 (0.4–1.0)	.524
IGF-1, ng/mL	200 (89–257)[b]	170 (116–207)[b]	288 (267–369)[b]	<.05[b]

[a] Kruskal-Wallis test.
[b] Results were significant.

CONCLUSIONS: A higher frequency of obesity and advanced BA was observed in children with benign premature adrenarche, with a strong correlation between BA and degree of obesity. Furthermore, obese children were characterized by higher levels of adrenal androgens compared with normal-weight children.

MANAGEMENT OF DIABETIC KETOACIDOSIS: SUCCESSFUL MANAGEMENT EXPERIENCE OF MORE THAN 32 YEARS

Submitted by Surendra Varma
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INTRODUCTION: Diabetic ketoacidosis (DKA) in children and adolescents has a mortality rate of 1% to 2%. The proper management of DKA requires intense monitoring and clear understanding of pathophysiology related to it. Potential complications include cerebral edema, hypokalemia, hypoglycemia, and relapse.
OBJECTIVE: Our goal was to describe our long-term experience in the management of diabetic ketoacidosis in children.
METHODS: This study comprised a 32-year experience of managing DKA in the pediatric age group. More than 900 episodes of DKA were encountered during this period. The age range of patients was from 9 months to 18 years. These episodes included patients presenting with new-onset type 1 diabetes as well as known patients with recurrent DKA. All patients were managed in a PICU by residents directly supervised by Dr Varma following an established protocol, including careful monitoring and paying particular attention to avoiding complications.
RESULTS: In >900 admissions during this period, the mortality rate was 0%, and the incidence of cerebral edema was <0.1%. Hypoglycemia and relapse occurred in <1% of the cases. The only occurrence of severe hypoglycemia (electrocardiographic changes and arrhythmia) was in a patient who was transferred from an outlying hospital after 36 hours of inappropriate treatment.
CONCLUSIONS: Our experience demonstrates that children with DKA can be managed successfully with minimal complications by adhering to the following principles:

1. early recognition and rapid transport to an ICU with experienced staff and physicians; and
2. adherence to well-established standards of treatment, including:
   - proper fluid and electrolyte management aimed at avoiding overhydration and extreme levels of electrolytes;
   - cautious correction of acidosis;
   - slow, steady reductions in plasma glucose and avoidance of hypoglycemia;
   - careful monitoring of clinical status (sensorium, state of hydration, vital signs, etc) and laboratory study results; and
   - frequent reassessment of the patient with adjustments and changes in treatment as dictated by the patient's needs.

Epidemiology

ASTHMA IN GREEK CHILDREN FROM BIRTH TO 18 YEARS: A LONGITUDINAL STUDY

Submitted by Flora Bacopoulou
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INTRODUCTION: The striking worldwide variation in the prevalence of asthma and its divergent changes over time necessitates regional longitudinal studies.
OBJECTIVE: We aimed to examine the asthma situation in Greece.
METHODS: Data from a longitudinal study of a representative nationwide sample derived from the National Perinatal Survey (11 049 consecutive births in April 1983) were analyzed in an attempt to describe the prevalence and natural course of asthma from birth throughout childhood to adolescence. We followed up with 2133 children (at the ages of 7 and 18 years) by using written questionnaires. The diagnostic labeling of asthma was confirmed by a physician on the basis of a history of wheeze attacks, nocturnal cough, exertional symptoms, and response to treatment.
RESULTS: Prevalence rates of current asthma were 7.7% and 4.7% and of lifetime asthma were 19.6% and 26.3% at 7 and 18 years, respectively. More than half (58.2%) of the children with early-onset asthma (onset before the age of 7 years) were free of symptoms at the

age of 7 years, and only 7.6% continued to be symptomatic at 18 years. In 6.7% of the participants asthma symptoms appeared between 7 and 18 years of age (late-onset asthma). In almost half (48.2%) of these children symptoms were persisting at the age of 18 years.
CONCLUSIONS: These findings illustrate that asthma remains a significant health care problem for Greek children and adolescents. Continued surveillance of asthma prevalence and its longitudinal predictors is necessary to assist health care professionals with adequately informing children and their parents on the course of the disease.

CONGENITAL MALFORMATIONS ASSOCIATED WITH PESTICIDES IN ENCARNACIÓN, PARAGUAY

Submitted by Stela Benitez Leite
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INTRODUCTION: Exposure to pesticides is a known risk to human health. The association between parental exposure and congenital malformations is described.
OBJECTIVE: We sought to study the association between exposure to pesticides and congenital malformations in newborns who were born at the Regional Hospital of Encarnación in Itapúa, Paraguay.
METHODS: This was a prospective case and control study from March 2006 to February 2007. A case was defined as a newborn who was born with congenital malformations, and a control case was defined as a newborn of the same gender who was born immediately after and was found to be healthy. The exposure to pesticides was considered along with other risk factors that are known to cause congenital malformations.
RESULTS: The cases (52) and controls (87) were analyzed. The average number of births per month was 216. The risk factors that were significantly associated were living near fumigated fields (odds ratio [OR]: 2.46 [95% confidence interval (CI): 1.09–5.57]; $P < .02$), having pesticides in the house (OR: 15, 35 [95% CI: 1.96–701.63]; $P < .003$), direct or accidental contact with pesticides (OR: 3.19 [95% CI: 0.97–11.4]; $P < .04$), and history of family malformations (OR: 6.81 [95% CI: 1.94–30.56]; $P < .001$). The other risk factors known to cause malformations did not have statistical significance.
CONCLUSIONS: The results show an association between the exposure to pesticides and congenital malformation in newborns who were born at the Regional Hospital of Encarnación. Future studies are required to confirm these findings.

THE GLOBAL BURDEN OF CHILDHOOD OTITIS MEDIA AND HEARING IMPAIRMENT: A SYSTEMATIC REVIEW

Submitted by Hasantha Gunasekera
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INTRODUCTION: The World Health Organization resolved that chronic otitis media and resultant hearing impairment are significant global health problems and called for more detailed epidemiological information, particularly the association between prevalence and socioeconomic variables.
OBJECTIVE: We sought to determine the worldwide prevalence of otitis media (OM) and hearing impairment (HI) and their risk factors.
METHODS: We searched Medline, Embase, and Cinahl for population-based studies with incidence or prevalence data on OM and HI (>25 dB) in children (<18 years), without language restrictions. Studies identified through reference lists were also included. We examined the effect of socioeconomic and health variables on OM and HI prevalence.
RESULTS: The search strategy identified 1504 studies with substantial methodologic variation. They included studies ($n = 108$) that provided a combined sample size of 250 978 children. Acute OM incidence ranged from 0.6 to 1.7 episodes per child per year. The highest OM prevalence rates were in Inuits (81%) and Australian Aborigines (84%). HI prevalence ranged from <1% (Greece) to 23% (Australian Aborigines), and HI was significantly more common in children with OM (odds ratio [OR]: 8.11 [95% confidence interval (CI): 6.91–9.52]). In meta-analysis, increased OM prevalence was associated with not breastfeeding (OR: 1.28 [95% CI: 1.03–1.59]) and parental smoking (OR: 1.73 [95% CI: 1.42–2.10]), but male gender (OR: 1.04 [95% CI: 0.90–1.20]) and urbanization (OR: 0.72 [95% CI: 0.28–1.83]) were not significant. Some studies reported increased OM prevalence with overcrowding, lower maternal education, and poorer household sanitation.
CONCLUSIONS: Indigenous children have the highest prevalence of OM and its complications. OM remains a significant cause of preventable childhood HI, and many of the risk factors are modifiable.

HUMAN BOCAVIRUS IN GREEK CHILDREN WITH RESPIRATORY TRACT INFECTION

Submitted by Katerina Haidopoulou

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INTRODUCTION: Human bocavirus (family *Parvoviridae*) was recently identified in children with respiratory tract infection (RTI), first in Sweden, and subsequently in different parts of the world.
OBJECTIVE: The aim of our study was to gain insight into the epidemiology of bocavirus in children with RTI in Greece.
METHODS: One hundred ten throat-swab samples were collected during the autumn and winter months of 2006–2007 from previously healthy children (aged 1 month to 13 years) who were hospitalized for RTI. DNA was extracted from the samples, and polymerase chain reaction was performed to amplify the *NS1* gene of the bocavirus genome. Polymerase chain reaction products were sequenced and compared with respective bocavirus sequences.
RESULTS: Bocavirus DNA was detected in 10 samples (9%). Comparison with previously identified bocavirus sequences showed a high degree of identity. Mean age of the children was 1.8 years (range: 2 months to 4 years). The most common symptoms were fever, cough, and various degrees of respiratory distress. A majority of the children (9 of 10) were clinically diagnosed as having lower RTI, mainly acute bronchiolitis and pneumonia.
CONCLUSIONS: This is the first report of human bocavirus infection in Greece, which suggests that the virus is spread worldwide, and it is associated with RTI in infants and young children.

GENETIC CHARACTERIZATION OF THE F PROTEIN OF RESPIRATORY SYNCYTIAL VIRUS STRAINS ISOLATED IN THE BEIJING, CHINA, AREA

Submitted by Qi Lu

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INTRODUCTION: Respiratory syncytial virus (RSV) is the most common viral pathogen for lower respiratory tract infection among young children. However, pathogenic mechanisms and molecular characteristics of RSV are still not completely understood, so the development of an effective vaccine has been hindered. F protein has been shown to be a potential RSV subunit vaccine candidate, so the study on genetic characteristics of F protein may be important for further investigation.
OBJECTIVE: Our goal was to determine the genetic characteristics of the F protein.
METHODS: Seventy-six strains of human RSV were isolated from 2001 to 2004 in Beijing, China, of which 6 representative strains were chosen.
RESULTS: Among the 6 Beijing isolates, 4 belonged to subgroup A. The F gene of the isolates shared 97.0% to 97.4% nucleotide sequence identity and 92.1% to 93.0% amino acid sequence identity. They were highly homologous with GenBank Nos. AY198175, AY198176, and AY198177 (China Hebei). The other 2 isolates belonged to subgroup B, and 97.3% and 98.2% sequence identity was seen at nucleotide and amino acid levels, respectively. The nucleotide sequences of subgroup B showed the highest identities with GenBank Nos. NC001781 and AF013254. Phylogenetic analysis of nucleotide sequences revealed that those 4 within group A were monophyletic and closely related to each other, but those 2 within group B were distributed in 2 distinct clusters. AA200-225 and AA259-278 on the F gene are conservative between subgroups A and B.
CONCLUSIONS: Subgroup A and B strains cocirculated, which indicates that there were different transmission chains in Beijing from 2001 to 2004. AA200-225 and AA259-278 are potential segments to develop an effective vaccine in Beijing or even in China.

SEROEPIDEMIOLOGY OF HEPATITIS A IN GREEK CHILDREN

Submitted by Vassiliki Papaevangelou

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INTRODUCTION: Hepatitis A is a vaccine-preventable disease with epidemiology that has changed over the past decades. In Greece, the vaccine has been available and recommended, but no universal mass vaccination has been implemented as yet.
OBJECTIVE: We sought to study the seroepidemiology of hepatitis A in Greek children.
METHODS: The seroepidemiology of hepatitis A in children 0 to 14 years of age living in Greece was studied. We collected 100 sera per year of age, stratified by geographic region. Demographic data and documented

hepatitis A vaccine history was entered into a specially designed anonymous database. Sera were tested for the presence of anti–hepatitis A virus immunoglobulin G antibodies (AxSYM, Abbott Laboratories, Hellas, Greece).
RESULTS: Data from 948 children analyzed revealed that 40.7% of the children had received at least 1 dose of hepatitis A vaccine. To date we have examined 498 sera. Among fully vaccinated children who had received at least 2 doses of vaccine, 91.2% were immune. The overall prevalence of anti–hepatitis A virus antibodies in unvaccinated children was 15.4%. In unvaccinated children >12 months of age, the rate of natural immunity was 11.7% (33 of 282). Interestingly, neither age nor ethnicity were associated with higher rates of natural infection. Among unvaccinated infants, the rate of passively maternal antibodies was surprisingly high (15 of 30 [50%]), mainly because of children from immigrant or Gypsy families, reflecting maternal natural infection.
CONCLUSIONS: The implementation of universal vaccination against hepatitis A in Greece should be discussed because, according to our results, 11.7% of unvaccinated children have serologic evidence of past natural infection.

SOCIAL FACTORS ASSOCIATED WITH CHILD ABUSE AND NEGLECT IN GUADALAJARA, MEXICO

Submitted by Maria Guadalupe Vega-Lopez
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INTRODUCTION: Cases of child abuse and neglect have increased in Mexico, but few studies have been carried out to examine the factors associated with this health problem.
OBJECTIVE: With this study we sought to identify social factors associated with child abuse and neglect and to construct a predictor model of child maltreatment in children younger than 7 years in Guadalajara, Mexico.
METHODS: A case-control study was designed; cases were selected randomly from the register of maltreated children younger than 7 years by the DIF (the public institution that provides assistance to families in Mexico) during 2002 ($N = 205$). Controls were chosen randomly from the register of children assisted in other DIF programs in 2002 ($N = 379$). A multivariate logistic regression model was used to estimate odds ratios (ORs) with 95% confidence intervals (CIs).
RESULTS: In the multivariate analysis, 6 factors were statistically associated with child maltreatment: maternal drug addiction (OR: 15.3 [95% CI: 1.8–127.6]), mother without steady partner (OR: 3.0 [95% CI: 1.9–4.6]), bad family relationships (OR: 1.3 [95% CI: 1.1–4.2]), the child has "tantrums" (OR: 1.8 [95% CI: 1.2–2.8]), the child's behavior irritates the parents (OR: 1.5 [95% CI: 1.1–2.1]), and overcrowding (OR: 1.5 [95% CI: 1.1–2.2]).
CONCLUSIONS: According to the constructed model, if a child were simultaneously exposed to all these risk factors, he or she would have a very high probability of being a maltreated child. The findings show that public health institutions can play an important role in designing timely intervention strategies directed at avoiding or reducing the cases of child abuse and neglect.

Gastroenterology, Hepatology, and Nutrition

EFFECT OF COBALAMIN SUPPLEMENTATION IN INFANTS: A RANDOMIZED, CONTROLLED TRIAL

Submitted by Anne-Lise Björke Monsen
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INTRODUCTION: A metabolic profile that suggests impaired cobalamin status is prevalent in breastfed infants. Whether this profile reflects immature organ systems or cobalamin deficiency has not been clarified.
OBJECTIVE: Our goal was to study serum cobalamin levels in breastfed infants.
METHODS: This study included 107 apparently healthy infants who at the age of 6 weeks were randomly assigned to receive either an intramuscular injection with 400 μg of cobalamin or no intervention. Concentrations of cobalamin and folate in serum and total homocysteine (tHcy), methylmalonic acid (MMA), and cystathionine in plasma were determined at inclusion and at the age of 4 months.
RESULTS: There was no significant difference in the concentrations of any vitamin marker between those in the intervention ($n = 54$) and control ($n = 53$) groups at 6 weeks ($P = .20–.78$). At the age of 4 months, infants who were given cobalamin had 75% higher serum cobalamin levels than those of controls. The intervention was associated with a remarkable reduction in median plasma tHcy (from 7.46 to 4.57 μmol/L) and MMA (from 0.58 to 0.20 μmol/L) ($P < .001$) levels, whereas both metabolite levels were essentially unchanged during follow-up in the control-group infants.
CONCLUSIONS: Cobalamin supplementation of infants changed all markers of impaired cobalamin status (low cobalamin, high MMA and tHcy, and slightly ele-

vated folate concentrations) toward a profile observed in cobalamin-replete older children and adults. Thus, high MMA and tHcy levels, reported for a large fraction of infants, do not reflect immature metabolism but, rather, insufficient cobalamin to fully sustain cobalamin-dependent reactions. Clinicians and researchers should address the possible developmental and clinical consequences of metabolic evidence of cobalamin deficiency in infants.

CENTRAL OBESITY IS THE MAJOR RISK FACTOR FOR FAILURE OF OBESITY MANAGEMENT DURING CONSOLIDATION PHASE IN CHILDREN

Submitted by Adel El Tajuri
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INTRODUCTION: A proportion of obese children who are treated with a multidisciplinary approach with behavior modification and parental involvement show no response to the consolidation phase of treatment.
OBJECTIVE: Our goal was to identify possible risk factors that led to failure of obesity management in children who were attending an equipped, busy, specialized outpatient clinic.
METHODS: We performed a case-control study in which cases were those whose conditions failed to respond to current multidisciplinary management as judged by no decrease in BMI *z* score. Controls were those who responded to treatment (lower subsequent BMI *z* scores).
RESULTS: Of the 519 children, 416 (80.2%) had BMI *z* scores of >3. Management was successful in 85% of the patients. In bivariate analysis, risk factors were age of <4 years (odds ratio [OR]: 4.00 [95% confidence interval (CI): 1.08–14.70]), previous obesity management (OR: 2.18 [95% CI: 1.10–4.32]), triglyceridemia (OR: 2.01 [95% CI: 1.10–3.65]), and higher abdominal fat content as measured directly by dual-energy radiograph absorptiometry (OR: 1.09 [95% CI: 1.00–1.19]) or relative to thigh (waist/hip index) (OR: 2.67 [95% CI: 1.13–6.72]). Duration of obesity, the initial BMI *z* score, and gender were not predictive of treatment failure. In multivariate analysis, central obesity was the single-most important factor. In more hierarchical conceptual framework, factors retained were maternal obesity (OR: 2.44 [95% CI: 1.22–4.86]), previous management of obesity (OR: 2.21 [95% CI: 1.11–4.37]), and waist/hip index (OR: 3.35 [95% CI: 1.18–9.49]).
CONCLUSIONS: We propose a model in which centrally obese children with obese mothers who have high triglyceride levels are more likely to show resistance to reversal of the pathologic process of excess fat accumulation. Central obesity is a well known correlate of increased morbidity.

NUTRITIONAL STATUS IN CYSTIC FIBROSIS

Submitted by Maria Fotoulaki
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OBJECTIVE: We aimed to investigate the nutritional status of patients with cystic fibrosis (CF) in relation to their clinical manifestations.
METHODS: In 68 patients with CF (aged 2–38 years), body weight, height, and composition (bioelectrical impedance analysis), respiratory function, *Pseudomonas* colonization, pancreatic function, CF-related diabetes mellitus (CF-DM), and genotype were measured.
RESULTS: BMI was <5th percentile in 12 patients (18%), between the 5th and 10th percentiles in 6 (7%), between the 10th and 85th percentiles in 41 (60%), between the 85th and 95th percentiles (overweight) in 4 (6%), and >95th percentile (obese) in 5 (7%). Among 18 patients with a BMI at <10th percentile, 18 (100%) had pancreatic insufficiency, 16 (89%) had *Pseudomonas*, and 7 (38%) had CF-DM. Among 41 patients with a BMI in the 10th to 85th percentile, 37 (90%) had pancreatic insufficiency, 28 (82%) had *Pseudomonas*, and 9 (22%) had CF-DM. Among 9 patients with a BMI at >85th percentile, 3 (33%) had pancreatic insufficiency, 1 (11%) had *Pseudomonas*, and none had CF-DM. Forced expiratory volume in 1 second was significantly better among overweight patients than among patients with a low or normal BMI ($P < .05$). In addition, forced expiratory volume in 1 second correlated with BMI ($P = .014$), age ($P = .029$), and percent free fat mass ($P = .039$). Overweight/obese patients were homozygotes for mild mutations.
CONCLUSIONS: Most patients with CF had an optimal nutritional status. A small percentage were overweight or obese, especially those with pancreatic sufficiency and carriers of mild mutations. These patients had mild-to-moderate lung disease and were less likely to be colonized with *Pseudomonas* or have liver disease.

TRANSMISSION OF *HELICOBACTER PYLORI* INFECTION IN MOTHER-INFANT PAIRS

Submitted by Selda Fatma Hizel Bulbul
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INTRODUCTION: Various pathways, such as person-person, fecal-oral, and oral-oral transmission, play a role in transmission of *Helicobacter pylori* infection. It can be transferred from mother to infant in either the perinatal or postnatal periods.
OBJECTIVE: The aim of this prospective study was to determine the course of *H pylori* infection in mother-infant pairs in early years of life.
METHODS: Forty-eight mother-child pairs were followed for 12 months. *H pylori* and hepatitis A virus immunoglobulin G levels were measured in maternal sera, infant sera, and breast-milk samples at birth and in breast-milk samples and infant sera at follow-up visits.
RESULTS: At birth, the seropositivity for *H pylori* was 81.25% and hepatitis A was 68.75% in breast milk and 95.8% in maternal and infant sera for both microorganisms. Although there was a decrease in seropositivities for both agents in both infant sera and breast milk at the age of 9 months, an increase was observed in the twelfth month.
CONCLUSIONS: High seroprevalence rates of *H pylori* and hepatitis A virus and similar monthly changes in seroprevalence could be indicators of the same transmission routes.

IMPACT OF ZINC SUPPLEMENTATION ON GROWTH: A DOUBLE-BLIND, RANDOMIZED TRIAL AMONG URBAN IRANIAN SCHOOLCHILDREN

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INTRODUCTION: The first study that linked zinc and growth was carried out in Iran and Egypt almost 3 decades ago. At the time, the circumstances leading to growth impairment secondary to zinc deficiency were believed to be unique in less developed countries. Multiple studies have been carried out to assess the effect of zinc supplementation on children's growth. The results of these studies have been inconsistent.
OBJECTIVE: The aim of this study was to investigate the impact of zinc supplementation on growth (weight and height) among schoolchildren who were underweight or had stunted growth.
METHODS: Our study was a randomized, double-blind, placebo-controlled trial of 90 Iranian urban schoolchildren (50 boys and 40 girls; 7–12 years old) who were underweight or stunted and were supplemented with 10 mg of zinc or placebo on school days for 6 months. Variables were weight and height.
RESULTS: Significant effects on weight gain (2.037 ± 1.240 vs 1.55 ± 0.64 kg; $P = .0167$) and height (2.030 ± 1.003 vs 1.403 ± 0.521 cm; $P = .0002$) in the children after zinc supplementation versus placebo administration, respectively, were seen over the 6-month period.
CONCLUSIONS: On the basis of this study, zinc supplementation improved growth in underweight or stunted children and should be considered for populations at risk for zinc deficiency, especially where there are elevated rates of underweight or stunting.

TEL/AML1$^+$ ACUTE LYMPHOBLASTIC LEUKEMIA IN THE GREEK PEDIATRIC POPULATION

Submitted by Sophia Polychronopoulou
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INTRODUCTION: *TEL/AML1*$^+$ acute lymphoblastic leukemia (ALL) is considered to be a distinct nosological entity with excellent prognosis, but recent studies have indicated significant clinical heterogeneity.
OBJECTIVE: In this study, we attempted to estimate the incidence and clinical features of *TEL/AML1*$^+$ ALL for the first time in a representative cohort of Greek pediatric patients.
METHODS: One hundred twenty children (<16 years old) diagnosed with ALL (107 of B-cell origin, 13 of T-cell origin) were screened for *TEL/AML1* with interphase fluorescence in situ hybridization by using a commercial probe set. All patients were treated as either standard risk (SR) or high-risk (HR) cases according to a modified BFM-95 (Berlin-Frenkfurt-Munster) protocol. Follow-up ranged between 5 and 87 months (median: 45 months).
RESULTS: Twenty-six patient (all of them will ALL of B-cell origin [24.3%]) were found to be positive for *TEL/AML1*. The presence of *TEL/AML1* was significantly associated with younger age and lower white blood cell count at diagnosis but not with remission duration or overall survival rate. The number of children who relapsed (1 vs 7) or succumbed (1 vs 5) was comparable between the *TEL/AML1*$^+$ and *TEL/AML1*$^-$ groups of children with ALL of B-cell origin.
CONCLUSIONS: The incidence of *TEL/AML1* in Greece seems comparable to that in other European and Med-

iterranean countries. As in most European studies, the independent prognostic value of *TEL/AML1* is in doubt, because it is closely associated with other favorable factors. In this series, the modification of the therapeutic regimen (ie, omission of the SR arm) may be responsible for the similar outcome in *TEL/AML1*$^+$ and *TEL/AML1*$^-$ cases, because it seems to lower the relapse risk for all children with ALL.

BEHAVIORAL VARIABLES IN FUNCTIONAL DYSPEPSIA: THE TYPE A BEHAVIOR PATTERN, SYMPTOMS OCCURRENCE, AND EFFECTIVENESS OF PHARMACOLOGIC TREATMENT IN SCHOOL-AGED CHILDREN

Submitted by Igor Radziewicz-Winnicki
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INTRODUCTION: Functional dyspepsia (FD) is the most prevalent type of abdominal pain. Several organic disorders that result in FD have been identified, whereas psychological trials have suggested that patients with functional gastrointestinal disorders may present behavioral disorders simultaneously. Defining the relationship between common personality aspects, type A and/or type B behavioral patterns (TABPs/TBBPs), and coexisting symptoms as well as their change during FD treatment might be helpful in establishing focused therapy strategies, including appropriate psychological interventions.
OBJECTIVE: Our goal was to evaluate the grade of TABPs in children with FD and FD subtypes to reveal correlations of behavioral patterns and experienced symptoms and to assess the relationship between analyzed factors and symptom relief during therapy.
METHODS: A total of 66 children (aged 11–18 years) were diagnosed with FD following the Rome II criteria. The control group consisted of 86 healthy children who denied recurrent abdominal pain. In all children, severity of 10 dyspeptic symptoms was measured with the FACES Pain Rating Scale and the created visual-analog Dyspepsia Symptoms Questionnaire. Psychological evaluation was carried out by using the Type A/B Behavior Scale for Children and Adolescents (TAB) by Ogińska-Bulik and Juczyński. All patients received typical treatment for 4 weeks. After 8 weeks, children were asked to complete the symptoms questionnaires again.
RESULTS: The general TABP pattern was significantly decreased in the FD group compared with the controls ($P = .0016$), especially in boys. Moderate or extreme TABP was diagnosed in 4.2% of the boys with FD in comparison with 29.7% of the male controls; 66.7% of the boys with FD (vs 24.3% of the controls) and 37.2% of the girls with FD (vs 22.5% of the controls) met criteria for moderate or extreme TBBP. Boys with ulcer-like FD revealed scores lower than those of the controls on total TABP ($P < .001$) and all of the TABP subscales: competition, impatience, sense of time urgency, and hostility. Correlation analysis exposed the positive relationship between total TABP, competition, and hostility with dysmotility-like symptoms. Sense of time urgency and total TABP correlated negatively to the pain. During the therapy observation, hostility was conducive to increasing most of the dyspeptic symptoms ($P < .037$), and competition was related to the nausea release in boys and to aggravation of heartburn and feeling full long after eating in both genders. The sense of time urgency was related to belching intensifying.
CONCLUSIONS: The behavioral pattern varied in the FD and control groups. The children with FD were more likely to present a TBBP than TABP, which is strongly restricted, especially in boys with ulcer-like FD.

1. The TBBP constituents are connected to dysmotilities, whereas reduced TABP compounds are more common among pain-suffering patients.
2. Behavioral pattern influences efficacy of FD treatment: behavioral compounds centered on emotions are conducive to increase dysmotilities, whereas behaviors connected with defeating stress situations encourage pain-symptom aggravation.

DOES INTRAFAMILIAL SPREAD PLAY A ROLE FOR *HELICOBACTER PYLORI* INFECTION IN CHILDREN?

Submitted by Eleftheria Roma
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INTRODUCTION: Acquisition of *Helicobacter pylori* (Hp) infection in children occurs mainly in those under 5 years of age.
OBJECTIVE: Our aim was to investigate intrafamilial spread of Hp infection.
METHODS: One hundred symptomatic children without previous eradication treatment were investigated by gastroscopy and the ^{13}C-urea breath test (UBT). All family members of each index patient were investigated by using the UBT. Infected members were estimated according to UBT results, and for those members who were UBT-negative and had recently received eradication therapy after confirmation of infection by endoscopy, the previous positivity was taken into account.
RESULTS: Hp infection was identified in 44 (44%) of 100 symptomatic index children. There was no statistical

difference between Hp^+ and Hp^- index children concerning demographic factors except age, which was higher in Hp^+ index children ($P = .009$). In all Hp^+ index children (100%) and in 71.4% of Hp^- children, at least 1 more family member was infected ($P < .001$); in all cases (100%) at least 1 parent in the group of Hp^+ index children, compared with 69.6% in Hp^- index children ($P < .001$), was infected. The rate of infected siblings of the Hp^+ index children was 43.2%, and that in the Hp^- group was 3.6% ($P < .001$). There were more infected mothers in the Hp^+ index children group (83.7% vs 50% in the Hp^- group; $P = .001$) and more infected fathers (76.7% vs 56.4%, respectively; $P = .035$).

CONCLUSIONS: The identification of at least 1 more infected member in each family of Hp^+ index patients, including a parent in all cases, strongly indicates family as the main source of infection for children and confirms the hypothesis of intrafamilial spread of Hp.

THERAPEUTIC EFFECT OF A MAGNESIUM-ENRICHED FORMULA ON INFANTS WITH CONSTIPATION

Submitted by Yvan Vandenplas
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INTRODUCTION: Infant constipation is a frequent condition in formula-fed infants.

OBJECTIVE: Our goal was to study the effectiveness of magnesium-enriched formula in relieving constipation in infants.

METHODS: A prospective randomized, clinical trial was performed with infants with constipation fed with a magnesium-enriched formula, Novalac-IT (IT group) in comparison with 20% strengthened formula (S group). Enrolled subjects had difficulties with defecating, hard stools, or low frequency of defecation (≤4 times per week).

RESULTS: Ninety-three infants (47 boys; mean age: 3.8 ± 1.7 months) were included because of hard consistence of (50.5%), low frequency of (44.1%), and painful (33.3%) defecation. Statistically significant improvement was observed after 4 and 8 weeks of intervention in the IT group ($P = .014$ and $P < .001$, respectively). In the IT group, significantly more infants were symptom free at 4 weeks (82.9% vs 50%; $P = .029$) and 8 weeks (89.1% vs 54.1%; $P < .001$). Increase of stool weight was significant in the infants in the IT group after 4 and 8 weeks ($P = .048$ and .029, respectively).

CONCLUSIONS: A magnesium-enriched formula improves constipation in formula-fed infants.

DOUBLE-BLIND TRIAL OF FORMULA IN DISTRESSED AND REGURGITATING INFANTS

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INTRODUCTION: Many parents seek medical help because of frequent regurgitation and inconsolable crying of their formula-fed infant.

OBJECTIVE: We aimed to assess the effectiveness of special formulas in distressed and regurgitating infants.

METHODS: We included 12 consecutive infants in a prospective, randomized, single-blinded (parents), cross-over trial (6 infants were started on G1 [80/20 casein/whey, tapioca starch, and locust bean] for 2 weeks and then switched for 2 weeks to G3 [partial whey hydrolysate, tapioca starch, and locust bean]; for the other 6 infants, the order of the formulas was opposite). Infants were exclusively formula fed, were crying for >3 hours/day for at least 3 weeks, and regurgitated several times after each feeding. Before inclusion, all of them had been given ≥3 different commercialized AR formulae, formulae for digestive comfort, and at least 1 extensive hydrolysate without success. All infants had been treated without success with a prokinetic agent (domperidone/cisapride) and an acid-blocking drug (H2-receptor agonist/proton-pump inhibitor).

