16 &17 MARCH 2023 THE EGG BRUSSELS

CLIMATE CHANGES IN PEDIATRICS: FROM SOCIETY TO ENVIRONMENT

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SOCIÉTÉ BELGE DE PÉDIATRIE

Groupement Belge des Pédiatres de Langue Française · ASBL

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De Belgische Vereniging voor Kindergeneeskunde

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FULL ABSTRACTS

LO 1.

Drug exposure at the target site: are children a neglected population in tissue pharmacokinetic research ?

J. Meersschaut, E. Hermans, J. Vande Walle, P. De Paepe, P. De Cock

Universiteit Gent

Background/Aims
Knowledge of drug tissue penetration is important, as most drugs have their target site in the interstitial or intracellular space. This scoping review aimed to give a summary of the existing data on drug tissue penetration in children.

Methods
A systematic search strategy was developed. Studies investigating the drug concentration in solid tissue with tissue biopsy, microdialysis, or imaging techniques in the pediatric population (0 – 18 years old) were included. All drug classes were considered. Only studies with intravenous and oral drug administration were eligible for inclusion. Tissue penetration into the central nervous system and bodily fluids were out of scope. The search was performed on the 28th of January 2022 in the PubMed and Embase databases. Two reviewers performed the double-blind screening of the articles. The ClinPK checklist [1] was used to evaluate the study quality.

Results
4304 records were retrieved. Forty-two studies were included, of which 31 were published more than 20 years ago. Thirty-seven were (small) cohort studies and five were case reports. The sampling method was tissue biopsy in 37 studies, microdialysis in four studies and one study used an imaging technique. In the majority of the studies (~75%) antibiotics were investigated. Other drug classes were sedatives, immunomodulators, cytostatics, thyreostatics, anthelmintics, and antiarrhythmics. Tonsil and adenoid tissue were the most frequently sampled tissues. In general, the quality of the studies was low.

Conclusion
There is scarce knowledge on drug tissue penetration in children. The studies that are available are generally of low quality, describe small patient populations, and/or included mainly the questionable sampling method of tissue biopsy. We hypothesize that the (semi-)invasive character of tissue sampling techniques hampers its widespread implementation in pediatric drug studies. To date, the impact of maturation on drug tissue penetration has been insufficiently studied and it thus remains uncertain to what extent the available adult data can be extrapolated to the pediatric population. More research should be initiated to fill this knowledge gap.

[1] Kanji S, Hayes M, Ling A, Shamseer L, Chant C, Edwards DJ, et al. Reporting Guidelines for Clinical Pharmacokinetic Studies: The ClinPK Statement. Clin Pharmacokinet. 2015;54(7):783-95.

SO 12.

Navigating the Unknown: Understanding and Managing Parental Anxiety When a Child is ill

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Background
Parents are often confronted with a difficult decision when their child falls ill: should they go to the general practitioner or not? They do not want to overlook a critical illness but neither do they want to consult the doctor unnecessarily. This study aims to describe this process comprehensively in order to allow clinicians to assess the extent to which parents can recognise clinical warning signs and act accordingly. The purpose of this study is to describe parents' decision-making process when deciding whether or not to consult a general practitioner for their sick child.

Methods
We used a qualitative study design based on semi-structured interviews to investigate the decision-making process of 25 parents. Four case scenarios describing a developing illness in a child were presented. At each decision point in the scenarios, parents were asked whether they would consult their general practitioner and, if so, why.

Results
Parents' reasons for seeking medical attention could be divided into two main categories. First, symptom-related factors lead parents to consult a doctor. Parents were alarmed by the persistence and progression of symptoms, the combination of symptoms, or changes in their child's behaviour. Second, several parent-related arguments were identified. Sometimes the parents just need reassurance, while at other times, they fear a specific disease or are concerned about warning signs. Parents' reasoning seems frequently affected by their previous experiences and familiarity with symptoms. Some parents, however, would not seek medical attention at any decision point, even though their child would be in a potentially life-threatening situation.

Conclusion
Although parents make carefully considered decisions on whether or not to consult a doctor, many appear to miss red flags, including more experienced parents. Conversely, some become overly concerned with certain specific symptoms such as fever, and few parents are familiar with self-management strategies. Evidence-based child health apps and parent education campaigns concerning self-limiting illnesses, alarm symptoms and self-management strategies could help ensure that a doctor gets to see sick children in time.

SO 34.

Online survey on first aid knowledge among primary school teachers in Flanders

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UZ Leuven, KU Leuven

Introduction
About one in seven accidents involving children occur in the school context, and 70% of these accidents occur in children under 12 years of age. This means that teachers are often confronted with situations where first aid could potentially improve the outcome. Despite the importance of first aid application by teachers, not much is known about the first aid knowledge of teachers in Flanders. Therefore, we conducted a case-based survey research on the first-aid knowledge of primary and nursery school teachers in Flanders.

Methods
Using snowball sampling, an online survey was distributed to primary school and kindergarten teachers in Flanders. The questionnaire consisted of 25 questions of which 9 were demographic in nature and 14 hypothetical first aid scenarios in a primary school context. The collected data were analyzed using SPSS version ##. Linear regression models were used to assess the relationship between the used variables and the overall score, as well as self-assessment of first aid knowledge.

Results
A total of 361 primary school teachers completed the questionnaire. Participants achieved an average score of 66%. When asked to rate their own first aid knowledge, the average score was 3.39/5 with >3/5 considered as high self-assessment. Participants who followed a first aid course and respondents with a high self-assessment had a significantly higher overall score. Linear regression analysis shows that among all variables only previous first aid training and self-evaluation of first aid ability could predict the teachers' first aid knowledge.