RESULTS: Gastric emptying time, as evaluated with a ^{13}C acetate breath test, was 117.1 ± 18.3 minutes with Novalac-AR (80/20 casein/whey and corn starch), 104.5 ± 15.5 minutes with G1, and 79.2 ± 14.0 minutes with G3 ($P < .001$ [Friedman test]). The mean number of regurgitations per day was 5.1 ± 1.2 with G1 and 1.8 ± 1.2 with G3 ($P = .002$). Quality of life, as assessed by the parents in a diary, was 4.20 ± 1.79 with G1 and 2.10 + 0.74 with G3 ($P = .005$). The mean duration of crying per day was 84.5 ± 50.1 minutes with G1 and 26.7 ± 18.1 minutes with G3 ($P = .003$).

CONCLUSIONS: The cross-over design protected for bias. G3 scored better than G1 for all parameters evaluated and decreased regurgitation and infant distress significantly.

General Pediatrics

PEDIATRICIANS' AWARENESS OF AND ATTITUDES ABOUT OTITIS MEDIA: RESULTS OF A MULTINATIONAL SURVEY

Submitted by Adirano Arguedas
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INTRODUCTION: Otitis media (OM) is a common problem in primary care and constitutes a significant health burden in <5-year-olds. Middle-ear effusion after acute OM is also a common problem that causes hearing loss in a substantial proportion of children and is a frequent reason why primary care providers refer children to specialists. However, there are limited non-US data on pediatricians' awareness and attitudes toward OM disease burden, complications, and causative pathogens.

OBJECTIVE: A multinational survey was undertaken to validate and measure primary care physicians' attitudes and behaviors toward OM.

METHODS: Two thousand pediatricians from 10 countries (4 European, 3 Asian, 2 Latin American, and 1 Middle Eastern) were interviewed. Questions focused on the number of children younger than 5 who were treated for OM in the previous year, perceptions about complications and sequelae, awareness of OM pathogens, and concerns about current disease-management practice.

RESULTS: Reported estimates of OM in <5-year-olds was 349 (range: 125–1000) cases per year per practice (ie, pediatricians treated at least 1 patient with OM per day). Eighty-two percent of the pediatricians reported that they treat OM with first-line antibiotics; they were generally satisfied but viewed antibiotic resistance as a serious issue. Nineteen percent of children were referred to an ear, nose, and throat specialist because of treatment failure, recurrent/chronic OM, or hearing problems or for surgery. Pediatricians associated OM with 2 main pathogens: *Streptococcus pneumoniae* (77%) and *Haemophilus influenzae* (73%). Association of nontypeable *H influenzae* was significantly lower (40%).

CONCLUSIONS: OM is frequently treated by pediatricians in daily practice. A majority of them seem to use antibiotics as first-line treatment. The most common reasons for specialist referrals include treatment failures, recurrent/chronic OM, hearing problems, and surgery. Hearing loss and antibiotic resistance are of concern. Nontypeable *H influenzae* is less well known as an otopathogen.

ASSESSMENT OF DIFFERENCES BETWEEN THE NEW WORLD HEALTH ORGANIZATION CHILD-GROWTH STANDARDS AND THE CENTERS FOR DISEASE CONTROL AND PREVENTION 2000 GROWTH CHARTS IN LATIN AMERICAN CHILDREN: WHICH REFERENCE SHOULD WE USE?

Submitted by Daniel Fuentes Lugo

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INTRODUCTION: Evaluation of growth patterns significantly depends on the reference used. Last year the World Health Organization (WHO) released new standards for assessing child growth during the first 5 years of life.

OBJECTIVE: Our goal was to assess differences between the 2000 Centers for Disease Control and Prevention (CDC) growth charts and 2006 WHO growth standards.

METHODS: A longitudinal study was conducted on a sample of 300 healthy children (167 boys and 133 girls) from a pediatric outpatient clinic in Mexico City. Weight-for-age *z* score, length/height-for-age *z* score, and weight-for-length/height *z* score were obtained yearly from birth to age 5 and compared by using the 2000 CDC growth charts and 2006 WHO growth standards.

RESULTS: Significant statistical differences were found at all ages in both genders. Main differences were found in early-infancy weight-for-age *z* scores. The prevalence of girls who were undernourished at birth was 3 times higher with the CDC reference than with that of the WHO (13.53% vs 4.50%, respectively), but the opposite was found for boys (2.99% vs 9.58%, respectively). During the first 4 years of life, a higher prevalence of length/height-for-age *z* scores less than −2.0 was found in both boys (10.77%) and girls (4.51%) when using WHO standards as opposed to the CDC charts. Furthermore, at the age of 5 years, obesity was significantly higher in girls according to WHO standards than in boys according to the CDC charts, although the CDC reference failed to detect a fast rate of weight gain in early infancy.

CONCLUSIONS: The new WHO standards are a better tool than the CDC charts for monitoring growth and detecting early overweight in Latin American children. Therefore, using this new international reference in daily clinical practice in our countries should be emphatically encouraged.

CHILDREN WITH PERSISTENT WHEEZING ASSOCIATED WITH HUMAN BOCAVIRUS INFECTION IN CHINA

Submitted by Enmei Liu

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INTRODUCTION: Human bocavirus (HBoV) is a newly identified human parvovirus that was originally

isolated from children with lower respiratory tract disease. The impact of HBoV on childhood persistent wheezing has not been identified.
OBJECTIVE: Our aim was to study the impact of HBoV on childhood persistent wheezing.
METHODS: In this study, a total of 40 tracheal aspirates were obtained by bronchofibroscope from children with persistent wheezing who had been wheezing for at least >4 weeks. HBoV was detected by polymerase chain reaction. A rapid immunofluorescence method was used for diagnosis of respiratory syncytial virus, adenovirus, influenza A and B, and parainfluenza 1, 2, and 3.
RESULTS: In 40 children with persistent wheezing, 13 (32.5%) had DNA sequences that were HBoV-positive. Age of the patients with HBoV-positive infection ranged from 1 month to 2 years. The results of polymerase chain reaction products sequencing proved that these 13 samples were exactly identical to the sequence of HBoV published in GenBank (accession Nos. DQ988934 and DQ457413). Two children with HBoV infection were found to have coinfection with respiratory syncytial virus.
CONCLUSIONS: This study confirmed that HBoV is a common pathogen for children with lower respiratory infection and might particularly be attributed to persistent wheezing. However, more studies should be performed to study the mechanism of HBoV on chronic airway inflammation.

THE CHILDREN IN DISASTERS PROJECT: ADDRESSING THE SPECIAL NEEDS OF CHILDREN IN MAN-MADE AND NATURAL DISASTERS

Submitted by Karen Olness
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INTRODUCTION: Natural and man-made disasters have increased dramatically over the past 15 years. Children are the most vulnerable population in disasters and suffer acute and long-term physical and psychological damage. In 2005, there were 17 million children displaced from their homes as a result of humanitarian emergencies.
OBJECTIVE: The Children in Disasters Project of the Rainbow Center for Global Child Health aims to reduce the traumatic acute and long-term effects of disasters for children by providing training to health professionals and relief workers, both in the United States and around the world, on how to recognize and respond to the special needs of children in disasters.
RESULTS: Since 1996 the project has provided intensive, interactive, 5-day training programs entitled "Management of Complex Humanitarian Emergencies: Focus on Children and Families." These were the first programs to emphasize that children need special attention in disasters. This course has been replicated with colleagues in 9 countries and has trained 980 people to help care for disaster-affected children. Course evaluations have been excellent, and trainees have done well in disaster work.
CONCLUSIONS: Because of ongoing humanitarian emergencies, there is a need to continue training relief workers about the special needs of children.

PROBIOTICS REDUCE INCIDENCE AND DURATION OF RESPIRATORY TRACT INFECTION SYMPTOMS IN 3- TO 5-YEAR-OLD CHILDREN

Submitted by Arthur Ouwehand
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INTRODUCTION: Probiotics are live microorganisms that have a beneficial effect on the host.
OBJECTIVE: Our aim was to investigate whether consumption of probiotics would be able to reduce symptoms of respiratory tract infections during the winter season.
METHODS: Children aged 3 to 5 years were recruited and randomly assigned to 1 of 3 groups to receive placebo (n = 92), *Lactobacillus acidophilus* NCFM (NCFM) (n = 77), or a combination of *L acidophilus* NCFM and *Bifidobacterium lactis* Bi-07 (NCFM+Bi-07) (n = 79). Probiotics were consumed daily at a dose of 10^{10} colony-forming units for 6 months from November to April. The study was performed in Shanghai, China, and approved by the local authorities.
RESULTS: The incidence of fever was reduced by 63% in the NCFM+Bi-07 group and by 48% in the NCFM group. Cough was reduced by 54% in the NCFM+Bi-07 group and by 42% in the NCFM group. Runny nose was reduced by 44% in the NCFM+Bi-07 group and by 9% in the NCFM group; the latter result was not significant. Antibiotic use was reduced by 80% in the NCFM+Bi-07 group and by 68% in the NCFM group. Children in the placebo group had, on average, 6.5 days with symptoms, those in the NCFM group had 4.5 days with symptoms, and those in the NCFM+Bi-07 group had 3.4 days with symptoms.
CONCLUSIONS: Daily consumption of NCFM and Bi-07 and of NCFM alone significantly reduced the incidence and duration of respiratory tract infection symptoms in children. The combination of the 2 probiotics tended to perform better than the NCFM alone.

PREVALENCE AND INCIDENCE OF A NEWLY DEFINED TYPE OF DIABETES IN CHILDREN, ADOLESCENTS, AND ADULTS IN THE LARGEST INTERNATIONAL SERIES TO DATE

Submitted by Annabelle S. Slingerland

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INTRODUCTION: Recently, interest in "neonatal" diabetes has increased because patients could stop taking insulin and improve glycemic control and associated neurologic features.
OBJECTIVE: Our objective was to determine the anticipated increase in prevalence and incidence of permanent neonatal diabetes in children, adolescents, and adults and investigate the impact of the new definition.
METHODS: We studied 293 (53% male) referrals to the Exeter Laboratory (Devon, United Kingdom) as part of the largest international series to date. The referred patients were diagnosed with diabetes below 6 months of age irrespective of current age, and their conditions had not remitted at the time of study. Data on 27 countries were collected, and age of diagnosis, date of birth, and gender were obtained from standardized forms. All referred patients were tested for *KCNJ11* mutations.
RESULTS: The minimum observed prevalence of the 5 most representative countries was 1.17 (1.01–1.31) per million population, with the estimated true prevalence twice as high. Prevalence was higher for the pediatric versus adult age range (odds ratio: 0.78 [95% confidence interval: 0.54–1.31] vs 0.42 [95% confidence interval: 0–0.50], respectively; $P = .009$). Seventy-five percent of the patients were below 16 years of age with a median (interquartile range) of 5.7 (2.4–10.2) years, which implies underdiagnosis beyond 5 years of age. Age of diagnosis was skewed to a median (interquartile range) of 6 (1–13) weeks, with 62% in the first 8 weeks. During 2000–2004, the minimum observed incidence was 2.95 (0–49.1) per million live births.
CONCLUSIONS: This is the first report to show 2 to 25 times higher prevalence than previous reports from 10 years ago. "Neonatal" should be changed to "diagnosed at <6 months of age irrespective of current age," and awareness should be increased, especially for those who are older than 5 years and present with treatment implications.

Genetics

IDENTIFICATION OF 7 NOVEL TRANSFORMING GROWTH FACTOR β RECEPTOR 2 MUTATIONS IN CHINESE PATIENTS WITH MARFAN SYNDROME

Submitted by Hon Yin Brian Chung

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INTRODUCTION: Marfan syndrome (MFS) (Online Mendelian Inheritance in Man [OMIM] No. 154700) is an autosomal-dominant connective tissue disorder that affects multiple systems including the cardiovascular, ocular, and musculoskeletal systems. Fibrillin 1 (FBN1) (OMIM No. 134797) mutations are causative in >90% of the cases, and recent studies have shown that transforming growth factor β receptor 2 (*TGFBR2*) (OMIM No. 190182) mutations could be identified in ~10% of non-*FBN1* probands (Mátyás G, Arnold E, Carrel T, et al. *Hum Mutat*. 2006;27:760–769).
OBJECTIVE: Our objective was to examine the mutation spectrum of *TGFBR2* in non-*FBN1* Chinese patients with MFS and related phenotypes.
METHODS: All Chinese probands who were referred for evaluation of MFS and tested negative for *FBN1* mutations were included. Mutational screening was performed by denaturing high-pressure liquid chromatography (Kosaki K, Udaka T, Okuyama T. *Mol Genet Metab*. 2005;86:117–123). Amplicons with an abnormal elution pattern were selected for direct sequencing.
RESULTS: Seven novel mutations were identified in 7 of 41 probands. All of them had prominent cardioskeletal phenotypes without ocular or dural involvement, which confirmed previous findings (Disabella E, Grasso M, Marziliano N, et al: *Eur J Hum Genet*. 2006;14;34–38). Six mutations were missense (R190H, D247V, T325P, G357R, I510N, and T530I), and 1 was frameshift (P501fsX17). Except for R190H, all were found in the functionally important kinase domain. Bioinformatic analyses showed that (1) all mutations occurred in conserved positions by cross-species comparison between 6 orthologs, and (2) R190H, T325P, T530I, and G357R were also found in conserved positions among 3 paralogs (*TGFBR1* and activin receptors AVR2A and AVR2B) in the TGFBR superfamily. None of the 7 were found in 50 unaffected individuals (100 normal alleles). With the *TGFBR2* mutations, 4 additional probands would fulfill the diagnostic criteria of MFS.
CONCLUSIONS: *TGFBR2* mutation was identified in 17% of our non-*FBN1* probands. It should be considered in the evaluation for MFS after *FBN1* screening, especially if there are compatible clinical features.

MUTATIONAL ANALYSIS OF *PTPN11* AND *KRAS* GENES IN TAIWANESE CHILDREN WITH NOONAN SYNDROME

Submitted by Fu-Sung Lo

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INTRODUCTION: Noonan syndrome (NS) is an autosomal-dominant disorder that presents with a characteristic face, short stature, skeletal anomalies, and congenital heart defects. Protein-tyrosine phosphatase nonreceptor-type 11 (*PTPN11*), encoding SHP-2, mutation was the first reported gene involved and accounted for 31% to 60% of cases of NS. The *KRAS* gene was the second reported gene and was recently identified in a small number of patients with NS.
OBJECTIVE: Our goal was to perform mutational analysis of *PTPN11* and *KRAS* genes in children with NS.
METHODS: In this study we screened for mutation of the *PTPN11* and *KRAS* genes in 73 Taiwanese patients with NS. The mutation analysis of the 15 coding exons and exon/intron boundaries was performed by polymerase chain reaction and direct sequencing of the *PTPN11* gene. The mutation analysis of 5 coding exons and exon/intron boundaries was performed by polymerase chain reaction and direct sequencing of the *KRAS* gene. We identified 12 different missense *PTPN11* mutations in 15 (21%) patients with NS and 2 different missense *KRAS* (V14I and I36M) mutations in 2 (3%) patients with NS. These *PTPN11* gene mutations were clustered in exon 3 ($n = 6$) encoding the N-SH2 domain and 13 ($n = 5$) encoding the PTP domain.
CONCLUSIONS: This study provides support that *PTPN11* and *KRAS* mutations are responsible for NS in Taiwanese patients.

SCREENING OF MUTATIONS IN THE *NPHS2* GENE IN GREEK PATIENTS WITH AUTOSOMAL-RECESSIVE STEROID-RESISTANT NEPHROTIC SYNDROME

Submitted by Spyridon Megremis

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INTRODUCTION: Mutations in the *NPHS2* gene, encoding podocin, are a major cause of autosomal-recessive steroid-resistant nephrotic syndrome (SRNS) in childhood and have been observed in 6.4% to 30% of sporadic and 20% to 40% of familial cases.
OBJECTIVE: We investigated mutations in the coding region of the *NPHS2* gene in Greek patients with SRNS and identified a novel A295T mutation.
METHODS: The study included 16 child patients with SRNS (14 families); 11 cases were sporadic, and 5 (from 3 families) were familial. All 8 exons of *NPHS2*, including intron boundaries, were screened for sequence variations by using denaturing gradient gel electrophoresis followed by specific characterization using direct DNA sequencing.
RESULTS: The results revealed 2 pathogenic genotypes in 2 patients with sporadic SRNS (R138Q/R138Q and R229Q/A295T). In addition, 3 previously described *NPHS2* intronic polymorphisms (IVS3–46C→T, IVS3–21C→T, and IVS7+7A→G), 1 thus-far-unreported intronic variant (IVS3–17C→T), and 4 known silent mutations (G34G, S96S, A318A, and L346L) were detected in sporadic and familial cases as well as in healthy controls.
CONCLUSIONS: These findings indicate that *NPHS2* mutations are not a frequent cause of familial SRNS in Greek patients. Among patients with sporadic SRNS, the genotypes R138Q/R138Q and R229Q/A295T account for an allelic frequency of 18.2%. The R138Q mutation is well characterized. The novel mutation, A295T (883G→A), is predicted in silico to cause a structural alteration in the cytoplasmic domain of podocin (see the PolyPhen database at http://genetics.bwh.harvard.edu/pph). This is the first report of *NPHS2* mutations in the Greek population and the first description of the A295T amino acid substitution.

CLINICAL STUDIES AND ANALYSIS OF THE RETT SYNDROME GENE (*MECP2*) IN CHILDREN WITH MENTAL RETARDATION IN THE GREEK POPULATION

Submitted by Stavroula Psoni

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INTRODUCTION: Mutations in the methyl CpG-binding protein 2 (*MECP2*) gene are responsible for 70% to 95% of cases of Rett syndrome (RS), an X-linked dominant neurodevelopmental disorder that mostly affects girls. Classical RS is characterized by normal early development followed by psychomotor regression and gradual onset of microcephaly, although variable atypical forms have also been observed. *MECP2* has also been implicated in a variety of other mental retardation (MR) phenotypes, including X-linked MR, fragile X syndrome–like and Angelman syndrome (AS)–like phenotypes.
OBJECTIVE: Our goals were to evaluate the incidence and spectrum of *MECP2* mutations in children with RS

and atypical MR and to correlate the phenotype and genotype.

METHODS: Exons 3 and 4 of the *MECP2* gene were analyzed by using denaturing gradient gel electrophoresis, sequencing, and gap polymerase chain reaction for (1) 124 children with FXS-like symptoms (102 boys, 22 girls) and 41 children with AS-like symptoms (14 boys, 27 girls) who tested negative for gene variation at the FXS and AS loci, respectively, (2) 23 girls with classical RS and 25 girls with atypical RS, and (3) 11 boys who were referred with possible RS. Statistical analysis (*t* and nonparametrical tests) included correlation of RS clinical severity score (Kerr, 2001) with *MECP2* mutations and frequency of *MECP2* mutations in the various patient categories.

RESULTS: Mutations were detected in 78.3% of classical and 20% of atypical RS cases, respectively. One boy carried the p.R106W mutation, and another boy showed a large rearrangement that required further characterization. Among AS- and FXS-like cases, 7.3% and 2.4% had *MECP2* mutations, respectively, including an X-linked MR case.

CONCLUSIONS: *MECP2* gene analysis provides an appropriate diagnostic tool for RS and contributes additional information for research into MR.

Hematology and Oncology

ASSESSMENT OF BONE MINERAL DENSITY AND MARKERS OF BONE TURNOVER IN CHILDREN UNDERGOING LONG-TERM ORAL ANTICOAGULANT THERAPY

Submitted by Maria Avgeri

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INTRODUCTION: Oral anticoagulants antagonize vitamin K action and potentially impair the carboxylation of osteocalcin, a protein that is essential for normal bone matrix formation.

OBJECTIVE: Our aim was to evaluate bone mineral density (BMD) and bone-turnover markers in 23 children who were undergoing long-term oral anticoagulant therapy (median age: 4 years) and 25 age- and gender-matched controls.

METHODS: BMD (characterized as a *z* score) of the lumbar spine was assessed by using dual energy radiograph absorptiometry. Osteoblast (bone alkaline phosphatase, osteocalcin, and amino-terminal procollagen 1 extension peptide) and osteoclast (urinary calcium and deoxypyridinoline and serum cross-linked C telopeptide) activity markers were measured. Vitamin D (25-hydroxy vitamin D, parathyroid hormone, whole and ionized calcium, phosphorus, and magnesium) and vitamin K (factors II, VII, IX, and X, protein C, protein S, and undercarboxylated osteocalcin [Glu-Oc]) statuses were determined.

RESULTS: Patients presented with higher levels of Glu-Oc, parathyroid hormone, and bone-resorption markers and lower levels of bone-formation markers and 25-hydroxy vitamin D; 52% of them showed signs of osteopenia ($-1.0 >$ BMD *z* score > -2.5). Statistical analysis demonstrated that anticoagulant therapy was an independent predictor of alterations in Glu-OC, osteocalcin, bone alkaline phosphatase, amino-terminal procollagen 1 extension peptide, and serum cross-linked C telopeptide levels.

CONCLUSIONS: Long-term use of coumarin derivatives may cause osteopenia in children with the risk of developing osteoporosis later in life.

IN VITRO ASSESSMENT OF MESENCHYMAL STROMAL CELL CHARACTERISTICS: IMPLICATIONS FOR THEIR CLINICAL USE

Submitted by Helen Dimitriou

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INTRODUCTION: Bone marrow (BM) stroma represents a source of progenitor stromal cells, termed mesenchymal stromal cells (MSCs), which are multipotent and can differentiate into cartilage, bone, and adipose tissue. Several questions have arisen regarding their long-term expansion and their safety before use.

OBJECTIVE: Our goal was to assess the long-term expansion and safety of MSCs in clinical practice.

METHODS: MSCs from BM of children with benign hematologic disorders and solid tumors without BM involvement were isolated and cultured for 10 consecutive passages (P). Immunophenotypic and functional characteristics, apoptosis, and the expression of cell cycle regulatory genes (*p53*, *p16*, and *Rb*) and signal transduction genes (*H-Ras*) involved in oncogenesis were assessed.

RESULTS: MSCs expressed mesenchymal-related surface antigens, >85% from P1. They had the ability to differentiate into osteocytes, adipocytes, and chondrocytes (reverse-transcription polymerase chain reaction). Colony forming units (fibroblast) ranged from 40.71 ± 4.3 at P1 to 15.5 ± 6.7 at P10. Their doubling time was 2.01 ± 0.14 days at P1 and 3.5 ± 1.19 days at P9. A low

percentage of apoptotic cells was detected (7-aminoactinomycin D [7AAD]) at P2 until P10. MSCs were resistant to apoptosis under serum-deprivation conditions. The expression of the cell cycle genes studied was not statistically different compared with controls, and cells did not grow on soft agar.

CONCLUSIONS: MSCs isolated from BM of children retain their characteristics for a serial number of passages and survive under serum-deprivation conditions, a necessary process in a transplantation setting. The cells do not have oncogenic properties, as shown by normal expression levels of oncogenes and tumor suppressor genes, and no growth on soft agar. These findings enhance the use of MSCs in clinical applications.

NDRG1 EXPRESSION IN CHILDHOOD LEUKEMIA AND ITS CORRELATION TO PROGNOSIS AND THERAPEUTIC RESPONSE

Submitted by Ju Gao

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INTRODUCTION: N-myc downstream regulated gene 1 (*NDRG1*) gene expression has been found to be downregulated in a variety of solid tumors and is now regarded as a suppressor gene. However, little is known about its possible role in hematologic cancers.

OBJECTIVE: Our goal was to study expression of the *NDRG1* gene in childhood leukemia and explore a possible correlation between expression and prognostic factors.

METHODS: Bone marrow or peripheral blood mononuclear cells from 65 children with leukemia and peripheral blood mononuclear cells from 12 healthy control children were isolated: *NDRG1* messenger RNA expression was determined by fluorescence real-time polymerase chain reaction.

RESULTS: *NDRG1* messenger RNA expression in acute leukemia groups collectively (acute lymphocytic leukemia [ALL] [41 cases] and acute monocytic leukemia [24 cases]) was significantly lower than that of normal controls (normalized ratios of *NDRG1* to glyceraldehyde-3-phosphate dehydrogenase copy numbers were 0.27 and 0.25 vs 0.30 and 0.86 in controls, respectively; $P < .01$), although there was no statistically significant difference between the ALL and acute monocytic leukemia groups. *NDRG1* expression was significantly lower in prednisone nonresponder ALL (13 cases) than in prednisone good-responder ALL (15 cases) (normalized ratios: 0.13 and 0.38, respectively). Similarly, *NDRG1* expression was significantly downregulated in high-risk ALL (17 cases) than that in lower-risk ALL (24 cases) (normalized ratios: 0.15 and 0.30, respectively).

CONCLUSIONS: *NDRG1* expression was remarkably downregulated in childhood leukemia, as in other human solid tumors. In addition, its expression in childhood ALL was closely associated with such prognostic factors as prednisone response and risk stratification. Our research suggests that *NDRG1* expression is negatively correlated to ALL prognosis and therapeutic response.

IMMUNE STATUS AND IMMUNE RECOVERY IN CHILDREN WITH LYMPHOMA AT THE END OF THERAPY (CHEMOTHERAPY AND/OR RADIOTHERAPY) AND IN FOLLOW-UP EVALUATIONS

Submitted by Helen Kosmidis

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OBJECTIVE: We aimed to evaluate the immune status and immune recovery after completion of chemotherapy and/or radiotherapy in children with lymphoma.

METHODS: We prospectively evaluated humoral and cellular immunity in 22 children with lymphoma (11 with Hodgkin's disease [HD] and 11 with non-Hodgkin's lymphoma [NHL]) at the completion of therapy and every 6 months thereafter.

RESULTS: Immunoglobulin (Ig) levels were normal before the onset of therapy in all but 1 child. At the end of therapy, Ig levels decreased: IgM in 18, IgG in 12, and IgA in 7 children. In addition, 17 of 22 had decreased CD19 levels. In HD after radiotherapy, IgG and CD19 levels increased significantly ($P = .013$ and .004, respectively). IgM levels remained abnormally low in 16 of 22 children up to 18 months after therapy completion. At the end of therapy, helper T lymphocyte (CD4) levels were low in 20 of 22 children, and suppressor (CD8) levels were elevated in 13 of 22 children. (For those with HD before radiotherapy, the CD8 level was high in 10 of 11 children, and the CD4 level was low in 6 of 11 children.) The suppressor CD8 level remained elevated in 12 of 20 children, and helper CD4 level remained abnormally low in 18 of 20 children for a period of 6 to 18 months after therapy. Some immunized children became nonimmune to polio (15 of 22), mumps (6 of 22), rubella (5 of 22), and measles (1 of 22).

CONCLUSIONS: In children with lymphoma, IgM levels remained low for long periods. Helper T lymphocyte levels were low and suppressor levels were

high at the end of therapy. Suppressor cells normalized faster, whereas helper cell levels remained abnormally low for a long period. Most children became nonimmune to polio, whereas the majority had antibodies to measles, mumps, and rubella. Despite depressed immunity, serious infections were not documented.

SUPPRESSION OF THE OLIVOCOCHLEAR REFLEX: A NEUROTOXIC ADVERSE EFFECT OF VINCRISTINE

Submitted by Helen Kosmidis

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OBJECTIVE: The purpose of this study was to examine the effects of a known neurotoxic regimen, such as the acute lymphocytic leukemia (ALL) Berlin-Frankfurt-Münster 95 (ALL-BFM-95) protocol, on the function of the medial olivocochlear bundle, which was assessed by recording suppression of the amplitudes of distortion-product otoacoustic emissions (DPOAEs) when white noise was applied simultaneously to the contralateral ear.

METHODS: Our population consisted of 3 groups of children with ALL. A baseline examination was performed before the beginning of therapy. DPOAE-suppression measurements were repeated after 4 weekly doses of vincristine in the first group ($n = 12$), after 8 weekly doses in the second group ($n = 12$), and 3 years after completion of the protocol in the third group ($n = 23$). In the third group, a subgroup of 12 children who were exposed to low-dose gentamicin (<13 days) and another 11 children who were exposed to high gentamicin doses (>23 days) were evaluated.

RESULTS: At baseline examination, all groups presented significant suppression at all frequencies. Efferent mediated DPOAE suppression was still present after 4 sessions of vincristine. However, after 8 vincristine sessions, instead of suppression, an increase of amplitudes was noted at 5 (of 12) frequencies. In the subgroups examined 3 years after ALL-BFM-95, the olivocochlear reflex had recovered.

CONCLUSIONS: Enhancement or no significant suppression of OAEs by contralateral noise indicates a probable vincristine-induced insult to the efferent cochlear innervation. This adverse effect seems to take place early in the course of chemotherapy and is slowly reversed a few years after chemotherapy. The clinical implications of these findings may need additional investigation.

SCREENING NEWBORNS FOR SICKLE CELL DISEASE IN GHANA

Submitted by Kwaku Ohene-Frempong

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INTRODUCTION: Screening of newborns for sickle cell disease (SCD) allows early initiation of prophylactic therapy, parental education, and comprehensive management, which results in reduced mortality. Since April 1993, a demonstration project to develop and implement a program of newborn screening for SCD has been conducted in Kumasi, Ghana, by the Comprehensive Sickle Cell Center at the Children's Hospital of Philadelphia in collaboration with the Ministry of Health and other institutions in Ghana.

OBJECTIVE: Our goal was to assess the program of screening and follow-up of children with SCD in Ghana.

METHODS: Infants are screened at birth or at well-infant visits within days or a few weeks after birth. Mothers are asked to come for results within 4 weeks, and failing that, an extensive tracking system is used to deliver results to the homes of families with infants with possible SCD. Tracking relies solely on information obtained from mothers at the time of screening. The goal is to enroll infants with possible SCD into the sickle cell clinic by 8 weeks of age. Pregnant women, parents with children, and the general public are educated regularly about the screening program. Children with SCD receive comprehensive care through the Sickle Cell Clinic at Komfo Anokye Teaching Hospital (Kumasi, Ghana).

RESULTS: From February 13, 1995 (when newborn testing was started), to December 31, 2005, a total of 202 244 infants were screened through 8 public health institutions and 14 private clinics in Kumasi and 1 private maternity center and 1 public health Center in Tikrom, a nearby, rural community. A total of 3745 (1.9%) infants were identified as having possible SCD with the following hemoglobin phenotypes according to isoelectric focusing: 2047 (1.04%) fetal sickle cell hemoglobin; 1684 (0.83%) fetal SC hemoglobin; and, 14 (0.003%) fetal SA hemoglobin (Table 1).

TABLE 1. Screening and Tracking Results: February 1995 to December 2005

	No.	%
Total No. of infants screened	202 244	100.0
Infants with possible SCD	3745	1.9 (of infants screened)
Under active tracking (newly diagnosed)	(125)	3.3 (of infants with possible SCD; excluded)
Total possible SCD accounted for	3620	96.7 (of infants with possible SCD; reported)
Lost to follow-up/never found	(494)	13.6 (of infants with possible SCD; reported)
Dead before contact made	(34)	0.9 (of infants with possible SCD; reported)
No. contacted with results (eligible for enrollment)	3092	85.4 (of infants with possible SCD; reported)
Came for results	651	21.0 (of those contacted)
Through home visiting	2441	79.0 (of those contacted)
Eligible but not enrolled after contact	477	15.4 (of those eligible)
Enrolled in clinic	2615	84.6 (of those eligible)
Known deaths after enrollment	109	4.2 (of those enrolled)

CONCLUSIONS: Screening and follow-up of newborns for SCD is feasible in a developing country in Africa. Extra effort in tracking is necessary to ensure that infants with disease are found early and referred for medical management.

PROSPECTIVE FOLLOW-UP OF PATIENTS WITH EWING SARCOMA WITHIN THE LATE EFFECTS SURVEILLANCE SYSTEM

Submitted by Marios Paulides

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INTRODUCTION: It is known that antineoplastic treatment may induce early and late organ toxicities depending on treatment modalities and intensity.
OBJECTIVE: The aim of this study was to determine the cumulative incidence of sequelae within our cohort of patients treated within the EICESS-92 (European Intergroup Cooperative Ewing's Sarcoma Study, 1992) treatment trial.
METHODS: Since 1998, the Late Effects Surveillance System (LESS) of the German Society for Pediatric Oncology and Hematology has prospectively registered late effects in patients of all ages with relapse-free bone and soft tissue sarcoma in Austria, Germany, and Switzerland. The follow-up is conducted locally in accordance with LESS guidelines. Data are reported to the LESS center for collation and analysis.
RESULTS: There were 67 patients available for analysis (42 male, 25 female) with a median age at diagnosis of 13 years and a median follow-up of 3.5 years. Registration had to be terminated for 17 patients as a result of relapse. In total, 43.3% (29 of 67) of the patients were reported to have at least 1 sequelae of treatment. Sixteen patients suffered toxicity in 1 organ system, 9 patients developed toxicity in 2 organ systems, and there were 3 organ systems affected in 4 patients. Nephrotoxicity was reported in 10.4% (7 of 67), cardiotoxicity in 8.9% (6 of 67), peripheral polyneuropathy in 5.9% (4 of 67), and other toxicities in 34.3% (23 of 67) of the patients.
CONCLUSIONS: Sequelae of treatment for Ewing sarcoma within this cohort of the EICESS-92 study were not more frequent than reported previously. Patients are at risk for the development of several toxicities after treatment for Ewing sarcoma, and they should receive adequate medical follow-up.

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR THE TREATMENT OF THALASSEMIA: THE GREEK EXPERIENCE

Submitted by Ioulia Peristeri

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INTRODUCTION: Although prevention remains the cornerstone for the management of thalassemia, hematopoietic stem cell transplantation (HSCT) is the only curative approach.
OBJECTIVE: Our goal was to assess our experience with HSCTs for the treatment of patients with thalassemia.
METHODS: From 1994 to 2006, 96 HSCTs have been performed in 84 thalassemic children from Greece, 3 with sickle cell/thalassemia and 1 with sickle cell disease. According to Pesaro classification, of these 84 children, 20 were in class I, 35 were in class II, and 29 were in class III. Donors were 84 histocompatible siblings and 4 unrelated volunteers. The graft was of bone marrow in 85, cord blood in 3, bone marrow and cord blood in 4, and peripheral blood stem cells in 4. The conditioning regimen consisted of busulfan, cyclophosphamide, and antilymphocyte globulin.
RESULTS: All except 1 patient received engraftments. Ten patients rejected the graft. Eight received another transplant from the same donor, 7 of which were successful. Four patients died; causes of death were graft-versus-host disease (GVHD) (2), disseminated toxoplasmosis (1), and brain hemorrhage (1). At a median follow-up time of 6.5 years, 84 of 88 children survived, 81 were cured and free from transfusions, and 3 remained transfusion-dependent. Severe acute GVHD developed in 18 children, and chronic GVHD developed in 8 patients. The overall survival rate, event-free survival rate, rejection rate, and transplant-related mortality rate were 95%, 94%, 11%, and 5%, respectively. Event-free survival was 100% for class I, 95% for class II, and 87% for class III. Eleven children had mixed chimera (residual recipient hematopoiesis) with normal levels of hemoglobin.
CONCLUSIONS: HSCT is a highly effective treatment for thalassemic patients who have a fully matched donor (related or unrelated). Younger age at transplant secures excellent results with reduced morbidity and mortality rates.

TWO-DECADE EXPERIENCE AND LONG-TERM SURVIVAL IN PEDIATRIC NON-HODGKIN'S LYMPHOMA

Submitted by Sophia Polychronopoulou

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INTRODUCTION: Treatment results for pediatric non-Hodgkin's lymphoma (NHL) continue to improve internationally.
OBJECTIVE: Our goal was to evaluate patient characteristics in our series of patients with NHL and outcomes for the last 16 years (1990–2006).
METHODS: Our patients included 52 newly diagnosed children (11 girls) with a median age of 8.40 years (range: 0.33–14.5 years). Histology results included B-lymphocyte NHL, T-lymphocyte NHL, and Ki-1 in 35, 12, and 5 patients, respectively. In each 5-year period, 14 (3), 17 (3), and 21 (5) patients (girls) were diagnosed, respectively. Common presenting sites were the mediastinum (16), neck area (14), and abdomen (10). Disease was at stage I, II, III, and IV in 3, 14, 23, and 7 patients, respectively. Treatment varied over time. Berlin-Frankfurt-Munich (BFM) protocols had been applied since 1995 (BFM-NHL-90), and since 1997 the BFM-NHL-95 protocol had been applied. Irradiation was given to 5 patients (2 with B-NHL, 3 with T-NHL), and autologous stem cell transplantation was performed on 4 patients, all with B-NHL (1 with central nervous system disease, 1 with residual disease at the end of treatment, and 2 at relapse).
RESULTS: At this writing, 41 patients are alive; 39, 2, and 1 are in first, second, and third remission, respectively. In total, 9 have succumbed (2 died soon after admission in other hospitals as a result of acute-phase complications), and 5 patients died during the first decade of our retrospective study (with T-histology and extensive disease). The event-free survival rate is 74.4% (39 of 52 patients), and the overall survival rate is 80.9% (41 of 52 patients), for a median follow-up time of 6.1 years (range: 0.01–14.7 years) for all patients. For the 39 patients treated with the BFM-95 protocol since 1997, event-free survival and overall survival rates are 79.4% and 88.2%, respectively, for a median follow-up time of 4.8 years.
CONCLUSIONS: Overall and event-free survival rates and outcome of our patients with NHL treated during the last 16 years are standing high. There has been limited use of irradiation and stem cell transplantation.

SERUM LEVELS OF *MYCN* AMPLIFICATION IN NEUROBLASTOMA WITH TUMOR-RELEASED DNA BY REAL-TIME QUANTITATIVE POLYMERASE CHAIN REACTION

Submitted by Tohru Sugimoto

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INTRODUCTION: *MYCN* amplification (MNA) indicates a poor prognosis in neuroblastoma and is routinely assayed for therapy stratification.
OBJECTIVE: We aimed to develop a diagnostic tool to predict *MYCN* status by using serum DNA, which, in patients with cancer, predominantly originates from tumor-released DNA.
METHODS: Using DNA-based real-time quantitative polymerase chain reaction, we simultaneously quantified *MYCN* (2p24) and a reference gene, *NAGK* (2p12), and evaluated *MYCN* copy number as a *MYCN*/*NAGK* ratio in 87 patients with neuroblastoma whose *MYCN* status had been determined by Southern blotting. Of these patients, 17 had *MYCN*-amplified neuroblastoma, and 70 had nonamplified neuroblastoma.
RESULTS: The serum *MYCN*/*NAGK* ratio in the MNA group (median: 199.32; range: 17.1–901.6 [99% confidence interval: 107.0–528.7]) was significantly ($P < .001$) higher than that in the non-MNA group (median: 0.87; range: 0.25–4.6 [99% confidence interval: 0.82–1.26], Mann-Whitney *U* test). The sensitivity and specificity of the serum *MYCN*/*NAGK* ratio as a diagnostic test were both 100% when the serum *MYCN*/*NAGK* ratio cutoff was set at 10.0. Among 6 patients in the MNA group whose clinical courses were followed, the serum ratios decreased to within the normal range in the patients in remission ($n = 3$), but they rose to high levels in the patients who had a relapse ($n = 2$) or failed to achieve remission ($n = 1$). The serum *MYCN*/*NAGK* ratio in the MNA group is likely to be the more sensitive tumor marker than conventional urinary vanillylmandelic and homovanillic acid markers and neuron-specific enolase markers to predict patients' clinical course.
CONCLUSIONS: Measurement of the serum *MYCN*/*NAGK* ratio seems to be a promising method for accurately assessing *MYCN* status in neuroblastoma.

RECURRENT IDIOPATHIC THROMBOCYTOPENIC PURPURA IN CHILDHOOD

Submitted by Maria Vranou

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INTRODUCTION: Idiopathic thrombocytopenic purpura (ITP) is usually a benign disease that remits within

weeks to years. The literature on recurrent ITP (rITP) is limited.

OBJECTIVE: The aim of this study was to retrospectively review patients with rITP who were followed up during the period of 1975–2004.

METHODS: We reviewed the outcome of 790 children with rITP

RESULTS: Among 790 children with ITP, 47 (5.2%) presented with >1 episode of thrombocytopenia. The median age of the children at onset of the disease was 55.9 ± 35.3 months and at final remission was 94.4 ± 58.9 months. The majority of patients (76.6%) had 1 recurrence, whereas the rest of them had >1 recurrence (up to 4); the total number of recurrences was 63. The interval between 2 episodes was <6 months in 25% of the episodes, 6 to 12 months in 29%, 12 to 24 months in 24%, 24 to 36 months in 8%, and >3 years in 14%. Almost half the patients demonstrated bleeding manifestations at diagnosis, whereas only a minority (5) showed bleeding symptoms during the first recurrence. Hemorrhages occurred at times of severe thrombocytopenia and were, in general, mild; however, 1 patient suffered intracranial hemorrhage. Of the episodes, 28.6% necessitated hospitalization and 17.5% required therapeutic intervention with corticosteroids or/and intravenous immunoglobulin. The long-term outcome of all patients was excellent, and none of them needed splenectomy.

CONCLUSIONS: rITP occurs mostly in young children, has a good outcome after >1 to 5 episodes, and a median age that ranges from months to years. The course is more often benign; however, life-threatening hemorrhage may occur in a severely thrombocytopenic patient.

SEASONAL AND GENDER DIFFERENCES IN THE PREVALENCE OF INFANT ANEMIA

Submitted by Songul Yalcin

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INTRODUCTION: Anemia is the most prevalent nutritional deficiency in the world.

OBJECTIVE: To estimate the prevalence of anemia among infants receiving routine health care in the Hacettepe University Ihsan Doğramacı Children's Hospital Well Baby Clinic in Ankara, Turkey, we conducted a cross-sectional study by using data from 469 healthy infants who had data available on their hemoglobin values at 6 months of age for the last 3 years.

METHODS: Infants with acute or chronic illness or thalassemia and infants who had taken or were taking iron supplementation at the time were not included in the study. Information regarding the children was obtained from hospital files. Infants with a hemoglobin level of <10.5 and <9.5 g/dL were considered to be mildly and moderately anemic, respectively, at 6 months of age.

RESULTS: The mean level of hemoglobin was 10.7 g/dL (SD: 0.90). The prevalence of anemia was 41.4%. Boys had significantly lower hemoglobin and hematocrit levels and mean corpuscular volume than girls. Infants born before 37 weeks' gestational age had moderate anemia more frequently. Infants born in spring or summer had anemia more frequently than those born in fall or winter (49.2% and 26.8%, respectively; $P < .001$). Birth weight and monthly weight gain from 6 to 9 months were positively correlated with hemoglobin value at 6 months ($r = 0.14$, $P = .003$ and $r = 0.10$, $P = .041$, respectively).

CONCLUSIONS: Anemic infants aged 6 months had an increased risk of developing growth failure from 6 to 9 months. In this study, the prevalence of anemia observed was of severe public health significance and justifies the need to emphasize, in prenatal and infant health programs, intervention measures that consider season of birth for anemia control.

SHOULD THE PELVIS BE INCLUDED IN ABDOMINAL COMPUTED TOMOGRAPHY SCANS OF CHILDREN WITH UPPER-ABDOMINAL PRIMARY MALIGNANT TUMORS?

Submitted by Maria Zarifi

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INTRODUCTION: There is increasing awareness of the potential risk associated with ionizing radiation in pediatric radiology. Children with abdominal cancer undergo multiple computed tomography (CT) scans both at diagnosis and for follow-up.

OBJECTIVE: We sought to estimate the potential contribution of pelvis CT findings in the management of children with upper-abdominal tumors in correlation with the effective radiation dose.

METHODS: Three hundred forty-two children (aged 1 day to 16 years) with histologically proven upper-abdominal primary malignant tumors (children with lymphoma were not included) were examined during the last 15 years in our department. Their upper- and lower-abdominal CT scans were reviewed retrospectively for clinically significant pelvic abnormalities.

The effective radiation dose for each abdominal area was calculated.
RESULTS: Nine children (2.63%) showed CT pelvic abnormalities that did not change clinical management, and 7 (2.04%) showed findings that affected tumor staging. Thirty-nine percent of the total effective radiation dose was from pelvic CT scans.
CONCLUSIONS: Our data indicate that clinically significant pelvic CT findings are rare in children with upper-abdominal primary malignant tumors. We suggest that the pelvis should not be routinely included in abdominal CT scans unless indicated by other clinical or laboratory findings, given the high level of effective radiation dose.

MONOCYTES EXPRESSING TISSUE FACTOR AS A DIAGNOSTIC MARKER FOR NEONATAL SEPSIS

Submitted by Ilham Youssry
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INTRODUCTION: For neonatal sepsis, several clinical and laboratory parameters have been proposed for its diagnosis but with variable sensitivity and specificity. The bacterial products in sepsis, including endotoxin, induce the production of proinflammatory cytokines that evoke the expression of tissue factor (TF) on monocytes and endothelial cells.
OBJECTIVE: Our goal was to estimate the percentage of monocytes that express TF (TF%) by flow cytometry in patients with neonatal sepsis and to delineate its significance in diagnosing neonatal sepsis.
METHODS: Twenty-seven neonates with neonatal sepsis and positive blood-culture results were recruited and evaluated clinically for their risk factors. Laboratory investigations including obtaining complete blood count and C-reactive protein level and estimation of the monocytes' TF expression by flow cytometry were performed. Twenty-four normal newborns were included as controls for the laboratory data.
RESULTS: The monocytes that expressed TF% of the studied patients was significantly higher than that of the controls ($P = .0001$). The level of TF% was significantly influenced positively by premature rupture of membranes, multiplicity, white blood cell (WBC) count, staff/segment ratio, and C-reactive protein level and negatively by gestational age, body weight, and platelet count. The sensitivity and overall accuracy of the TF% were higher than those of the staff/segment ratio and the WBC count for diagnosing neonatal sepsis. The areas under the receiver operating characteristic curve of TF%, staff/segment ratio, and WBC count were 0.84, 0.79, and 0.60, respectively.
CONCLUSIONS: The monocytes expressing TF% is a promising diagnostic and prognostic marker of infection in neonatal sepsis with high sensitivity and overall accuracy. Adding the estimation of monocytes expressing TF% to the sepsis screen may improve the diagnosis of neonatal sepsis.

Immunology

RESPONSE OF THE IMMUNE SYSTEM TO SURGICAL STRESS IN CHILDREN WITH CONGENITAL HEART DISEASES AND CONCURRENT THYMOMEGALY

Submitted by Nilufar Akhmedova
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INTRODUCTION: According to the World Health Organization, children with congenital heart diseases (CHDs) account for 1% of all newborns. High lethality, short lifetime, and unfavorable prognosis emphasize the urgency of the problem. According to the existing data in the literature, children with CHD often present with enlargement of the thymus. Prevention of complications after surgery directly depends on the condition of the immune system, the main organ in which is the thymus.
OBJECTIVE: Our aim was to study immune system condition in children with CHD and concurrent thymomegaly before and after surgery.
METHODS: Twenty-eight children (aged 1 month to 3 years) with CHD were observed. The control group was composed of 20 healthy children of the same age. Immunologic studies were carried out on all the children before and after surgery.
RESULTS: Before surgery, the children with CHD and thymomegaly presented a decrease of $CD3^+$ lymphocytes by 1.2 times and $CD4^+$ lymphocytes and immunoregulatory index by 1.5 times compared with the control children, with humoral immunity parameters being within normal limits. There was a characteristic increase of natural killer cell activity ($CD16^+$) by 1.2 times and an insignificant increase of relative and absolute content of $CD20^+$ cells. After surgery for CHD, a decrease of $CD3^+$ and $CD4^+$ cells and a sharp decrease of immunoregulatory index and relative content of lymphocytes was found compared with both the data before surgery ($P < .05$) and control values ($P < .01$). In the majority of children with CHD, a significant increase of $CD95^+$ ($P < .05$) and $CD25^+$ ($P > .05$) cells was noted compared with those before

surgery, whereas the number of $CD38^+$ cells was sharply reduced, which indicates depletion of compensatory capabilities of children after surgery.
CONCLUSIONS: Low content of activation markers, especially $CD95^+$ cells before surgery and $CD38^+$ cells after surgery, is an unfavorable prognostic sign in children with CHD and concurrent thymomegaly.

SYSTEMATIC REVIEW OF DIAGNOSTIC CRITERIA AND CLINICAL FEATURES OF FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

Submitted by Caroline Gholam
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INTRODUCTION: Familial lymphophagocytic histiocytosis (FHL) is an autosomal-recessive immunologic disorder that is fatal if untreated. The quoted incidence is 1.2 in 1 000 000; fewer than 1 of 3 patients are diagnosed while alive. The true incidence of FHL may be much higher.
OBJECTIVE: With this project we aimed to identify consensus information required for early recognition and diagnosis of patients with FHL to initiate life-saving treatment.
METHODS: An extensive Medline search that covered the last 20 years produced 17 relevant articles. The hemophagocytic lymphohistiocytosis 2004 protocol produced by the American Histiocyte Society provided additional information.
RESULTS: From this review, the consensus diagnostic criteria for FHL are (1) familial disease/known genetic defect, (2) clinical and laboratory criteria (5 of 8 criteria), (3) fever, (4) splenomegaly, (5) cytopenia in ≥2 cell lines, (6) hypertriglyceridemia and/or hypofibrinogenemia, (7) high ferritin level, (8) high levels of soluble CD25 (interleukin 2 receptor), and (9) hemophagocytosis in bone marrow, cerebrospinal fluid, or lymph nodes. Results of tests of initial bone marrow aspirate may be inconclusive, and repeated ones may be necessary. Half of the patients have abnormal cerebrospinal fluid findings. Several symptoms and laboratory findings provide supportive evidence.
CONCLUSIONS: Diagnostic criteria and supportive features are consistent throughout literature and are aided by the recent addition of genetic and protein-based testing. Diagnostic difficulty lies in the lack of pathognomonic features or specific diagnostic tests for FHL. Not all features present at the initial stage. Treatment should be initiated in cases of strong clinical suspicion.

MANNOSE-BINDING LECTIN (MBL) GENE POLYMORPHISMS AND SERUM MBL LEVELS IN CHILDREN WITH RECURRENT RESPIRATORY TRACT INFECTION

Submitted by Qiu Li
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INTRODUCTION: Mannose-binding lectin (MBL) is a plasma collectin and is considered an important component of innate immunity. Its plasma concentration is, for the most, part genetically determined by a series of single nucleotide polymorphisms located both in the structural gene and in the promoter region. MBL deficiency may be associated with increased susceptibility to infectious disease and autoimmune disorders.
OBJECTIVE: Our goal was to establish the reference serum level of MBL in children, investigate the correlation between *MBL* gene polymorphisms and its serum level in Chinese Han nationality, and *MBL* gene polymorphisms and serum level in children with recurrent respiratory tract infections.
METHODS: The concentrations of oligomerized MBL in plasma were measured by enzyme-linked immunosorbent assay, and *MBL* gene polymorphisms were analyzed by polymerase chain reaction-restriction fragment length polymorphism and polymerase chain reaction with sequence-specific primers.
RESULTS: The median MBL level in 470 normal children was 2536 ng/mL (range: 0–7860 ng/mL), and $P_{2.5}$ to $P_{97.5}$ was 161 to 5070 ng/mL. Two promoter polymorphisms, -550 and -221, and coding variants at codon 54 of the *MBL* gene affected the protein level significantly, and the most frequent genotype in Hans was *HYPA*/*HYPA*. Serum MBL levels were significantly lower in patients with recurrent respiratory tract infections (RRTIs) compared with healthy controls ($H = 6.661$; $P < .05$), and the frequency of the promoter *LXP* haplotype was significantly higher in patients with RRTIs than in controls ($\chi^2 = 4.71$; $P = .03$). The prevalence of the B allele in patients with RRTIs was higher than that in controls, but the difference did not reach significance ($\chi^2 = 0.18$; $P > .05$).
CONCLUSIONS: The MBL reference value in China is 161 ng/mL. Children with MBL concentrations of <161 ng/mL, therefore, were deemed to be MBL deficient, and *LXP* is a risk factor for recurrent respiratory tract infections in this population.

RESEARCH OF MANNOSE-BINDING LECTIN AND INTERLEUKINS 10, 12, AND 18 IN CHILDREN WITH HENOCH-SCHÖNLEIN PURPURA

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INTRODUCTION: Henoch-Schönlein Purpura (HSP) is a common vasculitis in children, and the unbalance of T-helper 1/T-helper 2 plays an important part in its pathogenesis. Mannose-binding lectin (MBL) is an important component of innate immunity and related with a lot of diseases with immunologic derangement. However, we do not know the relationship between MBL and HSP.
OBJECTIVE: We aimed to explore the serum level and gene polymorphisms of MBL and the levels of interleukin 10 (IL-10), IL-12, and IL-18 in supernatant of peripheral blood mononuclear cells of children with HSP and HSP nephritis (HSPN) and of healthy children.
METHODS: The concentrations of MBL and IL-10, IL-12, and IL-18 were measured by enzyme-linked immunosorbent assay: *MBL* gene polymorphisms were analyzed by polymerase chain reaction-restriction fragment length polymorphism and polymerase chain reaction with sequence-specific primers.
RESULTS: The serum MBL levels in the 23 children with HSP were not significantly different from 27 children with HSPN ($P = .95$) or 18 normal children. The levels of IL-18 in the supernatant of peripheral blood mononuclear cells in the 3 groups were not significantly different from each other ($P = .47$, .15, and .14). The levels of IL-10 in children with HSP and HSPN were not different from each other ($P = .70$), but both were significantly different from those in the normal children ($P = .04$ and .01). The levels of IL-12 in children with HSP were different from those in the children with HSPN ($P = .04$). The MBL promoter genotype and the frequency of alleles were not different between the children with HSP and HSPN or between those 2 groups compared with the normal group.
CONCLUSIONS: IL-12 probably plays an important role in the renal involvement in HSP. The position of MBL in the pathogenesis of HSP and HSPN remains to be confirmed.

RESPIRATORY SYNCYTIAL VIRUS INDUCED MORE SERIOUS INFECTION AND INFLAMMATION IN NUDE MICE THAN IN BALB/c MICE

Submitted by Juan Zhou
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INTRODUCTION: Respiratory syncytial virus (RSV) infection is ubiquitous and leads to severe disease in immunocompromised individuals.
OBJECTIVE: Our goal was to compare RSV infection and inflammation between immunocompetent BALB/c mice and immunodeficient nude mice.
METHODS: Pulmonary viral titers, histology, immunohistochemistry for CD14 and CD56, leukocyte counting, and cytokines were assayed by enzyme-linked immunosorbent assay in bronchoalveolar lavage fluid.
RESULTS: RSV titers peaked on the third day after inoculation in both types of infected mice. Infected nude mice had higher-level and more durative viral replication, more severe pulmonary histopathology, and a larger number of leukocytes in bronchoalveolar lavage fluid than infected BALB/c mice. Infected nude mice displayed more pulmonary ($CD14^+$) macrophages (114.34 ± 20.24 vs 75.46 ± 12.37; $P = .05$) and ($CD56^+$) natural killer cells (37.87 ± 8.07 vs 11.06 ± 5.37; $P = .05$) than infected BALB/c mice. RSV infection enhanced production of tumor necrosis factor α, interleukin 12 (IL-12), interferon γ, and IL-10 in both types of mice. Infected nude mice had a higher level of tumor necrosis factor α (40.30 ± 7.34 vs 24.24 ± 9.54; $P = .05$), IL-12 (83.96 ± 12.32 vs 68.21 ± 7.42; $P = .05$), and IL-10 (125.01 ± 18.97 vs 77.56 ± 9.01; $P = .05$) than infected BALB/c mice.
CONCLUSIONS: RSV-infected nude mice are a good model for assessing severe and persistent infection in individuals at high risk. RSV-induced inflammation is not parallel to the immune response of T cells, and macrophages and natural killer cells contribute to severe infection and inflammation of RSV-infected cellular-immunodeficient individuals.

Infectious Diseases

DIAGNOSTIC VALUE OF IN SITU POLYMERASE CHAIN REACTION IN CHILDHOOD LEPROSY

Submitted by Rajeshwar Dayal
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OBJECTIVE: Our aim was to assess the diagnostic value of in situ polymerase chain reaction (PCR) in leprosy, particularly for enhancing histopathological diagnosis.
METHODS: We prospectively studied 20 children (aged <16 years) with leprosy. Clinical examination of each case was performed, and skin smear for acid-fast bacillus was prepared. A biopsy of the lesion site was performed

for histopathological examination and in situ PCR testing.
RESULTS: Histopathological examination confirmed the clinical diagnosis in only 45% of the cases; nonspecific histopathology was reported for the remaining 55% of the cases. In situ PCR showed a positivity of 57.1% in the early/localized form of leprosy (indeterminate/borderline tuberculoid) and 61.5% in the borderline borderline/borderline lepromatous group. When compared with the histopathological examination, a significant enhancement of 15% in diagnosis was seen. With in situ PCR, the diagnosis could be confirmed in 4 (36.3%) of 11 cases with nonspecific histopathological features (which is common in early disease) in addition to confirmation of 8 (88.8%) of 9 histopathologically confirmed tissue sections. Histopathology and in situ PCR combined together confirmed the diagnosis in 13 (65%) of the 20 cases.
CONCLUSIONS: In situ PCR is an important diagnostic tool, especially in early and doubtful cases of leprosy.

DETECTION AND MOLECULAR SEROTYPING OF GROUP B *STREPTOCOCCUS* IN FATAL NEONATAL PNEUMONIA IN CHINA

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INTRODUCTION: Group B *Streptococcus* (GBS) has been recognized as an important pathogen in neonatal infectious disease. However, there are few data on the prevalence of neonatal GBS infection in China.
OBJECTIVE: Our aim was to estimate the infection rate of GBS in neonatal pneumonia in China and identify distribution of the GBS serotype.
METHODS: We retrospectively studied 200 children with fatal neonatal pneumonia who died between 1953 and 2004; 34 fatal neonatal cases without any infectious disease were used as a control group. Paraffin-embedded lung tissues were collected for total genomic DNA extraction. Polymerase chain reaction (PCR) and Southern blotting were used for GBS detection and molecular serotyping.
RESULTS: (1) The positive rate of GBS in the pneumonia group was significantly higher than that in the control group (PCR: 26% vs 3% [$P < .01$]; Southern blot: 65% vs 18% [$P < .01$]). (2) The positive rate in neonates younger than 7 days was significantly higher than that in neonates older than 7 days (PCR: 37% vs 13% [$P < .01$]; Southern blot: 72% vs 52% [$P < .05$]). (3) Risk factors were identifiable for most GBS-positive cases. (4) In the pneumonia group, 22 GBS-positive cases were serotypeable: 7 cases were identified as serotype Ia, 6 cases were serotype III, 5 cases were serotype II, and 1 case was serotype Ib.
CONCLUSIONS: In China, GBS is an important pathogen in fatal neonatal pneumonia, especially in early-onset cases. Serotypes Ia, III, and II were the most common serotypes identified.

PERIPHERAL BLOOD COUNT FOR DENGUE SEVERITY PREDICTION: A PROSPECTIVE STUDY IN THAI CHILDREN

Submitted by Nanthakorn Eu-Ahsunthornwattana
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INTRODUCTION: Dengue viral infection has a wide range of severity levels and requires different levels of medical attention. Early severity prediction using clinical features is difficult. Certain lymphocytic subtypes can be used to predict severity; we postulate that peripheral blood counts can also predict severity, which would be more useful in smaller rural hospitals.
OBJECTIVE: We aimed to compare the peripheral blood counts between patients with mild dengue infection and those with severe dengue infection and identify simple yet sensitive early severity predictors.
METHODS: We enrolled 91 patients with serologically confirmed dengue infection who were admitted to King Chulalongkorn Memorial Hospital. Their leukocytic counts on admission were compared. Potential predictors were identified by using receiver-operating-characteristic analysis.
RESULTS: Compared with patients with mild infection, those with severe infection (dengue hemorrhagic fever grade II or worse) had a higher leukocyte count (3580 vs 3050 cells per μL; $P = .04$), and fewer had leukopenia on admission (70% vs 89%; $P = .03$). They also had a lower percentage of "typical" lymphocytes (24% vs 40%; $P = .02$). Two predictors were identified; either one classified ~19% of all admitted patients as being at low risk. Typical lymphocyte counts of <40% excluded patients with mild disease with 89% sensitivity and 24% specificity (negative predictive value: 77%; positive predictive value: 45%). A combination of parameters [(white blood cells per μL) + 470 × (% typical lymphocytes) + 5 × (atypical lymphocytes per μL) $\geq -14\,950$] improved the sensitivity and specificity to 92% and 26% (negative predictive value: 82%; positive predictive value: 46%).
CONCLUSIONS: The absence of leukopenia and a low percentage of typical lymphocytes predict severe dengue illness. Simple hematologic parameters may be used to reduce unnecessary admissions of patients with sus-

pected dengue infection in the absence of more sophisticated predictors.

SPECTRUM AND MANAGEMENT OF OTITIS MEDIA IN AUSTRALIAN INDIGENOUS AND NON-INDIGENOUS CHILDREN: A NATIONAL STUDY

Submitted by Hasantha Gunasekera
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INTRODUCTION: The reported prevalence and severity of otitis media are highest among the world's Indigenous children, but whether their clinical management varies accordingly is unknown.
OBJECTIVE: Our aim was to study the spectrum and management of otitis media in Indigenous and non-Indigenous children in Australia.
METHODS: From a representative Australian cluster survey of consecutive primary health care consultations, we analyzed all consultations with children (aged 0–18 years). We compared the practitioners' investigation, treatment, and referral practices for Indigenous and non-Indigenous children with otitis media after adjusting for clustering.
RESULTS: Over 8 years (1998–2006), 7991 practitioners managed 141 693 problems in 119 503 consultations with children, including 2856 (2.4%) with Indigenous children. Ear problems were the fourth most common problems managed. Otitis media was managed slightly more commonly in Indigenous than non-Indigenous children (9.8% vs 7.3% consultations; $P < .05$). When otitis media was diagnosed, Indigenous children were significantly more likely to have severe otitis media (chronic and/or suppurative and/or perforation: 7.9% vs 1.7%; $P < .001$), discharging ears (3.9% vs 0.1%; $P < .001$), ear swabs (3.9% [95% confidence interval (CI): 1.6–6.2] vs 0.8% [95% CI: 0.6–0.9]), and topical eardrops administered (10.7% [95% CI: 6.8–14.6] vs 4.5% [95% CI: 4.1–5.0]) but not more likely to receive oral antibiotics (71.8% vs 75.9%), have ear syringing (1.1% vs 0.2%), or be referred to an otolaryngologist (6.1% vs 3.4%) or audiologist (1.8% vs 1.1%) (all $P > .05$).
CONCLUSIONS: In the Australian primary health care setting, Indigenous children are 5 times more likely to be diagnosed with severe otitis media than non-Indigenous children, but reported management is not substantially different, which is inconsistent with established national guidelines. This spectrum-management discordance may contribute to continued worse outcomes for Indigenous children with otitis media.

SEROLOGICAL STUDY ON IMMUNITY TO MEASLES AND MUMPS IN NORTHERN GREEK CHILDREN

Submitted by Katerina Haidopoulou
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INTRODUCTION: Routine immunization against measles and mumps has substantially reduced the number of these infections annually. However, outbreaks have been reported recently, even in highly vaccinated populations.
OBJECTIVE: Our goal was to determine the levels of serum antibodies against measles and mumps in a population of children who were vaccinated against measles-mumps-rubella (MMR).
METHODS: The study population consisted of 260 healthy children (aged 15 months to 14.5 years) who were separated into 2 groups according to the number of MMR vaccine doses previously administered: groups A (1 dose) and B (2 doses). Immunoglobulin G (IgG) and IgM antibody levels for measles and mumps were determined in blood serum by the enzyme-linked immunosorbent assay (Genzyme Virotech, Rüsselsheim, Germany) semiquantitive method.
RESULTS: Groups A and B consisted of 53 children aged 15 months to 8 years and 207 children aged 5 to 14.5 years old, respectively. A majority (93.08%) of the children were protected against measles. Group A and B protection rates were similar (92.27% and 96.23%, respectively). Although most of the children were protected against mumps, the total protection rate was significantly less (81.92%) ($P < .01$). The protection rate against mumps in group A was significantly lower than that in group B (67.92% vs 85.51%; $P < .03$).
CONCLUSIONS: Our results indicate high protection rates against measles conferred even by a single dose of the MMR vaccine. A respected percentage of the children were found to be susceptible to mumps even after completion of a 2-dose immunization schedule. Primary vaccine failure may be implicated as a cause of recent mumps outbreaks, but additional studies are needed.

COMPARISON OF PEDIATRIC LOGISTIC ORGAN DYSFUNCTION (PELOD) SCORE AND PEDIATRIC RISK OF MORTALITY (PRISM) III AS A MORTALITY PREDICTOR IN PATIENTS WITH DENGUE SHOCK SYNDROME

Submitted by Henny R. Iskandar
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INTRODUCTION: The mortality rate for dengue shock syndrome (DSS) in the PICU at Children's and Maternity Harapan Kita Hospital is still high (13.2%).
OBJECTIVE: We evaluated performance of the Pediatric Logistic Organ Dysfunction (PELOD) score compared with the Pediatric Risk of Mortality III (PRISM III) for predicting mortality in our PICU.
METHODS: A total of 42 patients (48% boys, 52% girls) admitted to the PICU from January to December 2006 were enrolled onto the study. Diagnosis of DSS was made according to 1997 World Health Organization criteria and confirmed with serologic-positive dengue blot taken on the fifth day of fever (93% secondary infection and 7% primary infection). PELOD and PRISM scores were evaluated on the first day.
RESULTS: From 42 admissions, 1 was excluded for insufficient data. Median age of the children was 7 years. Death occurred in 11.9% of the patients with DSS. Analysis showed that the mean PELOD score was 7.2 (Mann-Whitney *U* test between survivors and nonsurvivors was significant at $P = .001$) compared with the PRISM III (mean score was significant also at $P = .008$). The receiver operating characteristic curves for the PELOD and PRISM III were 0.954 and 0.868, respectively.
CONCLUSIONS: PELOD and PRISM III scores showed a good discrimination for predicting mortality in patients with DSS in our PICU.

MIDDLE-EAR FLUID *STREPTOCOCCUS PNEUMONIAE* SUSCEPTIBILITY AND SEROTYPE AND DISTRIBUTION IN MEXICAN CHILDREN WITH ACUTE OTITIS MEDIA

Submitted by Claudia Lopez-Enriquez
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INTRODUCTION: Acute otitis media (AOM) is the most common microbial respiratory tract infection in early childhood: *Streptococcus pneumoniae* is a common pathogen isolated from patients with AOM. The American Academy of Pediatrics advises immunization with a 7-valent pneumococcal conjugate vaccine for children with recurrent AOM.
OBJECTIVE: We aimed to establish the most common *S pneumoniae* serotypes present in the middle-ear fluid of Mexican children with AOM and to analyze antimicrobial susceptibility patterns and assess the potential protection provided by the new conjugated *S pneumoniae* vaccines.
METHODS: During 2002 and 2003, 72 *S Pneumoniae* isolates were obtained from 138 Mexican children with AOM. Serotyping distribution was performed by the quellung reaction with antisera from Statens Serum Institute (Copenhagen, Denmark). Tests for susceptibility were performed by using the agar-dilution method according to Clinical and Laboratory Standards Institute protocol for 18 antibiotics.
RESULTS: The most common *S pneumoniae* serotypes isolated were 6B and 19F (16.67% each) and 6A, 14, and 23F (15.27% each). The overall rate of resistance (defined as the rate of intermediate resistance plus the rate of resistance) for penicillin was 65.38% (intermediate and resistant categories were 29.17% and 36.11%, respectively), for cefotaxime was 19.45%, for azithromycin and erythromycin was 23.61%, for trimethoprim/sulfamethoxazole was 61.11%, for amoxicillin was 5.5%, and for clindamycin was 12.5%. With amoxicillin/clavulanate, ceftriaxone, imipenem, meropenem, teicoplanin, telithromycin, and vancomycin, we found susceptibility for 100% of the isolates. The most common resistant serotypes were 19F and 23F.
CONCLUSIONS: The serotype distribution of *S pneumoniae* that causes pediatric AOM in Mexico is similar to that reported from developed countries. The current heptavalent pneumococcal conjugate vaccine covers 63.89% of AOM episodes in Mexican children.

ROLE OF THROMBOMODULIN IN DETECTION OF ENDOTHELIAL CELL DESTRUCTION AFTER INFECTION WITH FALCIPARUM AND TERTIAN MALARIA

Submitted by Max Mantik
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INTRODUCTION: Thrombomodulin is an endothelial cell receptor for thrombin. In tropical and tertian malaria, thrombomodulin is secreted after endothelial cell

destruction after infections with *Plasmodium falciparum* or *Plasmodium vivax*.

OBJECTIVE: Our goal was to investigate whether thrombomodulin levels can be used to detect the endothelial cell destruction after tropical or tertian malaria and whether thrombomodulin is related to the severity of tropical malaria.

METHODS: This was a cross-sectional observational analytical study conducted in 5 hospitals in north Sulawesi, Indonesia, from June to September 2006, in patients aged 2 to 13 years with tropical or tertian malaria. Thrombomodulin levels were determined with an enzyme-linked immunosorbent assay using a thrombomodulin kit (Fujirebio Diagnostics, Inc, Malvern, PA). Data were analyzed by independent *t* test and Spearman rank correlation coefficient.

RESULTS: For 30 patients with tropical malaria (thrombomodulin level: 0.060–0.180 FU/mL) and 2 patients with tertian malaria (thrombomodulin level: 0.068–0.075 FU/mL), there was a significant difference in *t*-test results between tropical and tertian malaria ($P = .044$). For 11 patients with severe malaria (thrombomodulin level: 0.086–0.162 FU/mL), there was also a very significant difference in *t*-test results for complicated and uncomplicated tropical malaria ($P = .009$). The Spearman rank test showed significant positive correlation between thrombomodulin and parasitemia levels ($r_s = 0.686$; $P = .001$).

CONCLUSIONS: Thrombomodulin levels can be used to detect endothelial cell destruction in malaria; the thrombomodulin level in tropical malaria was found to be higher than that of tertian malaria. Thrombomodulin levels were very significantly different in complicated and uncomplicated tropical malaria and also correlated significantly with the degree of parasitemia.

ROTASCORE STUDY: EPIDEMIOLOGICAL OBSERVATIONAL STUDY OF ACUTE GASTROENTERITIS WITH OR WITHOUT ROTAVIRUS IN GREEK CHILDREN YOUNGER THAN 5 YEARS

Submitted by Vassiliki Papaevangelou

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INTRODUCTION: Pediatric rotavirus gastroenteritis (PRG) is the most frequent cause of severe acute gastroenteritis (AGE) in children up to 5 years of age worldwide.

OBJECTIVE: We sought to determine the proportion of PRG and compare its clinical burden to that of AGE caused by other pathogens.

METHODS: The study was conducted in 4 hospital emergency units (HEUs) and 50 private pediatric clinics between January and May 2006. Children up to 5 years of age were included. A rapid stool immunochromatographic test for rotavirus antigen detection was performed. Symptom-severity scores were calculated by using the Clark scale.

RESULTS: Seven hundred and six children participated in the study (median age: 20 months; 385 boys [54.5%]); 273 patients (38.6%) visited HEUs, and 433 (61.4%) visited private clinics. The proportion of PRG was 29% (95% confidence interval [CI]: 25.9%–32.6%) in the total study group, 18.3% (95% CI: 14.9%–22.3%) in private clinics, 45.7% (95% CI: 40.0%–51.7%) in HEUs, and 49.1% in hospitalized patients (95% CI: 42.3%–55.7%). Most children with PRG (71.7%) were between 6 months and 3 years old. Behavioral changes and signs of dehydration, weight loss, fever at ≥38°C, diarrhea, and vomiting were more prevalent with PRG ($P < .01$). In children with PRG, a higher incidence of moderate or severe gastroenteritis ($P = .013$ and .021, respectively), hospitalization ($P = .011$), and need for a clinical reevaluation ($P = .012$) was observed, as was longer hospitalization (5.14 ± 3.18 vs 3.69 ± 2.25 days; $P = .039$).

CONCLUSIONS: PRG was responsible for nearly half the patients with AGE who visited HEUs or required hospitalization. Vaccination against rotavirus would help prevent this frequent and often severe disease.

DIAGNOSIS OF TUBERCULOSIS LYMPHADENITIS IN CHILDREN

Submitted by Ileana Puiu

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INTRODUCTION: Tuberculosis represents a major health problem, and the most frequent cause of extrapulmonary tuberculosis is tuberculous lymphadenitis.

OBJECTIVE: The aim of this study was to determine the relative contribution of tuberculous lymphadenitis as a cause of persistent cervical lymphadenopathy.

METHODS: Our study included 87 children (aged 6 months to 18 years) suffering from tuberculous lymph-

adenitis who were admitted to our tuberculosis center during a period of 10 years.

RESULTS: Our 10-year study of 1112 children with lymphadenopathy showed that tuberculous adenitis was encountered in 87 children (7.8%). The disease was present at all ages but was found more frequently between the ages of 10 and 18 years (39.1%). The most common location was the anterior cervical space in 43 children (49.4%), followed by the axillary and supraclavicular areas. Systemic clinical signs (fever, weight loss, tiredness, night sweats) were encountered by 69 children (79.3%). Granulomatous infection was confirmed in 19 children (21.8%) who had abnormal chest radiograph findings. The diagnosis of tuberculous lymphadenitis was based on histological demonstration of caseating epithelioid cell granulomas in the specimen obtained by excision biopsy in 56 cases (64.3%). Tuberculin skin-test results were positive in 76 cases (87.3%). Positive family history of tuberculosis was discovered in 72 cases (82.7%).

CONCLUSIONS: In most cases, the diagnosis was established on the basis of the specific histopathological aspect, tuberculin skin-test result, positive family history of tuberculosis, and the abnormal chest radiograph findings.

SURVEILLANCE OF INFLUENZA IN CHILDREN YOUNGER THAN 5 YEARS IN A TERTIARY CARE HOSPITAL IN BANGKOK, THAILAND

Submitted by Piyarat Suntarattiwong

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INTRODUCTION: Influenza is a common febrile illness with a significant impact on the pediatric population. Few data regarding influenza in young children have come from tropical resource-limited countries.

OBJECTIVE: We aimed to study epidemiological data, clinical manifestations, influenza rapid tests, and oseltamivir treatment in children with influenza.

METHODS: We conducted influenza surveillance at Queen Sirikit National Institute of Child Health, a tertiary care children's hospital in Bangkok, Thailand. From July 5, 2004, to July 3, 2005, 2 groups of patients aged 0 to 5 years were enrolled: (1) patients diagnosed with lower respiratory tract infections (ie, viral croup, bronchitis, bronchiolitis, and pneumonia) and (2) patients diagnosed with influenza-like illness on the basis of World Health Organization criteria. Subjects must have had symptoms for <5 days. We collected nasal swabs to perform influenza A antigen tests by rapid-test kit and nasopharyngeal swab to perform viral cultures. Clinical signs and symptoms were recorded. Oseltamivir (Tamiflu) was given to the patients with positive rapid-test results, and parents agreed to receive an antiviral agent. Other treatment was provided by attending physicians as the routine standard of care.

RESULTS: We enrolled 495 patients, 49 (9.9%) of which had influenza virus. The virus was isolated year-round with 2 peaks (Fig 1). Fever and myalgia were symptoms with a statistically significant difference between patients with and without influenza infection. The rapid test for influenza A showed 51% sensitivity and 98% specificity compared with viral culture. Eighteen (37%) of 49 patients received oseltamivir treatment. The oseltamivir-treated patients had, on average, 1.12, 0.41, and 0.55 days' shorter oxygen duration, hospital stay, and time to improvement, respectively, but there was no statistically significant difference.

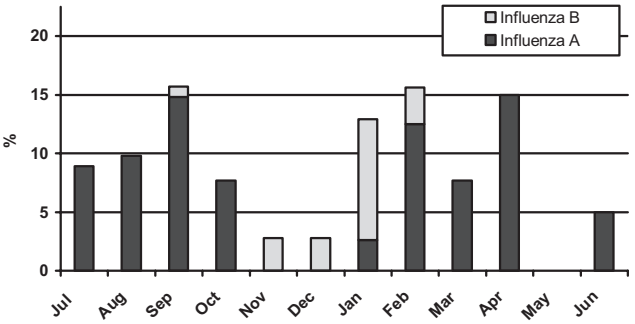

FIGURE 1. Percentage of influenza A and B cases according to month.

CONCLUSIONS: Influenza in young children in Thailand can be found in 10% of patients with lower respiratory tract and influenza-like illness. Two peaks occurred during July to October and January to April. Rapid-test kits have moderate sensitivity but high specificity. Benefit from oseltamivir treatment was observed but not statistically significant.

LITERATURE REVIEW OF ROTAVIRUS PREVALENCE IN AFRICA

Submitted by Zainab Waggie

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INTRODUCTION: Diarrhea kills 1.6 million children younger than 5 years annually, with rotavirus causing

600 000 of those deaths. Eighty-five percent of these deaths occur in sub-Saharan Africa and southeast Asia.
OBJECTIVE: We aimed to review rotavirus prevalence studies of children in Africa from 1975 to 2006.
METHODS: Three multilingual Medline searches (limited to humans) were performed: "RV," country/Africa, and epidemiology/diarrhea. Additional inclusion criteria included children <5 years of age, conducted over >3 months, and including >50 children. Data were analyzed in 4 periods.
RESULTS: Of the initial 189 studies identified, 75 in 18 countries met the additional inclusion criteria (Table 1). More than half of the studies were hospital based. In all studies the most common serotypes were G1 (25%), G4 (16%), G2 (13%), G3 (12%), P[8] (37%), P[6] (35%), and P[4] (11%). From 1996 to 2006 the common serotypes were G1 (22%), G4 (17%), G2 (13%), G3 (13%), P[6] (37%), P[8] (35%), and P[4] (11%).

TABLE 1. Results of 75 Studies on Rotavirus Prevalence in Children <5 Years Old in Africa

	All Studies	1976–1985	1986–1995	1996–2006
Total No. of studies	75	12	39	24
Duration, mo	12 (8.0–15.5)	12 (8.0–12.5)	12 (8.0–12.5)	14 (11–24)
Rotavirus-positive, %	26	25	25	30
Studies with serotyping, *n*	18	0	2	16
Rotavirus-positive with serotyping, %	24	—	5	67

— indicates that data were not available.

CONCLUSIONS: The current prevalence rate is 30% (range: 17%–38%). Present serotypes include G1 through G4, G8, G9, P[8], P[6], and P[4]. Rotavirus diarrhea represents a significant disease burden. Current rotavirus prevalence studies are important, because there are effective rotavirus vaccines available to prevent mortality and severe disease.

ASSOCIATION OF CYTOKINE-RELATED GENE EXPRESSION WITH DENGUE INFECTION SEVERITY

Submitted by Woraman Waidab

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INTRODUCTION: Dengue is the most prevalent mosquito-borne viral disease and one of the most serious infectious diseases worldwide. Infection by any of the serotypes of dengue viruses (DEN-1–DEN-4) may result in different severities ranging from a relatively benign fever, called dengue fever (DF), to fatal dengue shock syndrome. The pathogenesis of dengue hemorrhagic fever (DHF) and dengue shock syndrome is thought to be mediated by various host factors. Previous reports have suggested an involvement of immunoresponse mediators as well as apoptosis-related molecules in the severity of dengue infection.
OBJECTIVE: Our aim was to elucidate the cellular gene responses to dengue viral infection at the transcriptional level and to correlate expression levels with disease activity and/or clinical manifestation.
METHODS: Expression levels of interleukin 8 (IL-8), IL-1β, matrix metalloproteinase 9 (MMP-9), and Fas in peripheral blood cells were assayed for 10 children with DF, 10 children with DHF, and 5 healthy controls by using real-time reverse-transcription quantitative polymerase chain reaction.
RESULTS: Expression levels of IL-8, IL-1β, MMP-9, and Fas were higher in children who developed DHF than in those with DF.
CONCLUSIONS: The messenger RNA expression levels of IL-8, IL-1β, MMP-9, and Fas were significantly elevated in children with DHF, which suggests that these mediators are involved in the pathogenesis. The messenger RNA expression level might serve as a predictor of dengue disease activity. Reverse-transcription polymerase chain reaction has a potential to be another rapid and useful tool in assessing disease severity, leading to a proper therapeutic plan.

HIGH SEROPREVALENCE OF HUMAN METAPNEUMOVIRUS INFECTION IN CHILDREN IN THE CHONGQING, CHINA, AREA

Submitted by Xiaodong Zhao

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INTRODUCTION: Human metapneumovirus (hMPV), first isolated in 2001 in the Netherlands, was identified as a respiratory etiologic agent in a variety of regions. A number of reports have described evidence of hMPV infection on mainland China. However, the description of the seroepidemiology of hMPV infection remains limited.
OBJECTIVE: We aimed to define the seropositivity of hMPV immunoglobulin G (IgG) antibodies in different age groups of children in Chongqing, China.
METHODS: The specificity of the enzyme-linked immunosorbent assay was first validated by using respiratory syncytial virus (RSV)-infected cell lysates subtracted sera and Western blotting based on anti-hMPV animal serum. This assay was subsequently used to determine the presence of IgG antibodies to hMPV and RSV in 325 serum samples from children aged 0 to 6 years.
RESULTS: There was no cross-reaction between the hMPV and RSV enzyme-linked immunosorbent assays observed in our system. Seropositivity of anti-hMPV IgG antibodies in children aged 0 to 5 months was 74.5%,

64% for children aged 6 to 11 months, 72.7% for children aged 12 to 23 months, 87.1% for children aged 24 to 35 months, and 90.3% for children 3 to 6 years old, respectively. The seropositivity of hMPV and RSV was considerably similar in almost all age groups.
CONCLUSIONS: hMPV seems to be a common and important respiratory pathogen in Chongqing's children. Almost all individuals had been exposed to hMPV by the age of 6 years.

DETECTION OF HUMAN BOCAVIRUS IN CHINESE CHILDREN WITH RESPIRATORY TRACT INFECTION

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INTRODUCTION: Human bocavirus (HBoV), a parvovirus discovered in 2005, was identified as a respiratory pathogen in a proportion of respiratory tract diseases with an unknown causative agent.
OBJECTIVE: Our goal was to investigate the role of HBoV in acute lower respiratory tract infection in Chinese children.
METHODS: Two hundred forty-five nasopharyngeal aspirates collected from January to December 2006 from hospitalized children with acute lower respiratory tract infection were tested for the presence of HBoV DNA by using polymerase chain reaction (PCR) that targeted the *NP-1* gene. Bulk PCR products were subjected to nucleotide sequence analysis. Medical charts were reviewed for clinical features of HBoV infection.
RESULTS: HBoV DNA was detected in 11 (4.5%) of the 245 nasopharyngeal aspirates. HBoV infection occurred year-round and peaked in winter. The age range of the children was from 48 days to 18 months. Coinfections of HBoV and respiratory syncytial virus were found in 2 (18.2%) of 11 samples. Nucleotide sequence of the *NP-1* gene PCR products showed considerably high identity (99%). Clinical symptoms included cough and wheezing.
CONCLUSIONS: HBoV seems to be one of the respiratory pathogens for acute respiratory tract infection in the Chongqing area, particularly in young children. Understanding of the clinical relevance of HBoV infection will require additional studies.

COMBINATION OF ARTESUNATE-AMODIAQUINE AS A TREATMENT FOR UNCOMPLICATED FALCIPARUM MALARIA IN CHILDREN

Submitted by Syahril Pasaribu
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INTRODUCTION: Resistance of falciparum malaria to both chloroquine and pyrimethamine-sulfadoxine has been reported from Indonesia and other countries. Since the end of 2004, we have changed the standard treatment of uncomplicated falciparum malaria to use a combination of artesunate and amodiaquine.
OBJECTIVE: Our aim was to evaluate the efficacy and adverse reactions of artesunate-amodiaquine as a treatment for uncomplicated falciparum malaria in children.
METHODS: We conducted a cross-sectional study at Panyabungan, Mandailing Natal Regency, North Sumatera Province, Indonesia, from August to September 2006. The sample was school-aged children between 5 and 18 years old. The sample received an oral dose of artesunate (4 mg/kg body weight) combined with an oral dose of amodiaquine (10 mg/kg body weight) for 3 days. Parasitemia was assessed at days 0, 2, 7, and 28.
RESULTS: Peripheral blood smears were performed for 376 school-aged children; 135 of them tested positive for falciparum malaria. At the end of the study (28 days), 121 cases completed a full course of study. From the peripheral blood smears on days 2, 7, and 28, we found a 100% cure rate. Adverse reactions included 20 children (16.5%) with headache, 10 (8.3%) with vomiting, and 1 (0.8%) with tinnitus.
CONCLUSIONS: A combination of artesunate and amodiaquine can be used as treatment for uncomplicated falciparum malaria in children with the caution of headache as an adverse reaction of the drug combination.

INTERLEUKIN 18 GENE POLYMORPHISM AS A POTENTIAL HOST-SUSCEPTIBILITY FACTOR IN TUBERCULOSIS IN CHONGQING, CHINA

Submitted by Li-Ping Jiang
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INTRODUCTION: Interleukin 18 (IL-18), which is an important interferon γ inducer, regulates the expression of the proinflammatory cytokine interferon γ and the antituberculosis response.
OBJECTIVE: Our goal was to investigate polymorphisms of the IL-18 gene promoter and determine whether polymorphism of the IL-18 gene promoter is a

potential host-susceptibility factor in tuberculosis in Chongqing, China.

METHODS: A total of 123 patients (including 91 children and 32 adults) with tuberculosis and 249 normal controls (including 167 children and 82 adults) were selected randomly. The polymorphisms at positions -607A/C and -137G/C in promoter of the *IL-18* gene were analyzed by using polymerase chain reaction with sequence-specific primers.

RESULTS: The allele and genotype frequencies of IL-18/-607 gene polymorphisms were similar in patients with tuberculosis and in controls. However, frequencies of the -137GG, GC, and CC genotypes were 67.9%, 28.5%, and 3.6%, respectively, in controls and 78.9%, 19.5%, and 1.6%, respectively, in those with tuberculosis. Frequency of the -137GG genotype in tuberculosis was significantly higher than that in controls ($\chi^2 = 4.881$; $P = .027 < .05$). The frequency of allele G at position -137 in patients with severe tuberculosis was significantly higher than that in patients with pulmonary tuberculosis ($\chi^2 = 4.336$; $P = .037 < .05$).

CONCLUSIONS: Polymorphism of the IL-18 gene promoter at position -137 is a potential host-susceptibility factor in tuberculosis in Chongqing. The people with allele C at position -137 in the promoter of the *IL-18* gene may be protected against mycobacterium tuberculosis infection. The polymorphisms at position -137 of the *IL-18* gene may be associated with a severe degree of tuberculosis.

ASSOCIATION OF POLYMORPHISMS OF THE INTERLEUKIN 18 RECEPTOR: A GENE WITH SUSCEPTIBILITY TO TUBERCULOSIS IN CHONGQING, CHINA

Submitted by Li-Ping Jiang

Li-Ping Jiang

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INTRODUCTION: The interleukin 18 (IL-18) receptor complex is a heterodimer consisting of IL-18Rα and IL-18β. Both chains are required for IL-18 signaling transduction in T cells and natural killer cells.

OBJECTIVE: We aimed to determine whether polymorphisms of the IL-18Rα gene promoter were associated with susceptibility to tuberculosis in Chongqing, China.

METHODS: In 123 patients (91 children and 32 adults) with tuberculosis and 249 normal controls (167 children and 82 adults) in Chongqing, we analyzed the polymorphisms at positions -69T/C and -638T/C in the promoter of IL-18Rα by using polymerase chain reaction with sequence-specific primers.

RESULTS: Allele and genotype frequencies at position -638 of the IL-18Rα gene polymorphisms were similar in patients with tuberculosis and normal controls ($P > .05$). However, the frequency of -69/CC was significantly lower in patients with tuberculosis than in controls ($\chi^2 = 8.484$; $P = .004 < .05$). The frequency of -69/TT was significantly higher in patients with tuberculosis than in controls ($\chi^2 = 4.027$; $P = .045 < .05$). The frequency of allele C at position -69 in tuberculosis was significantly lower that than in controls ($\chi^2 = 9.816$; $P = .002 < .05$). The frequency of allele C at position -69 in patients with severe tuberculosis was significantly lower than that in patients with pulmonary tuberculosis ($\chi^2 = 4.664$; $P = .031 < .05$).

CONCLUSIONS: Polymorphisms of the IL-18Rα gene at position -69 were associated with susceptibility to tuberculosis in Chongqing. The people with allele C at position -69 may be protected against mycobacterium tuberculosis infection. Moreover, the position -69 of IL-18Rα may be associated with a severe degree of tuberculosis.

PLACENTAL ADENOVIRAL GENOME: POLYMERASE CHAIN REACTION DETECTION AND PLACENTAL HISTOLOGY IN PRETERM AND TERM INFANTS

Submitted by Eufrosini Tsekoura

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INTRODUCTION: Intrauterine infection is an important cause of spontaneous preterm birth. However, evidence-based etiology for the causative role of viral infection is still lacking. Intervillous trophoblasts express adenovirus receptor. Infection of trophoblast cells in vitro by adenovirus early in pregnancy has shown increased apoptosis. Adenovirus early in pregnancy may cause placental dysfunction. Mature syncytiotrophoblasts do not express adenovirus receptor.

OBJECTIVE: The aim of this study was to test the hypothesis that detection of adenovirus in placental tissue is associated with preterm birth and correlates with placental histopathological findings that are suggestive of infection.

METHODS: Placentas were prospectively collected from consecutive deliveries. Detection of the adenovirus genome was tested by polymerase chain reaction assay. Placental histology and immunohistochemistry studies with monoclonal antibody CD45 were evaluated for

signs of placental inflammation in the samples that tested positive for adenovirus.

RESULTS: Between January 2005 and December 2006, 193 placenta samples (71 from preterm deliveries and 122 from term deliveries) were collected in Alexandra's Maternity Hospital in Athens, Greece. The adenoviral genome was isolated in 54 (28%) of 193 placentas. The frequency of adenovirus detection in preterm placentas compared with those from term placentas was significantly increased (29 of 71[41%] vs 25 of 122 [20%]; $P = .002$; odds ratio [OR]: 2.6 [95% confidence interval (CI): 1.4–5.1]). Stratification by gestational age (GA) revealed a stronger association between preterm delivery and adenovirus detection as GA decreased below 33 weeks (GA ≤ 29 weeks, OR: 2.8 [95% CI: 1.1–7.0]; and GA 30–33 weeks, OR: 2.7 [95% CI: 1.1–6.5]). In the subgroup of deliveries at 34 to 36 weeks' GA, the association was no longer significant (OR: 2.6 [95% CI: 0.9–7.0]). Adenoviral genome detection followed the seasonal variation of adenovirus respiratory infections (beginning of March to end of June). Chorioamnionitis was present more frequently in the adenovirus-positive preterm placentas compared with term placentas ($P = .006$). The presence of villitis ($P = .03$) and chorioamnionitis ($P = .02$) was significantly increased in the adenovirus-positive preterm placentas compared with preterm adenovirus-negative placentas.

CONCLUSIONS: Our results indicate that there is an association between placental adenoviral genome detection and spontaneous early premature birth. Adenovirus may cause preterm birth through placental inflammation (chorioamnionitis and villitis).

OUTBREAK OF HUMAN METAPNEUMOVIRUS INFECTION IN CHILDREN IN CHONGQING, CHINA

Submitted by Xiaodong Zhao

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INTRODUCTION: Human metapneumovirus (hMPV) is a newly discovered respiratory pathogen. Understanding of the epidemiology of hMPV infection is limited in China.

OBJECTIVE: The objective of this study was to describe an outbreak of hMPV infection in Chongqing, China, and study the high coinfection rates of hMPV and respiratory syncytial virus (RSV).

METHODS: A total of 93 nasopharyngeal aspirates (NPAs) were collected from hospitalized children with acute respiratory diseases during December 2006 to January 2007. Total RNA was extracted from NPAs by using QIAmp viral RNA minikit and amplified for hMPV F gene and RSV G gene by real-time reverse-transcription polymerase chain reaction (RT-PCR) and traditional PCR, respectively. Most of the hMPV-positive samples were confirmed by traditional RT-PCR and subsequent nucleotide sequence analysis.

RESULTS: Of 93 NPAs, 38 (40.9%) were positive for hMPV and 52 (55.9%) were positive for RSV. Twenty-three (24.7%) revealed coinfection with both viruses. Ages of patients with hMPV infection ranged from 1 month to 31 months; 78.9% were younger than 2 years, and 47.4% were younger than 6 months. Cough was the most common symptom, 78.9% (30 of 38) had wheezing, and 42.1% had fever.

CONCLUSIONS: HMPV seems to be an important respiratory pathogen in young children in Chongqing, China. Coinfection of hMPV and RSV may frequently occur during the winter season. Whether coinfection leads to more severe disease remains unknown.

Neonatology

INFANT-VENTILATOR INTERACTION CAN AFFECT CEREBRAL BLOOD FLOW IN PRETERM INFANTS: COMPARISON BETWEEN 2 MODES

Submitted by Ehab Saoud Abd El-Moneim

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INTRODUCTION: Disturbance of cerebral blood flow (CBF) has been associated with neonatal brain injury. Because CBF is greatly influenced by mechanical ventilation, it is important to consider the effect of ventilation mode on CBF. We have shown that pressure-support ventilation combined with volume-guarantee mode (PSV-VG) would lower ventilation pressures and improve infant-ventilator synchrony when compared with synchronized intermittent mandatory ventilation (SIMV).

OBJECTIVE: Our aim was to compare the effect of PSV-VG and SIMV on CBF.

METHODS: To study an on/off effect, 33 preterm infants (mean gestational age: 26.6 ± 2.2 weeks) were switched from SIMV to PSV-VG and back again to SIMV. By using Doppler techniques, anterior cerebral artery pulsatility index (PIaca), superior vena cava flow (SVCF), and aortic minute distance (MDao) were measured in each phase. Infants were grouped according to patency of ductus arteriosus.

RESULTS: When the duct was closed, the PIaca decreased significantly ($P = .002$), which indicates higher

CBF, SVCF increased by 20.1% ± 7.4% ($P = .01$), and MDao increased by 14.6% ± 4.1% ($P = .007$) during PSV-VG. In the group with patent ductus arteriosus, although MDao decreased by 10.5% ± 4.4% ($P = .04$) during PSV-VG, the PIaca and SVCF remained constant. We also observed noticeable changes in the pattern of SVCF Doppler waveform as infant-ventilator interaction changed with switching the ventilation mode. Such pattern changes are described here for the first time.
CONCLUSIONS: The interaction between the ventilation mode, the shunt across the duct, and probably CBF autoregulation determines the effect of mechanical ventilation on CBF. Studying the SVCF Doppler waveform pattern may be a useful tool for assessing ventilator-patient interaction.

LIPID PROFILE OF PREMATURE INFANTS UP TO THE AGE OF 3 YEARS

Submitted by Helen Apostolou

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INTRODUCTION: Current literature indicates a high incidence of cardiovascular disease in later life of premature infants with low birth weight.
OBJECTIVE: The purpose of this study was to investigate serum lipid levels of prematurely born infants up to the age of 3 years.
METHODS: From 2001 to 2005, 171 premature newborns were studied in the follow-up clinic. Patients were divided into 4 groups according to gestational age (≤30 and >30 weeks) and birth weight (≤1000 and >1000 g). Serum levels of cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein were recorded at 12, 24, and 36 months of life.
RESULTS: Cholesterol levels were within the reference range in every given period, independent of age. Infants with low birth weight (≤1000 g) had significantly increased cholesterol levels compared with those with higher birth weight (>1000 g) ($P = .013$). All groups had significantly higher serum triglyceride levels ($P = .001$) during the first year of life in comparison to all other periods. In addition, infants with low birth weight had significantly higher serum triglyceride levels ($P = .015$) during the second year of life than infants with higher birth weight.
CONCLUSIONS: Premature infants with low birth weight have increased cholesterol and triglyceride levels during the early years of life, which is a finding that might be related to a high incidence of atherogenesis in later life and requires additional investigation.

IONIZED SERUM CALCIUM, NOT SERUM TOTAL MAGNESIUM, PREDICTS OUTCOME IN NEONATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Submitted by Hoda Atwa

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INTRODUCTION: Perinatal hypoxic-ischemic encephalopathy (HIE) is a significant cause of neonatal mortality. Previous studies have attempted to find a sensitive parameter that will accurately predict outcome in infants with perinatal asphyxia.
OBJECTIVE: With this study we aimed to determine whether the serum total magnesium (Mg), ionized Ca (iCa), and sodium (Na) levels could predict the outcome of HIE.
METHODS: This was a hospital-based prospective study of admission to a newborn NICU. A total of 60 term neonates with HIE were included in the study. HIE was classified according to the criteria of Sarnat and Sarnat. Twenty healthy term newborns were chosen as controls. Total Mg, iCa, and Na levels were measured in umbilical cord blood and after 48 hours in blood. Neurologic examination was performed at 6 and 12 months. Outcome was scored as normal, disability, or death.
RESULTS: In normal infants there was a significant increase in serum total Mg and decrease in iCa concentrations by the second day of life as compared with that from umbilical cord blood. Infants with mild HIE had significantly higher umbilical cord blood total Mg levels compared with that of infants with moderate ($P = .001$) and severe ($P = .02$) HIE. On the second day of life, infants with severe HIE had significantly higher serum total Mg levels ($P < .001$) and lower iCa levels ($P < .001$) compared with those in the mild-HIE group. No significant differences between infants with severe and moderate HIE were observed regarding cord blood and 48-hour total Mg, iCa, and Na levels. The serum cord-blood and 48-hour iCa concentrations were significantly lower in the group of infants with HIE who had a poor outcome (odds ratios: 0.82 ± 0.10 and 0.70 ± 0.09) as compared with those with a good outcome (0.91 ± 0.08 and 0.86 ± 0.08) ($P < .001$ and $P < .000$, respectively).
CONCLUSIONS: Cord-blood and 48-hour levels of iCa and 48-hour Na could predict poor outcome in infants with HIE.

CEREBRAL OXYGENATION RESPONSES DURING SKIN-TO-SKIN CARE IN LOW BIRTH WEIGHT INFANTS

Submitted by Esmot Ara Begum

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INTRODUCTION: Kangaroo care (KC) has been thought of as an important intervention for improving the care of low birth weight infants; however, the physiological effect of KC is still controversial.
OBJECTIVE: The aim of this study was to investigate physiological responses during KC.
METHODS: Sixteen low birth weight (<1600 g) infants with gestational ages of 24 to 32 weeks were studied. Heart rate (HR), respiration rate, pulse oxygen saturation (SPo_2), and regional cerebral oxygenation (rSo_2) were obtained in 3 periods continuously: before, during, and after KC. Spectral analysis was performed. Total amplitude, the power of low-frequency (LF; 0.06–0.10 Hz) band, high-frequency (HF, 0.15–0.40 Hz) band, and the ratio of LF/HF were calculated. Three groups were compared by analysis of variance.
RESULTS: Significant differences were not observed during KC in terms of mean HR, SPo_2, and rSo_2. By amplitude, these parameters were significantly decreased during KC ($P < .001$) and increased after KC ($P < .001$). The power of LF or HF was either significantly decreased during KC in HR, SPo_2, and rSo_2 ($P < .05$); however, the ratio of LF/HF was increased during KC in HR, whereas the ratio was decreased in rSo_2 ($P < .05$).
CONCLUSIONS: These results suggest that KC influences the stability of rSo_2 as well as HR and SPo_2. Discrete results in the LF/HF ratio of rSo_2 may indicate that KC has different effects on rSo_2 associated with cerebral function.

AMNIOTIC FLUID TRANSFORMING GROWTH FACTOR β AND THE DEVELOPMENT OF NEONATAL CHRONIC LUNG DISEASE

Submitted by Hiroyuki Ichiba

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INTRODUCTION: Chorioamnionitis can initiate fetal lung injury and result in neonatal chronic lung disease (CLD). Although neonates with CLD have higher amniotic fluid concentrations of proinflammatory cytokines, overexpression of transforming growth factor β (TGF-β) also seems to be important in the pathogenesis of neonatal CLD.
OBJECTIVE: Our goal was to investigate how TGF-β is related to fetal lung injury induced by chorioamnionitis.
METHODS: Forty-four amniotic fluid samples were obtained at delivery from preterm infants (median gestational age: 28 weeks; median birth weight: 908 g). TGF-β and interleukin 6 (IL-6) concentrations in amniotic fluid were measured with enzyme-linked immunosorbent assays.
RESULTS: TGF-β concentration in amniotic fluid correlated with IL-6 concentration ($P < .0001$). Both TGF-β and IL-6 concentrations in amniotic fluid increased with increasing histologic severity of chorioamnionitis (each $P < .0001$). Coexisting presence of neonatal CLD and histologic chorioamnionitis was associated with significantly higher amniotic fluid TGF-β and IL-6 concentrations than presence of neonatal CLD without histologic chorioamnionitis or absence of both (mean TGF-β level: 454.3 vs 119.2 vs 151.8 pg/mL [$P < .0001$]; mean IL-6 level: 5.14 vs 0.99 vs 1.64 ng/mL [$P = .0005$]). Both TGF-β and IL-6 concentrations in amniotic fluid correlated with duration of neonates' need for oxygen administration (each $P < .0001$).
CONCLUSIONS: Amniotic fluid TGF-β may be important in chorioamnionitis-induced fetal lung injury that results in neonatal CLD.

AGE-RELATED SERIAL PLASMA CITRULLINE LEVELS IN PRETERM NEONATES

Submitted by Hariklia Ioannou

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INTRODUCTION: Citrulline is a nonessential amino acid that is synthesized almost exclusively in the small intestine. In adults and children with short-bowel syndrome, citrulline has served as a reliable index of the remaining small intestine length. Citrulline is also a precursor of arginine, the role of which is crucial for neonatal metabolism and growth.
OBJECTIVE: We sought to determine serial plasma citrulline levels of preterm neonates to assess levels in accordance with age and intestinal maturation, which may serve as a baseline in the event of intestinal abnormalities such as necrotizing enterocolitis (a devastating complication in this age group).

METHODS: We measured serial plasma citrulline levels in 18 clinically stable neonates (gestational age: ≤32 weeks; birth weight: 1000–1750 g) on days 2, 7, 14, 21, and 28. Quantitative analysis of plasma citrulline levels was performed by ion-exchange chromatography with postcolumn derivatization.
RESULTS: In the study population, mean plasma citrulline levels showed a statistically significant increase from 19 ± 4 μmol/L on day 2 and 20 ± 4 μmol/L on day 7 to 23 ± 4 μmol/L on day 14, 29 ± 5 μmol/L on day 21, and 31 ± 5 μmol/L on day 28 ($P < .01$). The route of feeding did not seem to have an affect on plasma levels of citrulline (similar values were obtained from neonates who were fed enterally and parenterally on day 7).
CONCLUSIONS: Citrulline levels in normal preterm neonates seem to be age-related and may serve as reference values, which facilitates the evaluation of compromised intestinal function in preterm neonates with severe gastrointestinal problems.

SHORT-TERM AND LONG-TERM OUTCOME OF 596 INFANTS BORN TO MOTHERS WITH CARDIAC DISEASE

Submitted by Yumi Kono
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INTRODUCTION: The number of pregnancies of women with cardiac disease (CD) has been increasing. Previous studies on outcomes were reported mainly on maternal cardiac outcome.
OBJECTIVE: We focused on the outcome of infants who were born to mothers with CD.
METHODS: Study subjects consisted of 596 singleton live-born infants who were born at Tokyo Women's Medical University Hospital from 1991 to 2005. Women with maternal CD included 295 with congenital heart disease (CHD), 184 with arrhythmias, 84 with acquired valvular disease, 18 with cardiomyopathy, and 16 with miscellaneous CD. Gestational age, birth weight (BW), mortality rate, and complications in the subjects and long-term outcome of the preterm infants (<37 weeks' gestation) were evaluated.
RESULTS: Preterm birth was found in 74 (12.4%) infants, 3 of whom were born at <28 weeks' gestation. Low BW was found in 117 (19.6%) infants, 12 of whom weighed <1500 g. Rates of preterm birth (61%) and low BW (61%) in the infants of mothers with cardiomyopathy were significantly higher than those with other maternal CD. The overall mortality rate was 0.7%; 3 died (1 with Down syndrome with CHD, 1 with neonatal Marfan syndrome, and 1 extremely low BW infant born at 23 weeks' gestation) in the neonatal period, and 1 infant with CHD died at 1 year of age. Seven of the preterm infants (9.5%) had CHD. Other complications included anomalies/chromosomal disorders (5), cerebral palsy (1), mental retardation (2), borderline mentality (1), and hearing impairment (1). The prevalence of major neurologic handicap was 4%.
CONCLUSIONS: The rates of preterm birth and low BW were very high. Adverse outcome of infants born to mothers with CD was related to congenital disorders including CD of offspring and extremely preterm birth.

INVESTIGATION OF HEARING IMPAIRMENT IN POST–NEONATAL INTENSIVE CARE UNIT INFANTS BY USING AUTOMATED AUDITORY BRAINSTEM RESPONSE

Submitted by George Mitsiakos
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INTRODUCTION: Hearing impairment affects 2% to 4% of NICU graduates and is associated with several risk indicators.
OBJECTIVE: Our goal was to investigate the prevalence of hearing impairment in newborns hospitalized in an NICU and its association with risk indicators.
METHODS: Subjects consisted of 422 post-NICU infants who fulfilled 34 weeks of gestational age and were examined between March 2005 and December 2006. The following parameters were evaluated: perinatal asphyxia, craniofacial deformities, furosemide and aminoglycoside therapy (duration of administration), meningitis, duration of mechanical ventilation, and nursing duration in an incubator. Screening was performed with the last-generation automated auditory brainstem response (AABR) equipment, ALGO 3 (Natus Medical Inc, San Carlos, CA).
RESULTS: Results were considered normal when the newborn showed response to a 35-dBNA signal bilaterally. Newborns with hearing impairment were referred for early intervention. Multivariate analysis with logistic regression was used to identify the independent risk factors for hearing disturbances. The prevalence of AABR impairment was 2.84% (12 of 422 newborns); the impairment was unilateral in 7 of the infants and bilateral in 5 of them. These 12 infants were examined with conventional ABR with the following results: 6 of them showed normal responses, and in the other 6 infants the pathologic result was confirmed. Multivariate

analysis revealed a statistically significant association between hearing loss and craniofacial deformities, meningitis, and duration of mechanical ventilation ($P < .001$, $P = .001$, and $P = .038$, respectively).
CONCLUSIONS: Although the study sample was limited, the hearing-loss rate that we found was in accordance with that reported in the literature. The prevalence of hearing impairment found when using AABR is high. The only risk factors directly associated with hearing impairment proved to be craniofacial deformities, meningitis, and duration of mechanical ventilation.

INFANT OUTCOME AFTER ANTENATAL STEROIDS IN PRETERM PREGNANCIES WITH ABSENT UMBILICAL END-DIASTOLIC FLOW

Submitted by Florence Murila
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INTRODUCTION: Absence of the end-diastolic flow (EDF) is associated with adverse neonatal outcome. Administration of β-methasone to women with a pregnancy complicated by absent EDF is associated with the transient return of EDF in up to 70% of cases.
OBJECTIVE: We aimed to compare the hospital outcome of preterm infants for whom the absent EDF returned after antenatal administration of β-methasone with those for whom the absent EDF did not return.
METHODS: At Monash Medical Center, 80 pregnant women with absent EDF were given 2 intramuscular 11.4-mg doses of β-methasone 24 hours apart. In the majority of pregnancies, EDF returned after β-methasone treatment. The preterm infants born to these 80 pregnant women had their hospital outcome ascertained retrospectively. Statistical analysis was performed by using the χ^2 and Mann-Whitney rank-sum tests.
RESULTS: The 51 infants for whom the EDF returned were compared with the 29 for whom the EDF did not return. There were no significant differences in their gestational age, birth weight, or resuscitation and ventilation needs. The former group was less acidotic at birth (mean pH: 7.4 vs 7.3 [$P < .05$]; and mean base excess: −3 vs −5 mmol/L [$P < .05$]). There was no significant difference in the incidence of respiratory disease, intraventricular hemorrhage, necrotizing enterocolitis, and mortality rates.
CONCLUSIONS: Preterm infants born after return of an absent EDF after the administration of antenatal β-methasone were less acidotic at birth, but their hospital morbidity and mortality rates were not significantly improved compared with those for whom the absent EDF did not return.

TOPICAL COCONUT OIL APPLICATION REDUCES TRANSEPIDERMAL WATER LOSS IN PRETERM VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CLINICAL TRIAL

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INTRODUCTION: Topical emollients have been shown to reduce transepidermal water loss (TEWL). Such an effect of coconut oil (often used in traditional massage of infants in India) has not been studied.
OBJECTIVE: Our goal was to determine the efficacy of topical coconut-oil application in reducing TEWL in preterm very low birth weight (VLBW) neonates.
METHODS: Seventy-four preterm VLBW infants were randomly assigned at 12 hours of age to either 4 mL of topical coconut-oil application every 12 hours for 7 days ($n = 37$) or no oil application ($n = 37$). TEWL was measured at 12 hours of age and thereafter every 12 hours for 7 days in both groups by using a Vapometer (Delfin Technologies, Kuopio, Finland), a portable closed-chamber evaporimeter. The ambient and skin-surface relative humidity and temperature were recorded simultaneously.
RESULTS: Birth weight (1213 ± 214 vs 1164 ± 208 g), gestation (32 ± 2 vs 31 ± 2 weeks), and other baseline variables were comparable between the 2 groups. TEWL was significantly lower in the infants in the coconut-oil group at each point of measurement. Although TEWL declined for those in both groups during the first week of life, proportional reduction in TEWL in the infants in the coconut-oil group was much greater compared with controls. Significantly lower TEWL in the infants in the coconut-oil group persisted after adjusting for differences in baseline variables by using a generalized estimating equation population-averaged model (an advanced form of regression analysis) (mean difference: 6.8 g/m² per hour all during first week of life [95% confidence interval: 3.5–10.2]; $P = .000$).
CONCLUSIONS: Coconut-oil application in preterm VLBW neonates reduced TEWL by as much as 46%. Such an impact is expected to be of clinical importance, because it could reduce initial weight loss, promote better growth, and reduce fluid requirements.

N-TERMINAL PRO–BRAIN NATRIURETIC PEPTIDE AND PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

Submitted by Pracha Nuntnarumit
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INTRODUCTION: N-terminal pro–brain natriuretic peptide (NT-proBNP) in adults has been reported to be a diagnostic marker of ventricular enlargement and volume overload. However, clinical studies using NT-proBNP in premature infants have been very limited.
OBJECTIVE: We sought to determine whether plasma NT-proBNP in premature infants can identify hemodynamically significant patent ductus arteriosus (hsPDA) and determine the correlation between serial plasma NT-proBNP level and echocardiographic assessment of PDA.
METHODS: Thirty-nine preterm infants underwent clinical and echocardiographic examinations for PDA on days-of-life 2, 4, and 7 and simultaneous blood sampling to measure plasma NT-proBNP concentrations. When ≥2 clinical features of PDA were detected along with left-to-right ductal shunting demonstrated by echocardiogram, hsPDA was diagnosed and the patient treated with indomethacin or ibuprofen.
RESULTS: On day 2, the mean NT-proBNP concentration in the hsPDA group (n = 12) was significantly higher than that in the non-hsPDA group (n = 23) (3160.3 ± 3104.9 vs 618.1 ± 490.7 pmol/L; $P \leq .05$). Eight infants (72%) in the hsPDA group became asymptomatic after an initial course of indomethacin or ibuprofen, and their NT-proBNP levels concomitantly declined. NT-proBNP concentrations were significantly correlated with the magnitudes of the ductal shunt, such as left-atrium/aorta ratio and left-atrium volume index (r = 0.753 and 0.596, respectively). The cutoff of NT-proBNP concentration at 1204 pmol/L on day 2 gave the best predictive values for hsPDA with 100% sensitivity, 91% specificity, 86.7% positive predictive value, 100% negative predictive value, and a likelihood ratio of 11.5.
CONCLUSIONS: The plasma NT-proBNP level on day-of-life 2 is a sensitive marker for predicting hsPDA in preterm infants. Successful closure of PDA corresponds with a decline in plasma levels of NT-proBNP.

PREDICTIVE VALUE OF AMPLITUDE-INTEGRATED ELECTROENCEPHALOGRAPHY ON OUTCOME IN NEONATAL EXTRACORPOREAL MEMBRANE OXYGENATION

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INTRODUCTION: The early and accurate assessment of cerebral function in neonates who undergo extracorporeal membrane oxygenation (ECMO) may identify high-risk infants who are amenable to neuroprotective strategies or, at least, in need of more detailed neuroimaging and neurodevelopmental follow-up.
OBJECTIVE: The specific aims of this study were to assess the clinical utility and long-term predictive value of amplitude-integrated electroencephalography (aEEG) in neonatal ECMO.
METHODS: Thirty-four infants who required ECMO for respiratory failure were enrolled in the study prospectively. Serial aEEGs were recorded before, during, and after ECMO and classified by 2 independent interpreters on the basis of background pattern and amplitude criteria. Surviving infants were followed up to 18 to 22 months and assessed with a structured neurologic examination and formal developmental testing by using the Bayley Scales of Infant Development II. The primary outcome was death or neurodevelopmental impairment (defined as moderate-to-severe cerebral palsy and/or a Mental Developmental Index or Psychomotor Development Index score of <70).
RESULTS: Preliminary data analysis on the first 20 patients was performed. Thirteen patients survived, 3 died while on ECMO, and 4 died before discharge. All surviving infants were evaluated at follow-up. A severely abnormal aEEG predicted death or moderate-to-severe neurodevelopmental impairment with a sensitivity of 0.85 (95% confidence interval [CI]: 0.70–0.95), a specificity of 0.57 (95% CI: 0.3–0.76), a positive predictive value of 0.79 (95% CI: 0.65–0.88), and a negative predictive value of 0.67 (95% CI: 0.35–0.88).
CONCLUSIONS: aEEG is a useful neuromonitoring tool during neonatal ECMO.

FREEDOM OF BREATH, FOUNDATION OF LIFE

Submitted by Hongmao Ye
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Perinatal asphyxia is the leading cause of neonatal mortality, cerebral palsy, and mental retardation worldwide and accounts for ~1 million of the 4 million neonatal deaths that occur each year (World Health Organization, 2005). According to China's national maternal and children's health surveillance in 2005, neonatal mortality was 19 per 1000 live births. In China, the first top 3 causes of infant mortality are preterm birth and low

birth weight, birth asphyxia, and pneumonia. In 2005 asphyxia accounted for 20.5% of deaths in children under the age of 5 years. On the basis of a national sample survey from China Disabled Persons' Foundation in 2003, there are 199000 disabled children between 0 and 6 years old each year, 54.2% of whom are mentally disabled, primarily related to birth asphyxia.

The Neonatal Resuscitation Program (NRP) was introduced to China in the 1990s to reduce mortality and morbidity caused by asphyxia. NRP training was held in cities such as Beijing and Shanghai, which helped to build the foundation of the NRP in China. To disseminate the NRP throughout China, a multidisciplinary partnership was established among the Chinese Ministry of Health, Chinese Perinatal Society, Chinese Nursing Association, American Academy of Pediatrics, and Johnson and Johnson Pediatric Institute. In July 2003, a task force that consists of representatives from all partners made a 5-year commitment to set up "Freedom of Breath, Foundation of Life: China Neonatal Resuscitation Program." The objective was to ensure the presence of at least 1 trained health care professional at every delivery. It has been 3 years since the program launched, and many key accomplishments have been made:

1. The Chinese version of the fourth and fifth editions of the NRP manual (created by American Academy of Pediatrics and American Heart Association) was published.
2. Chinese NRP editions were made with Chinese cultural considerations to guide neonatal resuscitation practices in China.
3. Since July 2004, many training sessions have been organized, including a national instructors training, provincial instructors training(s) in 30 provinces (there are a total of 30 provinces in China), and cascading trainings in cities, counties, and townships. To date, 18 240 health care professionals have been trained, among them obstetricians, pediatricians, nurses/midwives, and anesthetists. By the end of 2006, NRP training had covered 99.1% of health care institutions in cities and 59.8% in 20 target provinces.
4. On September 20–23, 2006, the NRP Science Updates and Experience Sharing conference was held in Xian, capital city of Shaanxi in the northwest part of China. One hundred fifty health care professionals from 20 target provinces attended to learn of scientific updates from Drs Keenan and Niemeyer. Each province presented their training reports and summaries; a few of them were rewarded for their excellence of performance.
5. Since the launch of the NRP, many provincial health bureaus included neonatal resuscitation skills into midwifery service licensing. By the end of 2007, it will become a nationwide regulation in midwifery service licensing. Starting in 2007, the Chinese NRP expanded its program elements to add neonatal mortality and morbidity evaluation. We believe the data collected from this evaluation would be valuable, not only to the Chinese NRP but also to the international NRP.

ELECTRON MICROSCOPIC ANALYSIS OF BACTERIAL BIOFILM ON TRACHEAL TUBES REMOVED FROM INTUBATED NEONATES AND THE RELATIONSHIP BETWEEN BACTERIAL BIOFILM AND LOWER RESPIRATORY INFECTIONS

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INTRODUCTION: Recurrent neonatal lower respiratory infections caused by endotracheal tubes (ETTs) may be related to the bacterial biofilm on them.
OBJECTIVE: We aimed to investigate the microbial biofilm on the surface of ETTs removed from neonates with intubated ventilation to explore the relationship between ETT biofilm and the lower respiratory infections.
METHODS: Twenty ETTs used in intubated neonates were examined for the presence of biofilm on their surface by scanning electron microscopy, and bacteria harvested from the surface of ETTs and the secretions of lower respiratory tracts were isolated, identified, and assessed for antimicrobial susceptibility.
RESULTS: Scanning electron microscopy showed that the incidence of microbial colonization was 60% (12 of 20) when the use of tubes exceeded 2 days, biofilm formation was observed ~3 days after intubation, and its architecture became more mature and complex when the duration exceeded 3 days. There were 14 positive cultures from ETTs (70%, including 4 normal flora), in which 7 kinds of pathogens were isolated; in 13 cultures from the secretions of lower respiratory tract (65%, including 1 normal flora), 10 kinds of pathogens were isolated. Seven samples had the same pathogen both on the surface of ETTs and in the secretions of the lower respiratory tract, which accounted for 50 of the positive cultures from ETTs. The Gram-negative bacteria isolated from the surface of ETTs and the secretions of lower respiratory tract presented multiresistance to antibiotics.
CONCLUSIONS: The ETT biofilm develops into a mature and complex form on the basis of the duration of tube use. There is a possible positive correlation between them. There is correlation between microbial biofilm formation on the surface of ETTs and lower respiratory tract infection in intubated neonates who are ventilated

for a prolonged period of time. ETT biofilm could be a likely source of recurrent infection.

Nephrology

USING NONSTEROIDAL ANTIINFLAMMATORY DRUGS IN VOLUME-DEPLETED CHILDREN CAN PRECIPITATE ACUTE RENAL FAILURE

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INTRODUCTION: Nonsteroidal antiinflammatory drugs (NSAIDs) are ever increasing in popularity in hospital medicine and general practice and are readily available over-the-counter.
OBJECTIVE: Our goal was to illustrate the need to be aware of the effect of NSAIDs on dehydrated patients.
PATHOGENESIS: The risk of renal toxicity is increased in situations in which there is a stimulation of the renin-angiotensin system such as volume depletion. In these conditions, circulating vasoconstrictors are released, maintaining vascular resistance and blood pressure at the potential expense of regional organ blood flow. To maintain renal blood flow, counter-regulatory renal prostaglandins are released that counteract vasoconstrictors and normalize renal blood flow. NSAIDs blunt this counter-regulatory response and intensify the renal vasoconstriction, which leads to acute renal failure. In Table 1 we report 4 children with mild dehydration who developed acute renal failure after the use of therapeutic doses of NSAIDs in a children's hospital.

TABLE 1. Acute Renal Failure in 4 Children After Use of NSAIDs

	Patient No.			
	1	2	3	4
Age, y	13	7	14	13
Gender	Male	Male	Male	Female
Underlying pathology	Craniopharyngioma diabetes insipidus	Juvenile idiopathic arthritis; fasted for surgery	Juvenile idiopathic arthritis with vomiting	Relapse of Crohn disease
NSAID	Diclofenac sodium	Indomethacin diclofenac sodium	Diclofenac sodium	Diclofenac sodium
Highest urea level, mmol urea/L	10.7	12.9	10.7	22
Highest creatinine level, μmol/L	226	146	376	629
Normalization, d	5	3	3	Permanent impairment

CONCLUSIONS: We recommend that NSAIDs should be avoided in children with actual or potential intravascular volume depletion. Although we have not proven cause and effect, additional research is needed to define the true risk of the potential renal complications of using NSAIDs in patients who are at risk of dehydration.

NOTE: The cases of the 4 children described in this report have been published elsewhere (John CM, Shukla R, Jones CA. Using NSAID in volume depleted children can precipitate acute renal failure. *Arch Dis Child.* 2007;92:524–526).

ROLES OF SCAP (STEROL REGULATORY ELEMENT–BINDING PROTEIN CLEAVAGE-ACTIVATING PROTEIN) IN THE MECHANISM FOR MESANGIAL FOAM-CELL FORMATION UNDER INFLAMMATORY STRESS

Submitted by Qiu Li
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INTRODUCTION: Our previous studies have demonstrated that lipid abnormalities play a significant role in glomerulosclerosis. Inflammatory cytokines promote lipid accumulation in human mesangial cells (HMCLs) by disrupting low-density lipoprotein receptor (LDLr) feedback regulation. The sterol regulatory element–binding protein (SREBP) cleavage-activating protein (SCAP) carries SREBP from endoplasmic reticulum (ER) to Golgi, where it is known to cleave SREBP, thereby enhancing LDLr gene expression and cholesterol uptake when cells need cholesterol.
OBJECTIVE: We aimed to investigate whether inflammatory mediators interfere with SCAP translocation and its biological consequence.
METHODS: HMCLs were used in all experiments. Total cellular RNA was isolated from these cells for detecting LDLr, SREBP-2, and SCAP messenger RNA levels with real-time quantitative polymerase chain reaction. LDLr protein expression was measured by Western blot. Translocation of the SCAP-SREBP complex from the ER to Golgi was investigated by confocal microscopy.
RESULTS: In the absence of exposure to interleukin 1β, a high concentration of LDL retained SCAP in the ER, a low LDLr promoter activity, messenger RNA synthesis, and protein expression were found, respectively. However, exposure to interleukin 1β caused overexpression of SCAP and enhanced its translocation from the ER to Golgi. This disrupted normal feedback regulation and resulted in inappropriately increased LDL uptake with transformation of HMCLs into foam cells. Overexpression of SCAP in HMCLs resulted in an increased translocation of SCAP from the ER to Golgi, and high concentrations of LDL were unable to suppress SREBP-2 and LDLr gene expression.
CONCLUSIONS: These data suggest that inflammatory mediators promote abnormal translocation of SCAP from the ER to Golgi and play an important role in lipid accumulation in HMCLs.

NEITHER CLINICAL NOR BIOLOGICAL DATA CAN PREDICT RENAL INVOLVEMENT IN INFANTS WITH FEBRILE URINARY TRACT INFECTION

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INTRODUCTION: 99m Tc-dimercaptosuccinic acid (DMSA) scintigraphy is accepted as the gold standard in the diagnosis of acute pyelonephritis.
OBJECTIVE: In an attempt to reduce the number of investigations after urinary tract infections (UTIs), with this prospective study we aimed to evaluate the diagnostic value of acute-phase reactants in identifying renal involvement in infants with febrile UTI.
METHODS: Fifty-four infants (36 male, 18 female) aged 1 to 12 months were studied. For all infants, clinical findings such as duration and height of fever before antibiotic administration and laboratory parameters such as leukocytosis (white blood cell count of >15.000/μL), elevated erythrocyte sedimentation rate (ESR) (>20 mm/hour), and high levels of C-reactive protein (>10 mg/mL) were compared with the results of the DMSA scan obtained within 72 hours after referral.
RESULTS: Regarding microbial agents, *Escherichia coli* was identified in 42 (78%) of the 54 infants, and 16 (29.5%) of the 54 of infants were febrile for >2 days before diagnosis of UTI. Leukocytosis, elevated ESR, and high levels of C-reactive protein were present in 14 (26%), 41 (76%), and 38 (70%) infants, respectively. Acute-phase DMSA showed renal involvement in 10 (18.5%) infants. Vesicoureteral reflux was found in 16 (29.5%) infants. Gender, duration of fever before antibiotic administration, leukocytosis, elevated ESR, and high levels of C-reactive protein were not related to the severity of renal damage, as shown by DMSA. Only fever of >39°C was slightly correlated with an abnormal DMSA scan result ($r = 0.3$; $P = .032$).
CONCLUSIONS: Acute-phase DMSA scintigraphy remains superior to clinical and laboratory data for predicting renal involvement in infants with febrile UTIs.

IMMUNE FINDINGS IN CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME: COULD THEY PREDICT THE RESPONSE TO STEROID THERAPY?

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INTRODUCTION: Nephrotic syndrome (NS) is thought to be associated with primary immune disturbances.
OBJECTIVE: The aim of our study was to investigate prospectively the immune disturbances in steroid-sensitive (SS) and steroid-resistant (SR) NS and identify whether these immune disturbances may predict the response to steroid therapy.
METHODS: Thirty children with SS NS and 7 children with SR NS (aged 2 to 14 years) were studied. To evaluate the possible relationship between immune disturbances and response to treatment, patients were evaluated during different disease stages. Data were compared with those obtained from 25 age-matched controls. The following parameters were assessed: basic B- and T-cell populations, percentages of $CD23^+$, $CD3^+/CD69^+$/interferon γ^+ (IFN-γ^+) cells, and $CD3^+/CD69^+$/interleukin 4^+ (IL-4^+) T cells, and serum levels of IL-13 and IL-18.
RESULTS: In patients with SS NS percentages of $CD23^+$ and $CD19^+$ B cells, $CD3^+/CD69^+$/IL-4^+ T cells and serum levels of IL-13, IL-18 were significantly higher in the active stage compared with the remission stage on steroids, remission off steroids, and controls ($P < .05$). On the contrary, percentages of $CD3^+/CD69^+$/IFN-γ^+ T cells were significantly decreased ($P < .05$). In patients with SR NS, percentages of $CD23^+$B cells, $CD3^+/CD69^+$/IL-4^+ T cells, and serum levels of IL-13 and IL-18 presented no significant difference between active stage and partial remission. Percentages of $CD19^+$ B cells and $CD3^+/CD69^+$/IFN-γ^+ T cells were elevated in active stage compared with remission stage of patients with SR NS and in controls ($P < .05$).
CONCLUSIONS: These findings suggest that when a type-2 immune response is found in the active stage of NS, one could predict a good response to steroid therapy.

RENAL INVOLVEMENT IN CHILDREN WITH GLYCOGEN-STORAGE DISEASE

Submitted by Hesham Safouh
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INTRODUCTION: Long-term complications of glycogen-storage diseases (GSDs) include delayed puberty, hepatic adenomata, and renal disease.
OBJECTIVE: In this study, our aim was to detect renal involvement in children with GSD and to determine the most accurate laboratory test to be the gold standard for early detection of this renal dysfunction.

METHODS: Twenty-seven children known to have GSD were included in this study. Fifteen healthy age- and gender-matched children were also included as controls. Routine urine analysis and measurement of urinary β_2-microglobulin and microalbumin levels were performed for all patients and controls. Renal-function tests, measurement of serum electrolyte, alkaline phosphatase, urinary calcium, blood, and urine pH levels, creation of a urinary and plasma aminogram, calculation of the glomerular filtration rate, bone radiography to detect rachitic manifestations, and abdominal ultrasound to measure renal size were performed for all patients.
RESULTS: Twenty-one patients had ≥1 renal abnormality. The most common was increased urinary β_2-microglobulin level (15 of 21) followed by an abnormal glomerular filtration rate, whether low or high (8 of 21), and microalbuminuria (6 of 21). Sonographically, there was nephrocalcinosis in 1 case and renal stone in another. The area under the receiver operating characteristic curve for β_2-microglobulin was 0.86 (P = .01) and 0.7 for the urinary microalbumin/creatinine ratio (P = .15). The best cutoff level for predicting renal abnormality for urinary β_2-microglobulin was 0.22 mg/L with 70% sensitivity and 100% specificity, and the best cutoff value for the urinary microalbumin/creatinine ratio was 4.5 with 86% sensitivity and 50% specificity.
CONCLUSIONS: Renal abnormalities are common in patients with GSD. Urinary B_2-microglobulin level can be considered the gold standard for early detection of renal dysfunction in these patients.

LEPTIN AND LEPTIN RECEPTOR IN SERUM AND URINE FROM CHILDREN WITH NEPHROTIC SYNDROME ACCOMPANYING HYPERLIPIDEMIA

Submitted by Xi Qiang Yang

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INTRODUCTION: Hyperlipidemia may cause glomerulosclerosis in children with nephrotic syndrome (NS).
OBJECTIVE: Our goal was to observe the role of soluble leptin receptor (sOBR) and leptin in serum and urine on the mechanism of hyperlipidemia in children with NS.
METHODS: Twenty-three children with untreated NS and 15 age-, gender-, and BMI-matched healthy controls were enrolled onto the study. Leptin and sOBR in serum and urine were measured by enzyme-linked immunosorbent assay, and plasma lipid and insulin levels were detected by automatic biochemistry analyzer and radioimmunoassay, respectively. sOBR messenger RNA and membrane protein expression in peripheral blood mononuclear cells were detected by reverse-transcription polymerase chain reaction and immunocytochemistry.
RESULTS: Low-density lipoprotein, total cholesterol, triglyceride, and apolipoprotein A levels were increased. sOBR messenger RNA and membrane protein expression by peripheral blood mononuclear cells were significantly lower in the patient group compared with controls. The ratio of serum leptin versus sOBR (free leptin index) was significantly higher in the NS group. Urinary leptin in the patient group was higher than that in the control group. The free leptin index showed no correlation with BMI or total cholesterol, triglyceride, or apolipoprotein B levels in both groups but did show a correlation with plasma albumin, low-density lipoprotein, high-density lipoprotein, apolipoprotein A, and insulin levels in the patient group.
CONCLUSIONS: The reduced sOBR level, which enhanced the biologically active form of leptin in children with NS, might be correlated partly with serum lipid parameters, albumin, and insulin. Increased free leptin in serum might be a complementary mechanism against hyperlipidemia in children with NS.

LONG-TERM PROGNOSIS OF HENOCH-SCHÖNLEIN NEPHRITIS IN CHILDREN

Submitted by Ayse Oner

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INTRODUCTION: The long-term prognosis in Henoch-Schönlein purpura is determined principally by the development of progressive glomerulonephritis (>10% progress to end-stage renal failure).
OBJECTIVE: In this study we aimed to investigate the long-term prognosis of Henoch-Schönlein nephritis (HSN) in childhood.
METHODS: Between 1991 and 2003, 156 patients with HSN were investigated retrospectively.
RESULTS: There were 86 boys and 70 girls with a mean age of 9.6 years. They were graded according to the degree of renal involvement: grade 1, isolated microscopic hematuria (n = 31); grade 2, hematuria and mild proteinuria (n = 60); grade 3, acute nephritic syndrome (n = 4); grade 4, nephrotic syndrome ± hematuria (n = 18); grade 5, acute nephritic and nephrotic syndrome (n = 43). Renal biopsy was performed on 43 patients with grade 4 or 5 disease. Twenty patients had extensive crescent formation (>50%) as shown by the renal biopsy and were given triple therapy (intravenous pulse methylprednisolone [30 mg/kg per day for 3 days] fol-

lowed by oral prednisolone [OP], oral cyclophosphamide [2 mg/kg per day for 2 to 3 months], and dipyridamole). The other 23 patients with <50% crescent formation were given methylprednisolone followed by OP and dipyridamole. The patients with grade 3 or 4 disease were given OP and dipyridamole. Those with grade 1 or 2 disease were not given any immunosuppressive agent. During the follow-up period (mean: 30 ± 3.5 months; range: 12–96 months), 23 patients with grade 1, 38 patients with grade 2, 2 patients with grade 3, 8 patients with grade 4, and 21 patients with grade 5 disease showed complete remission (59%). Of the 5 patients with extensive fibrosis shown by renal biopsy, 2 (1%) had persistent nephropathy and 3 (2%) developed end-stage renal failure. The remaining 59 patients showed near-complete recovery with minimal urinary abnormalities (38%).

CONCLUSIONS: Although initial presentation of renal involvement determines the prognosis for those with HSN, intensive treatment with triple therapy seems to be effective for severe renal disease, especially if started before the development of fibrotic changes in crescents and tubulointerstitial tissue.

Neurology

THYROID FUNCTION IN EPILEPTIC CHILDREN TREATED WITH SODIUM-VALPROATE MONOTHERAPY: A PROSPECTIVE LONG-TERM STUDY

Submitted by Achilleas Attilakos

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INTRODUCTION: Sodium valproate (VPA) is widely used for the treatment of partial and generalized epilepsy in childhood and adolescence. The results of studies that have evaluated the effect of VPA monotherapy on thyroid function in children are controversial.

OBJECTIVE: The aim of this study was to investigate, prospectively, whether treatment with VPA has an effect on serum thyroid hormone concentrations in epileptic children.

METHODS: Serum levels of triiodothyronine, thyroxine, free thyroxine, and thyrotropin were determined in 30 epileptic children (aged 2 to 14 years [mean ± SD: 9.10 ± 3.74 years]) before and after 6, 12, and 24 months of VPA monotherapy.

RESULTS: Serum levels of thyroxine and free thyroxine were significantly decreased after 6 (P = .000 and .000, respectively), 12 (P = .000 and .015, respectively), and 24 (P = .000 and .003, respectively) months of treatment with VPA, whereas serum levels of triiodothyronine were significantly decreased only after 24 months of treatment (P = .043). Serum levels of thyrotropin were significantly increased after 6 (P = .000), 12 (P = .000), and 24 (P = .000) months of treatment with VPA. Thirteen children (43.3%) had thyrotropin values higher than the normal-range maximum after 6, 12, and 24 months of VPA monotherapy. Serum VPA concentrations remained within the therapeutic range during the period of study.

CONCLUSIONS: Our results showed that VPA monotherapy in childhood may cause early and persistent alterations in thyroid function, which suggests a need for early and careful monitoring of serum thyroid hormone concentrations in epileptic children who receive VPA.

CLINICAL MARKERS THAT ENHANCE ETIOLOGIC YIELD IN GLOBAL DEVELOPMENTAL DELAY

Submitted by B. H. Y. Chung

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INTRODUCTION: Etiology remains unknown in 30% to 50% cases of children with global developmental delay (GDD). A selective approach has been recommended to increase etiologic yield.

OBJECTIVE: Our aim was to identify clinical markers that enhance diagnostic yield of GDD at initial assessment.

METHODS: The charts of all patients with GDD (N = 577) followed up at the Duchess of Kent Child Assessment Centre were reviewed. GDD was defined as significant delay (<2 SD) in ≥2 developmental domains. Nine clinical items at initial assessment (gender, severity of delay, parental consanguinity, family history, behavioral disturbance, head size, facial dysmorphism, malformations, and neurologic deficits) were correlated with the likelihood of finding an etiology for GDD.

RESULTS: A significant threshold effect was found between mild and moderate GDD (positive likelihood ratio [LR^+]: 1.9; negative likelihood ratio [LR^-]: 0.72). Other items that significantly affected diagnostic yield were (1) female gender (LR^+: 1.62; LR^-: 0.79), (2) behavioral trait (LR^+: 0.24; LR^-: 1.67), (3) microcephaly (LR^+: 2.78; LR^-: 0.79), (4) presence of facial dysmorphism (LR^+: 2.65; LR^-: 0.65), (5) malformation (LR^+: 1.49; LR^-: 0.50), and (6) neurologic deficits (LR^+: 2.86; LR^-: 0.32). A dose-response relationship was found between LR^+ and the number of facial dysmorphisms and malformations.

CONCLUSIONS: Most checklists used for GDD are syndrome specific (eg, fragile X syndrome checklists). These 7 clinical markers are useful in the initial assessment,

even if no specific diagnosis is suspected. Unique statistical characteristics of LRs allow for a wide application in different clinical settings.

EFFECT OF DURATION OF STATUS CONVULSION ON NEURONAL APOPTOSIS AND EARLY APOPTOTIC EVENTS IN HIPPOCAMPUS OF RATS

Submitted by Li Jiang

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OBJECTIVE: Our goal was to explore the influence of duration of status epilepticus on neuronal apoptosis, mitochondrial membrane potential, and cytochrome c release in hippocampus in Wistar rats after status epilepticus (SE).

METHODS: SE that lasted for 30 minutes or 3 hours was induced by intraperitoneal injection with lithium chloride and pilocarpine. Rats were killed at different time points. The apoptosis, mitochondrial membrane potential, and intracellular cytochrome c level were investigated by flow cytometry.

RESULTS: The proportion of apoptotic cells, the decrease of mitochondrial membrane potential, and the release of intracellular cytochrome c significantly changed 30 minutes after 30-minute SE. The peak level was at the 12th hour after SE and 6th hour after SE in apoptosis and the 2 early apoptotic events, respectively. Compared with the same time point after 30-minute SE, the levels of apoptosis and the 2 early apoptotic events after 3-hour SE were much higher. The neuronal apoptosis and the 2 early apoptotic events in hippocampus after SE had a positive correlation with the duration of SE in partial correlation analysis.

CONCLUSIONS: Severe seizures could induce the changes of neuronal apoptosis and the early apoptotic events in hippocampus after SE; the longer the duration of SE, the more serious the change of apoptosis and early apoptotic events were.

PROTEOLIPID PROTEIN 1 GENE MUTATION IN CHINESE PATIENTS WITH PELIZAEUS-MERZBACHER DISEASE

Submitted by Yuwu Jiang

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INTRODUCTION: Pelizaeus-Merzbacher disease (PMD) is a rare X-linked recessive disorder that presents with nystagmus, impaired motor development, ataxia, and progressive spasticity.

OBJECTIVE: The objective of this study was to analyze the proteolipid protein 1 (*PLP1*) gene in 6 Chinese patients with PMD.

METHODS: Six unrelated Chinese patients had PMD (P1–P6), and 14 individuals were from family P2. Of these 6 patients, 3 had transitional, 2 had classical, and 1 had connate PMD according to the clinical and MRI features. Genomic DNA was extracted from peripheral blood samples. Gene dosage was determined by multiplex ligation-dependent probe amplification. All 7 exons and exon-intron boundaries of *PLP1* gene were amplified and analyzed by direct DNA sequencing.

RESULTS: *PLP1* duplications were identified in patients 1 through 4 with PMD. Their mothers were *PLP1* duplication carriers. Both duplication carriers and normal genotypes of *PLP1* were identified in the family members of patient P2. A c.517C → T (p. P173S) hemizygous missense mutation in exon 4 was found in patient 5, and his mother was a heterozygote of this mutation.

CONCLUSIONS: We identified 4 gene duplications and 1 missense mutation (p. P173S) of *PLP1* gene in 5 Chinese patients with PMD. This is the first report about *PLP1* mutations in patients with PMD in China.

IRON-DEFICIENCY ANEMIA IS ASSOCIATED WITH CEREBRAL SINOVENOUS THROMBOSIS: A CASE SERIES

Submitted by Fotini D. Kavadas

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INTRODUCTION: Iron-deficiency anemia is a relatively common but preventable condition in children that may have significant adverse implications on children's growth and development. Iron-deficiency anemia has also been sporadically reported in association with cerebral sinovenous thrombosis (CSVT).

OBJECTIVE: The objective of this study was to describe the largest case series to date of iron-deficiency anemia in association with CSVT as an advocacy measure for its prevention in children.

METHODS: Patients were identified through the Canadian Pediatric Ischemic Stroke Registry database (Toronto site). Included were patients who were older than 1 month to 18 years, met criteria for iron-deficiency anemia, and had radiographically confirmed CSVT.

RESULTS: Thirty-six patients who had CSVT and were older than 1 month to 18 years presented to the Hospital for Sick Children, Toronto, from January 2004 to December 2005. Six (17%) of these patients had iron-deficiency anemia; 2 were female adolescents, and 4 were male toddlers. All patients had historical and laboratory evidence of iron-deficiency anemia. Other risk factors, such as dehydration or inflammatory disorders, were present in all patients, but we did not detect significant inherited hypercoagulable disorders or acquired thrombophilia in any of them.
CONCLUSIONS: This report strengthens the evidence of an association between iron-deficiency anemia and CSVT. We suggest that children who have CSVT should be screened for iron deficiency. Advocacy to prevent iron deficiency is important, because this condition may have serious long-term and irreversible developmental consequences.

PREDICTION OF NEURODEVELOPMENTAL OUTCOME AFTER PERINATAL ASPHYXIA VIA TRANSCRANIAL CEREBRAL ARTERY DOPPLER ULTRASONOGRAPHY

Submitted by Haung-Chi Lin
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INTRODUCTION: Perinatal asphyxia is the most common cause of neurologic injury to the neonate and may lead to significant morbidity and mortality. Cerebral artery Doppler ultrasonography has been used for prediction of outcome after perinatal asphyxia in recent decades.
OBJECTIVE: We investigated whether cerebral artery Doppler ultrasonography is 1 of earliest markers of neurodevelopmental outcome.
METHODS: Cerebral artery Doppler ultrasonography was performed serially via temporal window during the first week of life in 24 asphyxiated neonates in our NICU from 1999 to 2007. The resistive indexes (RI) and blood flow velocities in the cerebral arteries of the circle of Willis were obtained. Neurodevelopmental outcomes were evaluated during follow-up.
RESULTS: Four patterns of cerebral artery Doppler ultrasonography were identified: pattern 1, normal RI with normal cerebral blood flow (6 neonates); pattern 2, normal RI with high cerebral blood flow (4 neonates); pattern 3, high RI after 48 hours of life (8 neonates); and pattern 4, low RI with high cerebral blood flow (6 neonates). Patterns 3 and 4 demonstrated grave prognosis, with severe cerebral palsy or mortality reported in more than 3 of 4 of neonates with either pattern, whereas all neonates with pattern 1 had favorable outcomes, free of delayed development or neurologic sequelae.
CONCLUSIONS: Cerebral artery Doppler ultrasonography is an early useful tool for predicting neurodevelopmental outcome after perinatal asphyxia. The outcomes turned out to be grave once abnormal RIs were detected, either low or high, indicating severe neurologic damage after asphyxia.

FOCAL AREAS OF HIGH-SIGNAL INTENSITY ON BRAIN T2-WEIGHTED MAGNETIC RESONANCE IMAGING SCANS ARE SIGNIFICANT FOR THE DIAGNOSIS OF NEUROFIBROMATOSIS VON RECKLINGHAUSEN TYPE 1

Submitted by Borivoj Petrak
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INTRODUCTION: Neurofibromatosis von Recklinghausen type 1 (NF1) is characterized by the following National Institutes of Health (NIH) diagnostic criteria: café au lait spots, freckling, neurofibromas, Lisch nodules, optic glioma, distinct osseous lesions, and first-degree relative with NF1. Focal areas of high-signal intensity (FASI) in white matter and deep gray matter are typical brain MRI findings in children with NF1.
OBJECTIVE: This study evaluated the frequency of FASI and the possibility of using FASI as a diagnostic criterion.
METHODS: In a group of 160 children, the diagnosis of NF1 was confirmed in keeping with the NIH criteria. All children had MRI examination of the brain. The MRI findings of FASI in the children with NF1 were compared both with the brain MRI findings of the control group of 160 children with different diagnoses and with frequencies of the NIH diagnostic criteria.
RESULTS: In 137 (86%) patients with NF1, ≥1 FASI were found. The difference between frequency of FASI in the NF1 group and in the control group (14 [9%]) is highly significant. The frequencies of the diagnostic criteria were as follows: café au lait spots: 157 (98%); freckling: 123 (77%); neurofibromas: 112 (70%); NF1 relatives: 89 (56%); Lisch nodules: 71 (44%); optic glioma: 45 (28%); and osseous lesions: 15 (9%; only partial examination of the group).
CONCLUSIONS: The findings of FASI in T2-weighted images of the brain MRI are significantly frequent in children with NF1. Frequency of FASI is comparable with frequency of NIH diagnostic criteria. FASI could be proposed as an additional or new criterion for the NF1, mainly in childhood.

BEHAVIORAL AND EMOTIONAL PROBLEMS IN CHILDREN WITH IDIOPATHIC EPILEPSY AND WELL-CONTROLLED SEIZURES

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INTRODUCTION: Children with epilepsy are at increased risk for developing behavioral and emotional problems.
OBJECTIVE: The aim of this study was to evaluate behavioral and emotional problems in children with idiopathic epilepsy and well-controlled seizures (without seizures for at least 6 months) and to investigate whether specific problems are associated with specific medical epilepsy-related factors.
METHODS: We studied 68 children who had epilepsy and were aged 6.5 to 9.5 years, divided in 2 subgroups: group A, 37 children (18 boys, 19 girls; mean age: 8.29 ± 1.00 years) with idiopathic generalized epilepsy, and group B, 31 children (18 boys, 13 girls; mean age: 8.35 ± 1.12 years) with idiopathic partial epilepsy. The Child Behavior Checklist by Achenbach was used to assess parent-reported behavioral and emotional problems.
RESULTS: A total of 45.9% of children in group A had behavioral and emotional problems, whereas 19.4% of children in group B had behavioral and emotional problems. Male gender was correlated with increased incidence of behavioral problems and the abnormal first electroencephalogram with increased incidence of attention problems in group A, whereas low socioeconomic status was correlated with increased incidence of behavioral problems and male gender with increased incidence of attention problems in group B.
CONCLUSIONS: The results of this study demonstrated a high prevalence of behavioral and emotional problems in children with idiopathic epilepsy. The findings emphasize the necessity to evaluate and address psychosocial problems in children with idiopathic epilepsy, even when their seizures are well controlled.

VISUAL SEARCH ATTENTION AND EXECUTIVE FUNCTION IN CHINESE CHILDREN WITH WILLIAMS SYNDROME

Submitted by Zheng-Yan Zhao
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INTRODUCTION: Williams syndrome (WS) is a rare neurodevelopmental disorder that is caused by a hemizygous deletion on chromosome 7q11.23. The interest of WS to neurocognitive scientists stems from the uneven profiles of cognitive abilities, with spatial cognition seriously impaired and language and face processing relatively proficient. We know relatively little about the visual search attention and executive function in children with WS.
OBJECTIVE: The objective of this study was to examine the nature of visual search attention and executive function in children with WS, compared with children with Down syndrome (DS), healthy chronological age–matched control subjects (CA), and healthy mental age–matched control subjects (MA).
METHODS: A total of 142 children were tested: 21 with WS, 25 with DS, 45 CA, and 41 MA. MA were matched to the children with WS and DS using the Peabody Picture Vocabulary Test. All participants were assessed on a set of computerized visual search tasks and Wilding Monster Sorting Test using a touch-screen.
RESULTS: The results showed that selective attention, switch, and sustained attention of children with WS all are less developed. Children with WS produced a large number of shape errors, and they also confused shape distractors with targets more than the other groups. Children with WS exhibited poorer executive performance as compared with both groups of typical children. They produced more repetitive errors than did children with DS.
CONCLUSIONS: These findings reveal distinct visual search deficits and atypically developing executive function in children with WS.

Obesity/Metabolism

IDENTIFICATION OF THE OBESE CHILD: ADEQUACY OF BODY MASS INDEX AND FAT MASS INDEX FOR CLINICAL PRACTICE AND EPIDEMIOLOGY

Submitted by Nayera Hassan
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INTRODUCTION: There is no agreement among researchers on adiposity indexes and on the best cutoff to define obesity.
OBJECTIVE: The objective of this study was to evaluate the validity of BMI and fat mass index (FMI) as indica-

tors of obesity in 272 boys and 242 girls who were aged 3 to 5 years.

METHODS: Bioelectrical impedance analysis was used to calculate percentage fat mass (%FM) and FMI (fat mass/stature^2). Boys and girls were considered obese when %FM was ≥ 25 and ≥ 30, respectively. Cutoffs of BMI (weight/stature^2) and FMI were tested at 90th, 95th, and 97th percentiles.

RESULTS: There were strong, significant correlations between BMI or FMI and %FM, but there was no significant correlation between BMI or FMI and stature; therefore, both BMI and FMI are useful indexes to assess fatness and obesity. With the use of %FM as the criterion for obesity, however, the highest prevalence of obesity was found at the 90th percentile for both genders. BMI and FMI had high specificities and lower but variable sensitivities. FMI is associated with a level of sensitivity that is somewhat higher than that of BMI. Almost all children who were not obese were classified correctly, whereas many obese children were not correctly identified.

CONCLUSIONS: FMI is a specific indicator of childhood obesity, and at 90th percentile, it has moderately high sensitivity. BMI should be used with caution as an indicator of childhood obesity.

COMPARISON OF INTERNATIONAL OBESITY TASKFORCE CUTOFFS, CENTERS FOR DISEASE CONTROL AND PREVENTION GROWTH CHARTS, AND BODY MASS INDEX *Z*-SCORE VALUES IN THE PREVALENCE OF CHILDHOOD OBESITY: THE GREEK OBESITY AND LIFESTYLE STUDY

Submitted by Nikolaos Mantzouranis

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OBJECTIVE: Few epidemiologic studies have compared classification methods of childhood obesity. The aim of the Greek Obesity and Lifestyle Study (GOALS) was to assess the prevalence of childhood obesity by comparing 3 classification methods.

METHODS: The GOALS was conducted on a representative sample of 2056 students (1148 boys and 908 girls), aged to 13 years. Body mass and height were measured, and the BMI (kg/m^2) was calculated. The comparisons of obesity prevalence were based on International Obesity Taskforce (IOTF) cutoffs, Centers for Disease Control and Prevention (CDC) growth charts and BMI-for-age *z* scores (overweight ≥1 SD, obese ≥2 SD).

RESULTS: The higher prevalence of obesity (including overweight) in GOALS was found by using the CDC growth charts (37.6%), whereas the obesity prevalence classified according to the IOTF cutoffs was recorded 1% lower (36.6%). In relation to CDC and IOTF classifications, significant lower prevalence was reported when obesity was estimated as BMI-for-age *z* scores (15.2%). Adjusted by gender, the Analysis of variance results showed that the obesity prevalence was significantly higher in boys in both CDC and IOTF classifications compared with BMI-for-age *z* scores.

CONCLUSIONS: The comparison among studies in Greece shows that the prevalence of childhood obesity in GOALS, based on both IOTF and CDC classifications, is the highest ever recorded in Greece and almost similar with the obesity prevalence reported in US teenagers. The lower obesity prevalence recorded in GOALS using the BMI-for-age *z* scores, compared with IOTF and CDC classifications, did not appropriately specify childhood obesity and cannot be used for public health applications.

ASSOCIATION OF COMORBIDITY WITH OBESITY IN MEXICAN CHILDREN AND ADOLESCENTS

Submitted by Arturo Perea-Martinez

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INTRODUCTION: Obesity is a chronic and recurrent inflammatory disease, associated with high risk to health. It is a world public health problem that affects children and adolescents. It is present in rich and poor countries. Type 2 diabetes, systemic arterial hypertension, blood lipid disorders, and cardiovascular disease together compose the metabolic syndrome (BMI > 95th percentile, weight circumference ≥ 85th percentile, serum glucose ≥ 100 mg/dL, high-density lipoprotein cholesterol ≤ 40 mg/dL, serum triglycerides ≥ 110 mg/dL); orthopedic lesions and psychosocial problems (marginalization and depression) are present early in life in obese individuals.

OBJECTIVE: The objective of this study was to describe the frequency of comorbidity in a cohort of 185 obese Mexican children and adolescents.

METHODS: A total of 185 obese Mexican children and adolescents were included in the study. The following parameters were measured: BMI, serum lipid profile, serum glucose, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and serum uric acid. Complete physical examinations were performed, including blood pressure measurements.

RESULTS: BMI was at the 95th percentile in 97% of cases; 75% had ≥1 clinical indicator of comorbidity associated with obesity. Skin lesions (nigricans acanthosis; folliculitis; and grooves in hip, abdomen, and upper and lower extremities), serum lipid disorders (high level of

serum triglycerides, low level of high-density lipoprotein cholesterol), systemic arterial hypertension, and others (eg, hypertransaminemia, hyperuricemia, orthopedic lesions) were the most common.

CONCLUSIONS: Obesity in children and adolescents is a severe world public health problem. Obese children and adolescents frequently had associated comorbidity. It is necessary to improve health, juridical, and educational world policies that prevent and support the treatment of obesity in early life.

THYROID FUNCTION AND GHRELIN AND LEPTIN LEVELS IN OBESE CHILDREN AND ADOLESCENTS WITH AND WITHOUT INSULIN RESISTANCE

Submitted by Charilaos Stylianou

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INTRODUCTION: Thyroid hormones ghrelin, leptin, and insulin are implicated in energy metabolism.

OBJECTIVE: The objective of this study was to investigate any relationship between thyroid function and ghrelin and leptin levels in selected euthyroid (thyrotropin: 0.35–4.94; free thyroxine [fT4]: 0.8–1.8; no autoimmune thyroiditis or iodine deficiency, no medications intake) obese children and adolescents with and without insulin resistance (IR).

METHODS: Forty obese children and 40 obese adolescents were enrolled. BMI, percentage of body fat, fasting glucose, insulin, ghrelin, leptin, thyrotropin, free triiodothyronine (fT3), and fT4 were measured. IR was estimated with homeostasis model assessment of IR index. The Mann-Whitney *U* test for independent samples was applied. Correlations were assessed by the Spearman coefficient.

RESULTS: In adolescents, fT3 levels were positively correlated with insulin and homeostasis model assessment of IR. In children, fT4 levels were negatively correlated with BMI and percentage of body fat (Table 1).

TABLE 1. Thyroid Function and Ghrelin and Leptin Levels in Obese Children and Adolescents With and Without Insulin Resistance

	Obese Children			Obese Adolescents		
	IR	NIR	*P*	IR	NIR	*P*
n	20	20		20	20	
BMI, kg/m^2	28.87 ± 3.84	27.11 ± 4.53	.121	30.54 ± 4.74	29.43 ± 3.87	.678
Body fat, %	35.68 ± 4.71	33.28 ± 4.98	.157	35.59 ± 6.01	34.33 ± 5.14	.461
Homeostasis model assessment, IR	5.00 ± 4.04	1.55 ± 0.64	.000	4.51 ± 1.53	1.80 ± 0.56	.000
Insulin, μIU/mL	22.53 ± 15.02	7.33 ± 2.64	.000	20.04 ± 5.76	9.01 ± 2.65	.000
Ghrelin, pmol/L	831.29 ± 379.19	902.96 ± 360.49	.355	860.12 ± 289.89	1102.09 ± 366.10	.043
Leptin, ng/mL	36.22 ± 14.94	35.20 ± 23.43	.301	42.31 ± 21.81	34.75 ± 17.93	.221
Thyrotropin, μIU/mL	2.28 ± 1.22	2.15 ± 0.75	.779	2.20 ± 1.15	2.06 ± 1.24	.659
fT3, pg/mL	4.61 ± 0.92	4.59 ± 0.64	.989	4.19 ± 0.68	4.12 ± 1.08	.529
fT4, ng/dL	1.32 ± 0.14	1.37 ± 0.22	.495	1.22 ± 0.12	1.29 ± 0.17	.398

CONCLUSIONS: The observed positive correlation between IR and fT3 in adolescents might indicate an interplay between thyroid function and IR. Ghrelin levels are negatively affected by IR but not directly associated with thyroid hormone concentrations.

Pediatric Research

ROLE OF NERVE GROWTH FACTOR IN ALLERGIC AND INFLAMMATORY LUNG DISEASES

Submitted by Basma Abdelmoez

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INTRODUCTION: Nerve growth factor (NGF) is a neurotrophin that exerts an important role in the development and functions of the central and peripheral nervous system, as it was originally discovered for its properties of simulating growth and differentiation of neurons; however, it was recently documented that several immune cells, such as mast cells, lymphocytes, and eosinophils, produce, store, and release NGF. Neurotrophins, including NGF, are constitutively expressed by resident lung cells and produced in increasing quantities by immune cells that invade the airways under inflammatory conditions. Furthermore, NGF appears as a promoter of allergic airway inflammation by increasing eosinophil and lymphocyte recruitment into the lungs. Neurotrophin receptors are expressed on several immune cells, including mast cells, T cells, B cells, and macrophages.

OBJECTIVE: The objective of this study was to clarify the role of NGF in allergic and inflammatory lung diseases.

METHODS: Our study was conducted of 90 children who attended the outpatient pediatric clinic or were admitted to the inpatient pediatric department of Elminia University Hospital. They were classified into 3 groups as follows: group 1, 35 children with asthma during the acute attack; group 2, 35 children with severe inflammatory lung disease and bronchopneumonia; group 3, 20 seemingly healthy children who were age and gender matched to the children with disease. For all children, the following were done: careful history taking, thorough clinical examination, chest radiograph,

complete blood count, erythrocyte sedimentation rate, and reverse-transcriptase polymerase chain reaction (RT-PCR) to detect NGF receptor mRNA expression on purified eosinophils that were obtained from peripheral blood.

RESULTS: We found only 3 patients who had asthma and had positive NGF receptors on isolated eosinophils from the peripheral blood by RT-PCR; however, all studied patients with bronchopneumonia had negative results. Moreover, there was a statistically significant difference between patients with positive and negative results for NGF receptors on isolated eosinophils by RT-PCR regarding age, the frequency of recurrence of asthma attacks, and positive history of other atopic diseases such as allergic dermatitis and allergic rhinitis; however, there was no statistically significant difference between patients with positive and negative results regarding gender, type of feeding, or family history.

CONCLUSIONS: There is a strong association between NGF receptors on isolated eosinophils and the severity of allergic lung diseases and bronchial asthma.

PREVALENCE OF TUBERCULOSIS AMONG CHILDREN WHO HAD TYPE 1 DIABETES AND WERE ADMITTED TO ELMINIA UNIVERSITY HOSPITAL

Submitted by Basma Abdelmoez

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INTRODUCTION: Tuberculosis has been a cause of significant morbidity and mortality for humans throughout history. There are 20 million cases of tuberculosis worldwide with 8 million new cases each year. Three million deaths annually are directly attributable to tuberculosis. Previous clinic-based studies in developed countries demonstrated an association between tuberculosis and diabetes but did not determine whether this is attributable an increase in recently transmitted or reactivated infection of tuberculosis.

OBJECTIVE: The objective of this study was to identify the epidemiologic relationship between tuberculosis and diabetes in children by using MycoDot, a simple, rapid, and reliable test.

METHODS: This study was a cross-sectional study of 2 groups. The first group was 110 children who had type 1 diabetes, were aged 5 to 10 years, and had a regular follow-up in the pediatric diabetes outpatient clinic in Elminia University Hospital. The second group consisted of 110 children (as a control group without diabetes) who were age and gender matched from the pediatric outpatient clinic in Elminia University Hospital. The children were subjected to tuberculin skin test and Ziehl Neelsen staining on sputum. The children with diabetes only were subjected to chest radiograph. The children's sera were subjected to MycoDot test.

RESULTS: Among the 110 children with diabetes, 6 (5.5%) were determined to have positive tuberculosis results using the MycoDot technique. Only 1 (0.9%) control patient was determined to have a positive tuberculosis result using the same test. Among the children with diabetes (110), 4 (3.8%) were found to have positive tuberculosis results by tuberculin skin test, whereas 2 (1.8%) were found to have positive tuberculosis results by Ziehl Neelsen staining on sputum.

CONCLUSIONS: Many studies have explored the association between diabetes and tuberculosis. In developed countries, studies dating to the first half of the 20th century demonstrated considerable increase in the frequency of tuberculosis among patients with diabetes, although the proportion with comorbidity ranged widely from 1.0% to 9.3%. Other studies have shown a higher frequency of diabetes among individuals with tuberculosis. In our results, 5.5% of children with diabetes had tuberculosis by MycoDot test, which is a simple and reliable test, whereas only 1 (0.9%) positive result was found in the group without diabetes by the same test. The former indicates that risk for tuberculosis increases among children with diabetes, which indicates that regular screening for the presence of active tuberculosis among children with diabetes should be conducted.

STUDY ON THE DAMAGE OF CULTURED HIPPOCAMPAL NEURONS INDUCED BY SEIZURE-LIKE DISCHARGE AND THE EFFECT OF BRAIN-DERIVED NEUROTROPHIC FACTOR ON THE INJURED NEURONS

Submitted by Li Jiang

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OBJECTIVE: The objective of this study was to observe the damage of cultured hippocampal neurons induced by seizure-like discharge and study the effects of brain-derived neurotrophic factor (BDNF) on such injury.

METHODS: Primary cultured hippocampal neurons were randomly divided into 3 groups: (1) control group: cultured neurons were exposed to regular extracellular solution for 3 hours, then returned to regular medium; (2) seizure-like discharge group: cultured neurons were exposed to magnesium-free extracellular solution for 3 hours, then maintained for 24 hours in regular medium; and (3) BDNF-treated group: cultured neurons were precultured with regular medium added to BDNF (200 ng/mL) for 24 hours and exposed to magnesium-free

extracellular solution for 3 hours, then maintained for 24 hours in regular medium that contained BDNF. The morphologic changes of neurons dyed by acridine orange/ethidium bromide were observed. Mitochondria membrane potential (MEP) by JC-1 dye was assessed with laser scanning confocal microscope. Lactic acid dehydrogenase (LDH) in supernatant was detected by autobiochemical analyzer. BDNF was detected by immunocytochemistry and assessed by optical density.

RESULTS: There were some apoptotic and necrotic neurons in the seizure-like discharge group. Compared with the control group, MEP was significantly decreased and LDH level and BDNF expression were significantly increased in the seizure-like discharge group. Compared with the seizure-like discharge group, MEP was significantly increased and LDH level was significantly decreased in BDNF-treated group, but there was no significant difference on BDNF expression between them.

CONCLUSIONS: Seizure-like discharge could induce injury to hippocampal neurons and could upregulate BDNF expression in hippocampal neurons. BDNF could relieve the damage of neurons induced by seizure-like discharge, so BDNF has protective effects on hippocampal neurons.

EFFECTS OF VITAMIN A ON LUNG DEVELOPMENT IN THE RAT FROM EARLY AGE TO ADULTHOOD

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INTRODUCTION: Epidemiologic studies show that nutritional deficiency can alter lung development and have later adverse effects on lung function and respiratory health. Vitamin A is an important nutrient and is considered important in lung development and maturation. Additional studies are required to address whether vitamin A deficiency adversely affects lung development from early age to adulthood and whether such effects can be blocked or reversed.

OBJECTIVE: Our aim was to study the effect of vitamin A on lung development in the rat from early age to adulthood.

METHODS: Female rats were divided into control, marginal vitamin A deficiency (MVAD), and vitamin A intervention (VAI) groups. Control dams and pups were fed a normal diet (6500 U/kg vitamin A). MVAD rats were fed an MVAD diet (400 U/kg vitamin A). VAI rats were fed an MVAD diet until the birth of the pups and thereafter were fed with normal diet while the pups were given vitamin A through intragastric administration. All pups were killed at 8 weeks of age. Blood serum vitamin A levels were measured. Lungs were weighed and stained for light microscopy.

RESULTS: The vitamin A level of the MVAD group was lower than that of the control group. Lung weight of MVAD rats was lower than that of the controls. Morphometric measurements showed that the alveolar number in MVAD rats was less than that of the controls, and alveolar septa were thicker than those of the controls. All results in VAI group were better than those in the MVAD group and showed no difference from the controls.

CONCLUSIONS: Vitamin A status in early life can affect the lung development from early age to adulthood. Such effects can be reversed by dietary intervention after birth.

MARGINAL VITAMIN A DEFICIENCY IN PREGNANCY CAN INDUCE MEMORY DEFICIT IN ADULT OFFSPRING

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INTRODUCTION: Vitamin A deficiency in pregnancy has a negative impact on the development of offspring; however, little is known about the effect of maternal marginal vitamin A deficiency (MVAD) on the function of the central nervous system in children later in postnatal life.

OBJECTIVE: We investigated whether MVAD during the gestational period can cause learning and memory impairment of adult offspring.

METHODS: There were 2 offspring groups: an experimental group that had MVAD only in pregnancy and a control group. Serum vitamin A was monitored by high-performance liquid chromatography. Both groups were trained by Marris water maze task at 8 weeks of age. The hippocampal CA1 long-term potentiation was detected by electrophysiologic technique, and the free calcium ion concentration in cells was examined by confocal laser scanning microscopy.

RESULTS: No significant difference in the serum vitamin A level was observed between the 2 groups; however, the escape latency of the experimental group (10.50 $\pm$ 1.58 seconds) was longer than that of the control group (8.75 $\pm$ 1.19 seconds) in the behavior test. Correspondingly, the changes of field excitatory postsynaptic potentials slope of the experimental group (29.5% $\pm$ 4.6%) was significantly less than that of the control group (57.5% $\pm$ 8.6%), and the lower relative intensity of fluorescence in cells was seen in the experimental group (85.8 $\pm$ 17.1) compared with the control group (113.6 $\pm$ 20.5) after the tetanus stimulation.

CONCLUSIONS: MVAD in pregnancy causes learning and memory impairment of adult offspring.

EFFECTS OF MARGINAL VITAMIN A DEFICIENCY ON LONG-TERM POTENTIATION IN YOUNG RATS

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INTRODUCTION: Vitamin A is an essential micronutrient for brain development. Marginal vitamin A deficiency (MVAD) remains a subclinical public health problem in children, but little is known about the mechanism by which it affects brain development beginning from embryonic period and early postnatal period.
OBJECTIVE: The objective of this study was to study the effects of MVAD on the hippocampal CA1 long-term potentiation (LTP) in young rats.
METHODS: The MVAD group was fed a vitamin A–deficient diet (400 IU/kg vitamin A), and the control group was fed a vitamin A–sufficient diet (6500 IU/kg vitamin A) at 3 weeks before coitus. Serum vitamin A was assessed by high-performance liquid chromatography. Hippocampal CA1 LTP was detected by electrophysiologic technique, and the ultrastructure of synapses was observed by electron microscope.
RESULTS: The changes of field excitatory postsynaptic potentials slope (25.4% ± 2.01%) in MVAD rats aged 7 weeks was much lower than that in the control group (57.5% ± 8.6%). The changes of slope of field excitatory postsynaptic potentials induced by MVAD in young rats could be replenished after addition of retinoic acid (RA); however, LTP impairment was observed again after addition of RA antagonist into the solution of the control group. No differences of LTP were found after addition of $FeSO_4$ or $ZnSO_4$. The curvature of the synaptic interface of the MVAD group was less than that of the MVAD group that was supplemented with RA and of the control group.
CONCLUSIONS: MVAD during the embryonic and early postnatal period can directly impair the hippocampal CA1 LTP of young rats.

EFFECT OF BCG VACCINATION ON SPLENIC DENDRITIC CELL DEVELOPMENT IN NEONATAL BALB/C MICE

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INTRODUCTION: As an immunoregulator, Mycobacterium BCG has the potential to be applied in allergic disease such as asthma prevention in clinic. Previous studies showed that neonatal BCG vaccination promoted mouse splenic T helper 1 development.
OBJECTIVE: The objective of this study was to investigate further the impact of BCG vaccination on dendritic cell (DC) development in neonatal mice.
METHODS: Neonatal and adult BALB/C mice were divided into 2 groups: the control group and the BCG-treated group in which BALB/C mice were inoculated with 1×10^5 colony-forming units of BCG intraperitoneally. After 4 weeks, splenic cells were isolated and co-stimulatory molecules and major histocompatibility complex molecules were analyzed by flow cytometry on CD11c-positive cells.
RESULTS: $CD11c^+CD8\alpha^+$ and $CD11c^+CD8\alpha^-$ DCs were found in spleen cells of BALB/C mice. In comparison with the control group, the percentage of $CD8\alpha^-$ DCs was significantly decreased (45.00 ± 14.14 vs 67.00 ± 8.27) and that of $CD8\alpha^+$ DCs was strikingly increased (55.00 ± 14.14 vs 33.00 ± 8.27) in BCG-treated neonatal mice. In contrast, the percentage of $CD8\alpha^-$ DCs markedly increased from 57% to 70% and that of $CD8\alpha^+$ DCs noticeably decreased from 43% to 30% in adult mice that were vaccinated. BCG vaccination upregulated the expression of co-stimulatory molecules on DC in adult and neonatal mice.
CONCLUSIONS: Our results indicate that development of T cells was induced by BCG vaccination through an effect on DC differentiation and maturation in BALB/C mice, possibly not only by DC phenotype but also by cytokines.

IMPACT OF ZINC SUPPLEMENTATION ON RESPIRATORY AND GASTROINTESTINAL INFECTIONS: A DOUBLE-BLIND, RANDOMIZED TRIAL AMONG URBAN IRANIAN SCHOOLCHILDREN

Submitted by Nahid Masoodpoor
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INTRODUCTION: In addition to inhibiting growth, mild zinc deficiency is probably associated with reduced resistance to infection in children, but it has been difficult to establish this link; however, children with severe

zinc deficiency have been found to be at increased risk for diarrhea and respiratory diseases.

OBJECTIVE: The aim of this study was to evaluate the roles of zinc supplementation in the episodes of respiratory and gastrointestinal infections in children.

METHODS: This study was a randomized, double-blind, placebo-controlled trial of 90 children (50 boys and 40 girls aged 7–12 years) who were underweight or had stunted growth. They were supplemented with 10 mg of zinc or placebo on school days for 6 months. Episodes of respiratory and gastrointestinal infections were recorded monthly.

RESULTS: At the end of this study, significant effects of zinc supplementation on the decreased number of episodes of respiratory and gastrointestinal infections were seen during the full 6 months.

CONCLUSIONS: On the basis of this study, zinc supplementation decreased the number of episodes of respiratory and gastrointestinal infections in schoolchildren who were underweight or had stunted growth.

SEVERE LUNG HYPOPLASIA IS OBSERVED IN *DHCR24*-KNOCKOUT MICE: A MOUSE MODEL OF DESMOSTEROLOSIS

Submitted by Rusella Mirza

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INTRODUCTION: The *DHCR24* gene encodes an enzyme that converts desmosterol to cholesterol in the last step of cholesterol synthesis. Desmosterolosis is an autosomal-recessive disorder that is caused by mutation in the *DHCR24* gene, resulting multiple developmental anomalies.

OBJECTIVE: The objective of this study was to understand the pathophysiology of desmosterolosis.

METHODS: *DHCR24*-knockout mice were used in this study. All homozygous mice (−/−) died soon after birth. *DHCR24*$^{-/-}$ mice demonstrated features of lethal restrictive dermopathy, associated with impaired skin barrier function as a result of hyperproliferation of undifferentiated keratinocytes throughout the epidermis. One other possible cause for neonatal death in *DHCR24*$^{-/-}$ mice is respiratory failure, as evidenced by severe cyanosis immediately after birth. We therefore studied the lung development of these mice. Lungs from the newborn alive pups were subjected to weight measurement and histologic and Western blot analyses.

RESULTS: *DHCR24*$^{-/-}$ mice were identified by their phenotype and genotyping. Lung-to-body weight ratio was decreased in *DHCR24*$^{-/-}$. The space between lung surface and the thoracic wall was significantly increased as a result of less expansion of the lung. The majority of the lung portion consisted of collapsed alveoli and decreased saccular space in *DHCR24*$^{-/-}$ mice. No differentiation defect in alveolar type I cell was detected by Western blot and immunohistochemistry with anti-T1 α antibody, a type I cell–specific marker. Immunohistochemistry with anti–caveolin 1 demonstrated no change in vascular development.

CONCLUSIONS: A distinct saccular hypoplasia in *DHCR24*$^{-/-}$ mice suggests that there is an important role of *DHCR24* in lung development. Additional experiments with surfactant compositions are needed to explore the underlying respiratory pathology.

USING Q-METHODOLOGY TO EXPLORE PREFERENCES FOR CARE OF ADOLESCENTS WITH CHRONIC DISORDERS: 4 PROFILES

Submitted by AnneLoes Van Staa

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INTRODUCTION: Adolescents with chronic disorders are seldom asked to give opinions about their preferences for care, even though they are frequent health care users and soon need to take over the responsibility of managing their own care.

OBJECTIVE: The aim of the study was to investigate care-related preferences of adolescents with chronic disorders.

METHODS: A Q-methodologic study was conducted in a random sample of 31 adolescents with various congenital and acquired disorders from the total population of Erasmus Medical Center-Agia Sophia Children's Hospital (12–19 years). Adolescents rank-ordered 37 statements about preferences for care and self-care using a quasi-normal distribution. Factor analysis was applied to identify clusters in the Q-sorts, groups of adolescents with common preferences.

RESULTS: Four profiles were distinguished: concerned and compliant, backseat patient, opinionated and careless, and worried and insecure. Differences between profiles are related to independence competencies, level of involvement in management of the illness, adherence to therapeutic regimens, and appreciation of their parents' role. All adolescents want to have an important say in treatment-related decisions. Although adolescents are used to being accompanied by their parents in the con-

sultation room, they sometimes prefer to be on their own.

CONCLUSIONS: Four different preference profiles were uncovered. Caregivers recognize these profiles in daily practice. Because the goal of Q-methodology is to establish different patterns but not their prevalence, the distribution of profiles will be explored in a large follow-up survey. Additional use of these profiles in daily practice will be also explored, because rank-ordering the statements stimulated adolescents to talk about care issues.

EFFECT OF PERINATAL IRON DEFICIENCY ON BEHAVIORAL DEVELOPMENTS AND MYELINATION AROUND THE HIPPOCAMPUS IN RATS

Submitted by Lingling Wu
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INTRODUCTION: Iron deficiency is a common nutritional disorder. The effect of iron deficiency on myelination of specific brain regions and their relevant behavior has not been well documented.

OBJECTIVE: The objective of this study was to determine the consequences of perinatal iron deficiency on behavioral and myelination of specific brain regions in rats.

METHODS: Sixteen dams were randomly assigned to iron-sufficient or low-iron diets during gestation and lactation. Thereafter, all offspring were fed the iron-sufficient diet and were assessed for behavioral and neurologic developments. Behavioral assessments included sensorimotor function tests, a recognition memory task, and a spatial learning task. The density of myelination around the hippocampus was measured by 2′,3′-cyclic nucleotide 3′-phosphohydrolase (marker of oligodendrocyte) by means of immunohistochemistry and quantified by analysis of integrated optical density. The regions of interest included the corpus callosum and the fimbria of the hippocampus.

RESULTS: Iron-deficient rats showed behavioral impairments in sensorimotor functions and recognition memory task but no significant differences were found in the spatial learning task. Iron-deficient rats had significantly reduced density of myelination than control rats in the corpus callosum but had no difference in the fimbria of the hippocampus.

CONCLUSIONS: This study shows that perinatal iron deficiency can significantly alter the behavioral outcomes in rat pups and can profoundly influence the development of myelination in specific brain regions.

EXPRESSION AND MODULATION OF AQUAPORIN 5 IN HYPEROXIA-INDUCED LUNG INJURY

Submitted by Feng Xu
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INTRODUCTION: Bronchopulmonary dysplasia (BPD) is a common disease that is caused by mechanical ventilation with persistent high-concentration oxygen in newborns, especially in preterm infants. One of the most important reasons is oxygen toxicosis. In physiologic conditions, liquid in the lung tissue is also transferred by aquaporins (AQPs), but the mechanism of aquaporins in hyperoxia-induced lung injury and lung dropsy is not clear.

OBJECTIVE: The objective of this study was to explore the expression and the modulation of AQP5 in hyperoxia-induced lung injury.

METHODS: Lung tissue was harvested after high-concentration oxygen exposure on the third, seventh, and 14th days in rats. The expression of AQP5 mRNA level and the location were detected by reverse-transcription polymerase chain reaction and immunohistochemistry, respectively, and compared with that in rats that were administered an injection of dexamethasone.

RESULTS: AQP5 was strongly labeled in alveolar epithelial cells. The expression of AQP5 in hyperoxia groups (3, 7, and 14 days) revealed a notable decline as compared with the control group, with no change even in the hyperoxia 14-day group. There was no difference between hyperoxia groups and hyperoxia + dexamethasone groups on AQP5 mRNA level.

CONCLUSIONS: The significant decrease of AQP5 expressed in hyperoxia-induced lung injury may be an important reason for abnormal water movement, which leads to pulmonary edema. Dexamethasone seems to have no effect in modulating AQP5 expression in acute lung injury.

PROTECTIVE EFFECT OF *N*-ACETYLCYSTEINE ON HYPEROXIA-INDUCED LUNG INJURY AND ITS INTERACTION WITH P38 MITOGEN-ACTIVATED PROTEIN KINASE SIGNALING PATHWAY

Submitted by Feng Xu
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INTRODUCTION: *N*-Acetylcysteine (NAC) is an effective oxidation inhibitor, but the protection of NAC in hyperoxia-induced lung injury is unknown.

OBJECTIVE: The objective of this study was to explore the protective effect of NAC on hyperoxia-induced lung injury and change of p38 mitogen-activated protein kinase (MAPK) expression caused by NAC treatment.
METHODS: Forty Wistar rats were randomly assigned to room air (A), hyperoxia injury (B), hyperoxia + NAC (C), hyperoxia + SB203580 (D), or hyperoxia + NAC + SB203580 (E). The lung wet/dry ratio, pathology, and location and quantity of p38 protein were detected.
RESULTS: Although pathologic changes in group B included severe alveolar edema with inflammatory cell aggregation and red blood cell leakage, the lung micrographic pictures in groups C, D, and E were improved significantly compared with group B; p38-positive cells increased in group B compared with that in group A and labeled in many types cells in lung tissue, especially in infiltrative inflammatory cells. In groups C, D, and E, the positive cells remarkably decreased compared with those in group B; the quantity of p38 MAPK was higher in group B than in group A, and p38 expression in groups C, D, and E decreased significantly compared with group B but was higher than that in the control group. There was no significant difference of p38 quantity among the 3 groups.
CONCLUSIONS: Reactive oxygen species activated phospho-p38 MAPK signaling pathway, and NAC and SB203580 treatments reduced the extent of hyperoxia-induced lung injury, as evidenced by reduction of the wet/dry ratio and lung pathology. NAC may exert a protective effect on hyperoxia-induced lung injury through attenuation of reactive oxygen species–induced p38 MAPK activation.

STUDY OF PULMONARY SURFACTANT AND SURFACTANT PROTEIN IN RATS WITH LIPOPOLYSACCHARIDE-INDUCED ACUTE LUNG INJURY

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INTRODUCTION: The abnormal metabolism of pulmonary surfactant (PS) may have some relationship to acute lung injury (ALI).
OBJECTIVE: The objective of this study was to examine the alteration trend of PS and surfactant-associated protein (SP) in rats with lipopolysaccharide (LPS)-induced ALI.
METHODS: Fifty-six adult Wistar rats were randomly divided into the normal saline (NS) group and the ALI group. The levels of mRNA of surfactant protein A (SP-A) and SP-B were measured by reverse-transcription polymerase chain reaction during intravenous LPS administration at 1, 3, 5, and 7 hours. The content and component of PS in the bronchoalveolar lavage fluid (BALF) were measured by high-performance liquid chromatography. In addition, lung dry/wet weight ratio, the protein content of BALF, alveolar oxygen partial pressure, and histologic changes were detected.
RESULTS: Compared with the NS group, the ALI group developed severe lung damage; edema, hemorrhage, and inflammation were found. Total phospholipids in BALF at 1, 3, 5, and 7 hours were lower than those in the NS group; phosphatidylcholine at 3, 5, and 7 hours was lower than that in the NS group, whereas lysophosphatidylcholine at 1, 3, 5, and 7 hours was higher than that in the NS group. The expression of SP-A and SP-B mRNA at 3, 5, and 7 hours was less than that in the NS group.
CONCLUSIONS: The changed metabolism of PS may be responsible for the pathogenesis of ALI. It is mainly demonstrated by the decrease in total phospholipids and phosphatidylcholine and the decreased expression of SP-A and SP-B mRNA. Decrease in content and change in components of PS may play an important role in severe hypoxemia in ALI.

EXPRESSION CHANGE OF AQUAPORIN 1 IN HYPEROXIC LUNG INJURY

Submitted by Feng Xu
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INTRODUCTION: Bronchopulmonary dysplasia (BPD) is a disease that is caused by prolonged high-concentration oxygen therapy, and its typical pathologic character is edema of pulmonary alveolus. Aquaporins play an important role in the fluid transition.
OBJECTIVE: The objective of this study was to examine the expression change of aquaporin 1 (AQP1) in hyperoxia-induced lung injury and the mechanism of action in lung edema.
METHODS: Thirty-two juvenile Wistar rats were randomly divided into breathing room air ($n = 8$) and hyperoxia exposure ($O_2 > 95\%$; $n = 8$ at 3, 7, and 14 days, respectively). The distribution of AQP1 in the lung tissues and its mRNA expressions were detected by immunohistochemistry and reverse-transcription polymerase chain reaction.
RESULTS: Light microscopic findings in the hyperoxia group included edema, hemorrhage, and extensive inflammatory cells. The lung wet/dry ratio, the protein content in bronchoalveolar lavage fluid, and the lung leak index in the hyperoxia group were significantly higher than those in room air group. The expression of AQP1 mRNA in the lungs was significantly decreased at

3 days of hyperoxia exposure, minimized at 7 days, and increased from 14 days. Immunohistochemistry for AQP1 was seen primarily in microvascular endothelia cells around bronchus and alveolus and interstitial cells; the positive regions were similar between the room air group and the hyperoxia group, AQP1 protein expression in the lungs was significantly decreased at 3 days of hyperoxia exposure, minimized at 7 days, but increased at 14 days. The dynamic changes of AQP1 protein level coincided with the changes of AQP1 mRNA expression.
CONCLUSIONS: Hyperoxic lung injury may induce regulative imbalance of aquaporin expression. It may be 1 of the reasons for lung edema caused by hyperoxic lung injury.

BASIC FEATURES OF HUMAN METAPNEUMOVIRUS CHINESE ISOLATE PROTEINS

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INTRODUCTION: Human metapneumovirus (hMPV), initially described in 2001, is an enveloped RNA virus of the genus *Metapneumovirus*, subfamily Pneumovirinae, family Paramyxoviridae.
OBJECTIVE: We sought to clarify the basic features of hMPV proteins.
METHODS: Rabbits were immunized with inactivated virions of hMPV Chinese isolate, CHN05-01, to yield anti-hMPV antiserum. Antiserum was used as primary antibody to detect hMPV proteins by Western blotting. NetNglyc 1.0 server, NetOglyc 3.1 server, and the NetPhos 2.0 server were applied for predicting potential glycosylation and phosphorylation sites of proteins of prototype virus of subtype A, CAN97-83.
RESULTS: The highest reactive titer of the antiserum with hMPV antigens reached 1:500 in enzyme-linked immunosorbent assay. Potential glycosylation sites of G protein and phosphorylation sites of P protein were greatest among all hMPV proteins. G protein was shown as a narrow band with molecular weight between 55 and 72 kd (~68 kd), indicating that its glycosylation level is consistent and remarkably different from that of CAN99-80 and CAN99-81. F1 subunit of fusion protein displayed molecular weight between 40 and 55 kd (~48 kd), which is consistent with previous reports.
CONCLUSIONS: Basic features of 2 major membrane proteins of Chinese hMPV isolate were clarified, which will benefit future studies on protein function and the pathogenesis of this virus.

APOPTOSIS OF ALVEOLAR TYPE II CELL AND C-JUN N-TERMINAL KINASE SIGNAL TRANSDUCTION INDUCED BY OXIDATIVE STRESS

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INTRODUCTION: Alveolar epithelial apoptosis has been described in the early stages of bronchopulmonary dysplasia. The production of reactive oxygen species during hyperoxia is thought to contribute to alveolar epithelial apoptosis, but the molecular mechanisms of oxidative stress–induced alveolar epithelial cell death is unclear.
OBJECTIVE: The objective of this study was to explore the role of the c-Jun N-terminal protein kinase (JNK) pathway in the apoptosis of alveolar epithelial cells that is induced by oxidative stress.
METHODS: Primary cultured rat alveolar type cells were treated with 500 μM hydrogen peroxide (H_2O_2) at various time intervals (0, 1, 3, 6, and 9 hours), whereas some cells were pretreated with a specific JNK inhibitor (SP600125). Mitochondrial membrane potential (MMP) change, cell survival, and apoptotic ratios were measured by fluorescence microscopy, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay, and flow cytometry analysis, respectively. The expression of phosphorylated JNK and Bax was detected by Western blot.
RESULTS: H_2O_2 treatment resulted in cell apoptosis and a decrease of MMP and cell viability in a time-dependent manner. Meanwhile, the JNK was activated and peaked at 30 minutes, and the Bax expression level was increased. Pretreated SP600125 enhanced cell viability and decreased apoptotic ratios after H_2O_2 treatment. The expression of Bax declined after using SP600125 compared with cells that were treated with H_2O_2 only.
CONCLUSIONS: High levels of oxidative stress induced cell apoptosis in a time-dependent manner. The mechanisms of oxidative stress–induced cell apoptosis involves JNK activation, Bax upregulation, and MMP decrease. JNK activation could improve the expression of Bax and play a proapoptotic role in the regulation of apoptosis that is induced by oxidative stress.

EFFECTS OF MESENCHYMAL STEM CELL TRANSPLANTATION ON CARDIAC FUNCTION, STRUCTURE, AND ELECTROPHYSIOLOGY IN RABBITS WITH DILATED CARDIOMYOPATHY

Submitted by Tian Jie

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OBJECTIVE: The objective of this study was to explore the influence of implanted mesenchymal stem cells (MSCs) on cardiac function, structure, and electrophysiology in rabbits with dilated cardiomyopathy (DCM).
METHODS: Thirty-eight rabbits were randomly assigned to 3 groups: (1) normal rabbits (n = 12); (2) rabbits with DCM cell implantation (n = 13); or (3) DCM control rabbits (n = 13). Adriamycin was applied to create the rabbit DCM model. Rabbits for cell transplantation received an intramyocardial injection of MSCs. Four weeks later, heart function morphology and electrophysiology changes were observed. The expression of cardiac Troponin T and connexin 43 was investigated through immunohistochemistry.
RESULTS: Compared with normal rabbits, the cardiac function of DCM rabbits was impaired, but this impaired function was improved by MSC implantation. The value for monophasic action potential amplitude and the maximum velocity in ¡°0¡±phase decreased significantly in DCM rabbits, whereas the value for 50% monophasic action potential durations (MAPD) and 90% MAPD were increased significantly. The effective refractory period increased also. The comparison of both DCM groups showed that the prolongation of MAPD was shorter in the cell implantation group than in the DCM control group, and no after-depolarization was observed, whereas early after-depolarization was recorded in 2 rabbits in the DCM control group. Histology analysis showed that the structural abnormalities in the cell implantation group were less than those in the DCM control group, and the implanted MSCs could express cardiac Troponin T and connexin 43.
CONCLUSIONS: Implanted MSCs can improve heart function, reduce the structural abnormalities, and possibly inhibit the progression of electrophysiologic derangement.

Pulmonology

DIAGNOSIS OF AIRWAY MALACIA VIA VIRTUAL BRONCHOSCOPY

Submitted by Nemat Bilan

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INTRODUCTION: The term "malacia" refers to softness; in medical terminology, it refers to weakness of bone or cartilage. Laryngomalacia is the most common congenital abnormality of the larynx, and the patient may experience recurrent aspiration. Tracheomalacia refers to tracheal weakness and usually causes airway collapse as a result of cartilage defect. Bronchomalacia describes the weakness and collapsibility of 1 or both main bronchi. All of these diseases can be diagnosed by bronchoscopy, but this method is invasive and may interfere with the diagnosis. Furthermore, it is intolerable in young individuals who are severely ill and in patients with coagulopathy.
OBJECTIVE: This study was conducted to examine the role of virtual bronchoscopy in the diagnosis of laryngotracheobronchomalacia.
METHODS: In a periexperimental study during 3 years (November 2003 through October 2006), 35 patients who had clinical signs and symptoms of airway malacia were surveyed via virtual bronchoscopy.
RESULTS: The percentage of boys and girls was 65.7% and 34.3%, respectively, and the mean age was 3.7 ± 1.6 months. The result of virtual bronchoscopy for laryngomalacia, bronchomalacia, tracheomalacia, laryngotracheomalacia and laryngobronchomalacia was 42.8%, 25.7%, 20%, 8.5%, and 2.9%, respectively.
CONCLUSIONS: Virtual bronchoscopy, because of its noninvasive character, its speed imaging, and its excellent ability of assessment of airway stenosis can be considered as a substitution for bronchoscopy.

IDIOPATHIC PULMONARY HEMOSIDEROSIS IN CHILDREN: A ROMANIAN EXPERIENCE

Submitted by Catalina Bulucea

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INTRODUCTION: Idiopathic pulmonary hemosiderosis (IPH) is a rare disease with unknown cause and variable outcome. It is characterized by recurrent episodes of severe hypochromic anemia, alveolar bleeding, and typical radiologic findings.
OBJECTIVE: The objective of this study was to develop an early diagnosis of IPH with real therapeutic benefits.
METHODS: We conducted a multicenter, retrospective, and prospective study using patients who were admitted to 3 Romanian pediatric clinics between 1984 and 2006. Secondary causes of pulmonary hemosiderosis were excluded.
RESULTS: Fifteen patients received a diagnosis of IPH during a 22-year period (1984–2006). The symptoms started at a mean age of 6.8 years (range: 9 months to 13 years), with a mean delay of 2.4 years before diagnosis. From the beginning, all patients had anemia, and only 6 children presented with pulmonary symptoms as well.

The classical triad (anemia, hemoptysis, and pulmonary infiltrates) was found from early in the disease in only 4 patients. The majority of patients' disease was diagnosed by bronchoalveolar lavage, and 3 were diagnosed at necropsy. Eight patients died in a period of 1 to 3 years from the diagnosis. The clinical course was variable: treatment with corticosteroids alone was not effective because 12 patients continued to have recurrent bleeding. Three patients who received immunosuppressive agents had a better outcome.
CONCLUSIONS: IPH is a severe condition with variable prognosis and has a better outcome when diagnosis is made at an early age. We believe that it is necessary to include in the screening of any severe, recurrent, hypochromic anemia a well-interpreted chest radiograph and to look for hemosiderin-laden phages in bronchoalveolar lavage.

BLOOD LEVELS OF INTERFERON γ IN NEWBORNS AND CHILDREN WITH OR WITHOUT RESPIRATORY PATHOLOGY

Submitted by Juan Peuchot
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INTRODUCTION: There is evidence that long-term exposure to bacterial endotoxins at an early age is related to a protective effect for the development of allergic sensitivity. The endotoxin would be a powerful inductor of type I cytokines. Interferon γ (IFN-γ) would regulate the production of type II cytokines. There would be an increase of interleukin 4 and a decrease of IFN-γ in the airway and peripheral blood.
OBJECTIVE: The objective of this study was to determine in blood the levels of IFN-γ, immunoglobulin E, and eosinophil count in newborns and children with or without recurrent wheeze.
METHODS: Fifty-one newborns were recruited. The sample was processed through enzyme-linked immunosorbent assay method to determine levels of IFN-γ. In addition, 53 children with or without recurrent wheeze were recruited as well as 53 healthy children.
RESULTS: A total of 157 patients divided into 3 groups were analyzed. Group A: 51 newborn patients; group B: 53 patients who had recurrent wheeze and were aged 4 to 10 years; group C: 53 patients who had no history of wheeze and were aged 4 to 10 years. The average value of IFN-γ in children with a history of wheeze was 0.48 UI/mL. They had average values of immunoglobulin E of 7.89 and eosinophils of 9%. Children without history of wheeze had average values of IFN-γ of 0.91 UI/mL; newborns had average values of IFN-γ of 1.10 UI/mL.
CONCLUSIONS: IFN-γ could be used as an early diagnostic marker in atopic diseases.

INTRAVENOUS MAGNESIUM FOR TREATING ACUTE EXACERBATIONS OF ASTHMA IN CHILDREN: A SYSTEMATIC REVIEW

Submitted by Oliver Rackham
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INTRODUCTION: Inhaled bronchodilators and systemic corticosteroids are the mainstay of treatment for acute exacerbations of asthma. A systematic review of the use of magnesium has been published, but the results are incomplete and the recommendation is "weak."
OBJECTIVE: The objective of this study was to determine the effect of intravenous magnesium in children with acute asthma.
METHODS: Randomized, controlled trials were identified by searching the Cochrane, Medline, Embase, CINAHL, and ProQuest databases. Other sources were used to identify "gray literature." Randomized, controlled trials in which children with an acute exacerbation of asthma were treated with intravenous magnesium versus placebo were included. Data were extracted from the full papers, and methodologic quality was assessed using a scale from 0 to 5.
RESULTS: Six studies involving 215 patients were included. Hospital stay was reduced in the magnesium-treated group. The percentage improvement in the percentage predicted peak expiratory flow rate was 43.5% greater in the treatment group. Significant differences were also seen in the forced expiratory volume in 1 second (weighted mean difference: 74.5%) and the forced vital capacity (weighted mean difference: 64.5%). There was improvement in asthma scores in 3 of the 4 studies that reported this outcome. There were no clinically significant differences in vital signs. No major adverse events were reported.
CONCLUSIONS: Intravenous magnesium is safe and beneficial as adjuvant therapy in the treatment of children with moderate to severe acute asthma. Magnesium should be for children who have moderate to severe acute exacerbations of asthma that do not respond to nebulized β-2 agonist.

DIAGNOSTIC BRONCHOALVEOLAR LAVAGE FOR PULMONARY FUNGAL INFECTIONS IN CRITICALLY ILL CHILDREN

Submitted by Malak Shaheen
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INTRODUCTION: The incidence of pulmonary fungal infection is increasing worldwide, particularly in critically ill patients.
OBJECTIVE: The objective of this study was to assess bronchoalveolar lavage (BAL) as a diagnostic specimen for clinically and radiologically suspected fungal pneumonia in critically ill children.
METHODS: Thirty-five children who were admitted to the PICU of Ain Shams University because of their critical illness were included. All children underwent full medical history; thorough clinical examination, including general and local chest examination and basic laboratory investigations (from that, the Pediatric Risk of Mortality [PRISM] score was calculated to evaluate the critical illness severity); chest imaging; and bronchoscopic collection of BAL and microbiological assessment of BAL and blood using direct microscopic examination, cultured on Sabouraud dextrose agar, and fungal antigen detection using the enzyme-linked immunosorbent test for both *Aspergillus galactomannan* antigen and *Candida mannan* antigen.
RESULTS: Pulmonary fungal infection was documented in 77% of the studied children. BAL investigations proved to have a higher diagnostic yield in comparison with blood. Positive fungal antigens in BAL fluid were significantly higher than positive BAL fungal cultures in studied children. Analysis of the risk factors for fungal infection among the studied patients revealed that prolonged PICU stay (≥1 week) and high PRISM score (mean: 35.9 ± 6.46) were significant risk factors for fungal infection.
CONCLUSIONS: BAL fluid investigation has a significantly higher diagnostic value for pulmonary fungal infections than that of the blood. The results may be further improved especially if both culture and antigen fungal detections are combined.

COMPARISON OF THE 2 BRONCHIAL PROVOCATION TESTS OF DIFFERENT DOSAGE CONCENTRATION GRADIENTS FOR INFANTS

Submitted by Ying Huang
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INTRODUCTION: Bronchial provocation tests (BPTs) assist in diagnosing and evaluating the curative effect of asthma.
OBJECTIVE: The objective of this study was to compare the sensitivity, reliability, and safety between 2 tidal breathing methods in BPT.
METHODS: Sixty-five infants, including those with asthma and chronic cough, were divided into groups A and B at random. BPT by the improvement of tidal breathing method was performed in group A (35 infants), and the traditional tidal breathing method was performed in group B (30 infants). In 10 normal infants (control subjects), the traditional tidal breathing method was used. In addition, we observed arterial oxygen saturation, respiratory system resistance, %T-PF, percent of tidal volume of peak tidal expiratory flow, and lung symptoms and monitored the vital sign and adverse effects of the test.
RESULTS: Results of the BPTs for all children with asthma were positive. The positive rates for children with chronic cough were 69.57% and 60.00% in groups A and B, respectively; the results of BPTs in control subjects were completely negative. There was no significant difference in positive rate, and both methods had a similar degree of airway hyperresponsiveness; however, in group A, the effect was of shorter duration and the test was more efficient. During the BPT, 6 infants in group A and 9 in group B had cough, but none exhibited an acute asthma episode.
CONCLUSIONS: The improved tidal breathing method, used as a BPT, outweighs the traditional method in sensitivity, specificity, efficiency of detection, dosage of medicine, and safety.

EVALUATION OF TUBERCULIN SKIN TEST IN UNVACCINATED 0- TO 7-YEAR-OLD CHILDREN OF NORTHERN GREECE

Submitted by Georgia Zardava
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INTRODUCTION: The tuberculin skin test (TST) is an important tool in the diagnosis of tuberculosis in children.
OBJECTIVE: The purpose of this study was to evaluate the proportion of 0- to 7-year-old children with induration of 5 to 9 or ≥10 mm after TST.
METHODS: During the 5-year period 2001–2005, 65401 0- to 7-year-old children (50.2% female) were enrolled in this study and TST was performed before BCG vaccination. Mantoux reaction and the extent of induration of the transversal diameter were evaluated. Among 65 401 children, 8018 were 0 to 5 years of age (group A) and 57 383 were 6 to 7 years of age (group B).
RESULTS: In group A, 19 (0.23%) children had induration within 5 to 9 mm (mean diameter: 6.81 mm) and 42 children (0.52%) had induration within 10 to 25 mm (mean: 14.4 mm). In group B, 62 (0.1%) children had induration within 5 to 9 mm (mean: 7.27

mm) and 186 (0.32%) children had induration within 10 to 30 mm (mean: 14.57 mm). Children with TST induration ≥10 mm were given treatment for tuberculosis; for those with induration of 5 to 9 mm, their environment was examined for the presence of risk factors.
CONCLUSIONS: The discovery of a high number of children with positive TST results (≥10 mm) in both groups indicates a remaining tuberculosis problem in Greece. The extent of induration up to 30 mm reveals the exposure of children of these age groups to high mycobacterial burden from adults with tuberculosis, especially immigrants from countries of Eastern Europe.

Rheumatology

CLINICAL COURSE AND OUTCOME IN CHILDREN WITH RARE CONNECTIVE TISSUE DISEASES: A RETROSPECTIVE REVIEW OF A 17-YEAR EXPERIENCE

Submitted by Christina Dracou-Kakava
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INTRODUCTION: Juvenile dermatomyositis/juvenile polymyositis (JDM/JPM), juvenile systemic scleroderma (JSCL-SYST), and juvenile mixed connective tissue disease (JMCTD) are rare in childhood.
OBJECTIVE: The objective of this study was to evaluate the prognosis of the rare connective tissue diseases (RCTDs) in children,
METHODS: We reviewed the medical charts of children with a diagnosis of RCTD since 1989 and a minimum follow-up of 5 years.
RESULTS: Twenty-four (16 female, 8 male) children with JDM/JPM, JSCL-SYST, and JMCTD were studied. The age at disease onset ranged from 4 to 13 years. The follow-up duration was 5 to 12 years. Sixteen children had JDM, and 2 had JPM. Four had JSCL-SYST, and 2 had JMCTD. Until now, 13 children have reached clinical remission, lasting >3 years after stopping drug therapy. Twelve children had JDM/JPM, and 1 had JMCTD. Persistent disease activity was noted in 11 children: 4 with JSCL-SYST, 6 with JDM/JPM, and 1 with JMCTD. Severe pulmonary disease developed in 3 children: 2 with JSCL-SYST and 1 with JMCTD. None of the children with JDM had pulmonary disease. Pulmonary hypertension (PH) was found in 2 children with JMCTD or JSCL-SYST. The child with JSCL-SYST and PH died. Persistent scleroderma pattern by wide-field capillaroscopy was noted in 4 children who had JDM and had had skin ulcerations and have developed subcutaneous calcifications. One of them has also had marked muscle atrophy and severe contractures.
CONCLUSIONS: Persistent activity and/or severe pulmonary involvement may be present during the clinical course of RCTD. The presence of PH indicates very poor prognosis in JSCL-SYST/JMCTD cases. Capillaroscopy may identify children who have JDM and are candidates for aggressive therapy.

RE-TREATMENT AND RISK FACTORS OF REFRACTORY KAWASAKI DISEASE

Submitted by Zhong-Dong Du
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OBJECTIVE: The objective of this study was to evaluate the incidence and risk factors of children with refractory Kawasaki disease (KD).
METHODS: All children with KD were analyzed in Beijing from 2000 through 2004. Risk factors were analyzed by logistic regression. Refractory KD was defined as persistent fever of ≥38.5°C 36 hours after initial intravenous immunoglobulin (IVIg) treatment.
RESULTS: A total of 1052 patients (aged 1 month to 13.8 years) with IVIg treatment were included; of them, 135 did not respond to IVIg treatment, with an incidence of 12.8%. Refractory KD occurred more frequently in children who received 1 g/kg per day IVIg for 2 days (20.9%) than in those who received a single dose of 2 g/kg (9.9%) or 400 to 600 mg/kg per day for 4 days (8.7%). Logistic regression revealed that erythrocyte sedimentation rate, alanine aminotransferase, white blood cell count, serum albumin, time from onset to IVIg treatment, and IVIg dosage were independent risk factors for refractory KD. Children with refractory KD were re-treated: 8 received 2 g/kg IVIg, with 5 (62.5%) responding; 114 received 1 g/kg IVIg, with 35 (30.7%) responding; and 11 received 400 to 600 mg/kg IVIg, with (9.1%) responding. In addition, 2 received corticosteroids, with 2 responding.
CONCLUSIONS: The incidence of refractory KD in Beijing is 12.8%. A 2-g/kg dose of IVIg is probably the best re-treatment option for refractory KD.

NEUROPSYCHIATRIC SYMPTOMS IN CHINESE CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Submitted by Yu-Lung Lau

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INTRODUCTION: There is a paucity of clinical studies on children with neuropsychiatric systemic lupus erythematosus (NPSLE).
OBJECTIVE: The objective of this study was to define the clinical characteristics of and the potential predictors for NPSLE in Chinese children.
METHODS: Sixty-two children with SLE diagnosed between 1990 and 2006 were retrospectively reviewed. Patients were evaluated according to the American College of Rheumatology case definitions (1999) for classification of neuropsychiatric symptoms. The demographic data, clinical manifestations, laboratory parameters (complete blood count, erythrocyte sedimentation rate, C-reactive protein, complement levels, anti-cardiolipin antibodies, and autoimmune markers), treatment, and SLE disease activity index score were analyzed.
RESULTS: Nineteen (30.65%) patients with SLE and 21 neuropsychiatric events were identified. Mean age at NPSLE manifestations was 13.57 ± 4.33 years. The most common neuropsychiatric manifestations were cognitive dysfunction (47.62%), seizure disorder (42.86%), and headache (28.57%), followed by mood disorder (19.05%), myelopathy (19.05%), cerebrovascular disease (14.29%), psychosis (9.52%), cranial neuropathy (9.52%), and mononeuropathy multiplex (4.76%). Renal involvement at diagnosis of SLE was significantly less common in patients with NPSLE than in those with non-NPSLE. Apart from that, we could not identify other clinical or laboratory parameters that could predict the development of NPSLE. Six patients presented with neuropsychiatric symptoms at onset of SLE. Comparing them with patients with later neuropsychiatric development, their mean age was younger and the SLE disease activity index score was significantly higher.
CONCLUSIONS: Neuropsychiatric symptoms were common in Chinese children with SLE. Early-onset NPSLE occurred in younger patients with higher disease activity score. Neuropsychiatric development was negatively associated with renal involvement at diagnosis.

RECURRENT MAJOR INFECTIONS IN JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: A CLOSE LINK WITH LONG-TERM DISEASE DAMAGE

Submitted by Pamela Pui-Wah Lee

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INTRODUCTION: Infection is a significant cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). We postulated that patients with recurrent infections are more likely to have poorer disease outcome.
OBJECTIVE: The objectives of this study were to describe the pattern of infections and disease damage that occurred in a cohort of patients with juvenile-onset SLE and to determine whether cumulative disease damage was associated with recurrent infections in these patients.
METHODS: We retrospectively reviewed (1988–2004) the clinical characteristics, infective complications, and disease damage as measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index Score (SDI) in 47 patients with juvenile-onset SLE. Potential risk factors for disease damage were evaluated by univariate analysis and logistic regression. The correlation between number of major infections and disease damage was determined.
RESULTS: Thirty-two (68.1%) patients had lupus nephropathy, and 16 (34.0%) patients had neuropsychiatric lupus. Sixty-one episodes of major infections, defined as infections that required more than 1 week of antimicrobial agents, occurred in 27 (57.4%) patients, and 18 (31.4%) patients had recurrent major infections (≥2 episodes). Organ damage (SDI ≥ 1) was documented in 21 (44.7%) patients. By logistic regression, occurrence of major infections was the only significant risk factor for disease damage. There was a positive correlation between SDI score and the number of recurrent major infections.
CONCLUSIONS: Infections and disease damage are common comorbidities in juvenile-onset SLE. Recurrent infections could predict poorer disease outcome and associated organ damage in SLE.

Surgery

TRANSLUMINAL ENDOSCOPIC TREATMENT OF FENESTRATED DUODENAL MEMBRANES

Submitted by Gerardo Blanco-Rodriguez

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INTRODUCTION: Duodenotomy and resection or lateral duodenoduodenostomy by open or endoscopic sur-

gery has been the traditional treatment of fenestrated duodenal membranes. A radial endoluminal incision of the membrane can widen its diameter and resolve the duodenal obstruction.

OBJECTIVE: We describe a new endoscopic procedure for membranectomy of fenestrated duodenal membranes.

METHODS: Under general anesthesia and endotracheal intubation, we introduced a flexible videopanendoscope into the second duodenal portion to visualize the membrane. Through the fenestration, we inserted a triple-lumen stone extraction balloon of 15 mm. After insufflation, we performed gentle traction to expose the membrane and distinguish its border from the duodenal wall. We dilated the orifice and advanced the endoscope to localize Vater's ampoule. Using a sphincterotome, we performed 1 or 2 radial cuts of 1.5 to 2.0 cm in the membrane in an opposite direction to the ampoule.

RESULTS: We performed this procedure on 10 patients. The mean duration of the procedure was 50 minutes. No patient had postoperative pain. Abdominal condition was normal, and all patients started oral intake 18 to 24 hours after the endoscopy. Patients were discharged asymptomatic. They completed 4 months to 4 years of follow-up. Eight continued to be asymptomatic. One had a double duodenal membrane and after 2 endoscopic cuts has occasional vomiting. Another 1 was lost to follow-up.

CONCLUSIONS: Transluminal endoscopic treatment of fenestrated duodenal membranes has been a safe procedure that may be an effective and less invasive alternative to open or laparoscopic surgery.

PYLORIC STENOSIS: A RETROSPECTIVE STUDY OF AN AUSTRALIAN POPULATION

Submitted by Lisa Gotley

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INTRODUCTION: Infantile hypertrophic pyloric stenosis (IHPS) is a common cause of nonbilious vomiting in infants. The "classic" presentation is one of a firstborn boy who is aged 2 to 8 weeks and has projectile vomiting; palpable olive, visible peristalsis; and hypochloremic metabolic alkalosis. With increased awareness of the condition and readily available ultrasonographic diagnosis, classic presentations may be becoming less common.

OBJECTIVE: We sought to describe the epidemiology, clinical features, and outcomes of children with IHPS at our institution.

METHODS: We conducted a retrospective case review of all cases of IHPS that presented to our tertiary pediatric hospital in an 11-year period.

RESULTS: The inclusion criteria were met by 330 children with confirmed IHPS. A total of 84% of patients were male, and 19% were born preterm. Preterm infants tend to present later, reflecting postmenstrual age. The median age at presentation was 36 days (range: 7–218 days) with mean symptom duration of 11 days (range: 1–95 days). Whereas 87% of patients had at least 1 classic finding on history or examination, only 14% had the classic triad. Elevated bicarbonate was present in 61% of blood samples, whereas hypochloremia was found in only 29%. Ultrasound confirmed the diagnosis in 89%. Surgical techniques were similar in outcome, except that incomplete pyloromyotomy was more common with the laparoscopic approach compared with the periumbilical approach (6% vs 1%).

CONCLUSIONS: IHPS occurs more frequently in boys and infants who were born preterm. It commonly presents without the full spectrum of classic findings. Given the availability of ultrasound diagnosis, IHPS should be considered in infants with any 1 of these findings.

LAPAROSCOPIC CHOLECYSTECTOMY IN CHILDREN: A 5-YEAR EXPERIENCE

Submitted by Evangelos Papandreou

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INTRODUCTION: Cholecystectomy in children is not a common surgical procedure. In the past 5 years, we have performed it laparoscopically. There was no difference in insufflated pressure between 2 groups while no drainage catheter was placed.

OBJECTIVE: We present a modified laparoscopic technique in children.

METHODS: In a 5-year period, 54 children underwent laparoscopic cholecystectomy. Their ages ranged from 14 months to 15 years (mean: 7.6 years). Depending on the applied technique, the patients were separated into 2 groups. The first group comprised 17 patients on whom we performed the conventional 4-port technique. The second group comprised 37 patients on whom a modified technique was performed. We used 3 ports: an umbilical port for the camera, another in the subxifoid region for the dissector, and a third in the right lower quadrant for the grasping clamp and the extraction of the gallbladder. Vessel sealing electrocautery was used

for ligation of the cystic artery and detachment of the gallbladder.
RESULTS: Reduction of the number of ports had no effect on accessibility and duration of the procedure; however, it simplified access and handling, particularly in the smaller patients. Conversion to open cholecystectomy was performed in 1 case with major deformities of the vertebral column. The duration of hospitalization varied from 1 to 4 days (mean: 2.7 days).
CONCLUSIONS: The decreased number of ports and the use of vessel sealing electrocautery make laparoscopic cholecystectomy in children easier and safe, without affecting the perioperative time.

PROCALCITONIN AS A PREDICTOR OF SEVERE APPENDICITIS IN CHILDREN

Submitted by Ioanna Velissariou
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INTRODUCTION: Procalcitonin is an amino acid peptide that can contribute in the diagnosis and management of severe bacterial infections because it reaches high concentrations in patients with severe bacterial infection, septicemia, or meningitis and decreases rapidly after appropriate antibiotic therapy.
OBJECTIVE: The objective of this study was to assess the diagnostic value of procalcitonin in 212 children with appendicitis and compare it with the standard diagnostic modalities, C-reactive protein, white blood cell count, and abdominal ultrasonography, in relation to the surgical and histologic findings of the appendix.
METHODS: Prolactin levels were measured in 212 children with appendicitis, and the results were compared with standard diagnostic modalities such as C-reactive protein level, white blood cell count, and abdominal ultrasonography, which are useful aids for detecting severe appendicitis and/or perforation.
RESULTS: A procalcitonin value of >0.5 ng/mL was indicative of perforation or gangrene with 73.4% sensitivity and 94.6% specificity, C-reactive protein level of >50 mg/L and white blood cell count of $>10^4/\mu L$ are useful diagnostic aids for perforation, and abdominal ultrasonography had a sensitivity of 82.8% and a specificity of 91.2%.
CONCLUSIONS: Procalcitonin seems to be a useful adjunct diagnostic tool for acute necrotizing appendicitis or perforation, and surgical exploration will probably be required in patients with procalcitonin values of >0.5 ng/mL.

Vaccination

IMMUNOGENICITY AND SAFETY OF CONCOMITANT ADMINISTRATION OF MEASLES-MUMPS-RUBELLA VACCINE AND VARICELLA VACCINE BY THE INTRAMUSCULAR OR SUBCUTANEOUS ROUTE

Submitted by Yves Gillet
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INTRODUCTION: In Europe, recommended administration route for vaccines and physicians' preferences vary.
OBJECTIVE: The aim of this study was to compare the immunogenicity and safety profile (injection-site and systemic adverse events) of a measles-mumps-rubella vaccine (M-M-RvaxPRO) and a varicella vaccine (Varivax) when given by intramuscular or subcutaneous route.
METHODS: A total of 752 healthy children who were 12 to 18 months of age were randomly assigned to receive concomitantly at 2 separate injection sites 1 dose of both vaccines by the same route, either intramuscular or subcutaneous.
RESULTS: Six weeks after vaccination, response rates in patients who were initially seronegative were similar for all antigens (intramuscular noninferior to subcutaneous), and geometric mean titers were comparable irrespective of the administration route (Table 1). Similar numbers and types of systemic adverse events were observed in both groups, excepted for varicella/varicella-like rashes, which were less frequent in the intramuscular group. Injection-site reactions were also less frequent for both vaccines in the intramuscular group compared with the subcutaneous group (15.8% and 25.8% of patients for M-M-RvaxPRO and 20.9% and 34.3% for Varivax, respectively), but the safety pattern was comparable between groups.

TABLE 1. Response Rates and Geometric Mean Titers of the Measles-Mumps-Rubella and Varicella Vaccines When Given by Different Routes

Per-Protocol Analysis	Intramuscular			Subcutaneous		
	n	Relative Risk, %	GMTs	*n*	Relative Risk, %	GMTs
Measles, ≥255 mIU/mL	349	94.3	2396.4	363	96.1	2560.6
Mumps, ≥10 ELISA Ab U/mL	349	97.7	86.4	363	98.1	89.8
Rubella, ≥10 IU/mL	321	98.1	97.2	318	98.1	94.4
Varicella						
≥5 gpELISA U/mL	336	88.4	9.8	345	85.5	9.2
≥1.25 gpELISA U/mL	336	98.5	9.8	345	99.4	9.2

CONCLUSIONS: These results support both intramuscular and subcutaneous administration routes for M-M-RvaxPRO and Varivax.

NATIONAL VACCINE INJURY COMPENSATION PROGRAM IN KOREA: A 12-YEAR EXPERIENCE

Submitted by Jung Soo Kim

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INTRODUCTION: In Korea, the vaccine injury compensation program, which is essential for the successful national immunization program, was established in 1995.
OBJECTIVE: This study was conducted to evaluate the safety of each vaccine and the vaccine injury compensation program in Korea.
METHODS: We analyzed the data of adverse reactions filed with the advisory committee on vaccine injury compensation of Korea from 1995 through 2006.
RESULTS: A total of 1127 cases of adverse events were reported to the committee. The number of reported adverse reactions gradually increased. BCG was the most commonly reported vaccine (616 [54.7%] cases, mostly localized suppurative lymphadenitis), followed by diphtheria-tetanus-acellular pertussis (160 [14.2%] cases, mostly neurologic responses) and measles/rubella vaccine (127 [11.3%] cases). A total of 119 cases were requested for vaccine injury compensation. The most commonly compensated vaccine was measles/rubella (31 [26%] cases), showing mostly the anxiety responses during the measles catch-up program in 2001. The second most commonly compensated vaccine was diphtheria-tetanus-acellular pertussis with or without other vaccines (21 [16.5%] cases), followed by Japanese B encephalitis (11 [8.7%] cases) and influenza vaccine (9 [7.1%] cases). The most common and serious adverse events for injury compensation were neurologic complications such as seizure, encephalopathy, and encephalomyelitis.
CONCLUSIONS: During a 12-year period, adverse reactions were reported in 54.7% of BCG vaccination cases, 14.2% of diptheria-tetanus-acellular pertussis vaccination cases, and 11.3% of measles/rubella vaccination cases. Vaccine injury compensation was requested in 26% of measles/rubella cases and 16.5% of diptheria-tetanus-acellular pertussis cases. Neurologic complications were the most common and serious adverse events for injury compensation.

Internet Use and Abuse in an Adolescent Population in Athens: Associations with Psychological Profile and Lifestyle of Users: Submitted by Eleftheria Konstantoulaki

Elli Tripodaki, Georgios Kormas, Eleftheria Konstantoulaki, Elisabeth Andrie, Georgios Nassis, Aliki Freskou, Maria Sfiri, Helen Georgouli, Artemis Tsitsika and Andreas Constantopoulos

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