Conclusion
The results of this study showed that having followed a first aid course as well as following a refreshing course predicts the ones first aid knowledge. This is why we think that first aid training should be mandatory in teacher training, as we see that so many teachers need first aid.

SO 35.

'I am worried about my child, doctor' A qualitative assessment of physician's appraisal of parental concerns

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UZ Leuven, KU Leuven

Background / Aims
Parents worrying about their children is a natural instinct. Physicians, in order to adequately advise, reassure, alert or redirect parents, are expected to base themselves on scientific evidence. In the field, they do not only rely on analytical reasoning but use their non-analytical reasoning and intuition as well. Sometimes physicians have an inexplicable feeling that something is wrong, better known as gut feeling. Many symptoms trigger such a gut feeling. However, little research has been done on whether other factors can influence this feeling. We investigated which parent-related factors influence a physician's assessment of gut feeling and which physician-related factors have an impact on their clinical reasoning process.

Methods
Qualitative research, with a heterogeneous sample of 30 Flemish paediatricians and general practitioners, was performed. Nine semi-structured focus group interviews (2-6 participants/interview) were conducted. To analyze the transcribed interviews, we used the constant comparative analysis method with a structured coding system.

Results
Several factors can influence how physicians appraise their gut feeling. Generally, we can divide these into four categories, being parent-, physician-, context- and child-related factors. Within each category, there are multiple determinants of which the most influential are having multiple children, the physician's work experience and disease severity.

Conclusion
The determining factors already described in literature are largely confirmed. Additionally, this study reveals new determinants (e.g. having multiple children as parent and physician fatigue) which remain to be confirmed with further research. It would be interesting to examine, by quantitative research, to what extent the identified factors are involved in the appraisal of gut feeling.

SO 36.

The importance of the SARS-CoV-2 pandemic on the seasonality of Respiratory Syncytial Virus in Belgium

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Jessa Ziekenhuis Hasselt, GZA Antwerpen, Sciensano

Background/Aims
Before the SARS-CoV-2 pandemic, in Belgium the main burden of RSV-disease was seen within the 'typical RSV season'. To secure proper preventive actions and in view of the acceleration in the development of new candidate RSV vaccines, monoclonal antibodies and therapeutics, close monitoring of the RSV epidemiology is very important.

Methods
A literature search was performed to map data on the impact of SARS-CoV-2 pandemic on RSV seasonality in Belgium and compared to local date collection from the Jessa-hospital.

Results
Very few publications with Belgian information on RSV seasonality and burden of disease are available. Before the Covid-19 pandemic, the start of the RSV season was found to be relatively consistent, most often around week 41/42, (beginning of October), with a median peak at week 49 (December). This was in line with another analysis on 24 Belgian winters, where all the peaks fell between weeks 47 and 52. The end of the season was more difficult to define with season duration ranging from 13 to 28 weeks. The findings of the literature are in line with the seasonality reported by the Belgian Institute for Public Health (Sciensano). Since the emergence of SARS-CoV-2, lockdowns, physical distancing, face masks and other non-pharmaceutical interventions (NPIs) influenced the dynamics of seasonal infectious diseases, including RSV. In Belgium, there was no 2020 winter peak. Local and national data show a delayed RSV wave in the 2021 spring season. The epidemic threshold was exceeded twice, between weeks 11 and 13 and again between weeks 16 and 19. Peak values did not exceed the regular winter peaks, but an 'ongoing plateau' from early spring to mid-summer. Also 2022 showed atypical seasonality, lacking a high winter peak but continued reporting of RSV infections beyond the normal end of season in March (week 13). The 2022 winter season is ongoing, with clear increase of RSV-positive cases since October 2022.

Conclusion
Precise monitoring of the RSV epidemiology is key for taking adequate preventive and organizational health care measures. The COVID-19 pandemic situation showed the importance of surveillance and the need for real-time registration of in- and out-of-season RSV outbreaks. In Belgium, current RSV surveillance could be optimized to allow efficient RSV prophylaxis guidelines. This improvement is ongoing, involving using better case definitions and raising the representativeness of the sentinel surveillance system

PW 21.

Clinical case of perinatal hydrometrocolpos: diagnosis and initial handling

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Introduction

Hydrometrocolpos (HMC) is a vaginal and uterine dilation due to fluid retention. A simplified classification features the level and nature of the obstruction. Types I to III are limited to genital tract, type IV extends to urinary tract and type V to digestive tract. HMC can be isolated or associated with other malformations, occasionally in syndromic contexts. Its presentation varies according to age. The perinatal period sees frequent dilated abdomen and symptoms of compression. The most severe complication is the infection of the stagnant fluid (referred to as pyocolpos) which can lead to sepsis. At puberty, the patient can suffer from painful primary amenorrhea (hematometrocolpos). Diagnosis revolves around clinical and radiological characteristics. Treatment is primarily surgical. It can range from simple drainage to urological/gynecological reconstructive surgery.

Discussion

We report the case of a 5-day-old infant born at term from a biamniotic monochorionic twin pregnancy. Two major events occurred during pregnancy: the discovery of a cystic hygroma with normal chromosomal and molecular karyotype and later on, the fortuitous discovery of an ovarian-like pelvic cyst and a bilateral ureterohydronephrosis. The delivery was eutocic with good neonatal adaptation. Nothing to report through clinical examination apart from a pedunculated growth next to the xiphoid appendix. Ultrasound on day one described a pelvic cyst with fluid level. However, NMR hinted at the presence of hydrometrocolpos associated with hydrosalpinx. The patient remained asymptomatic until the fifth day when she developed cyanosis, right unilateral pedal edema associated with a bloated abdomen and a swelling at the opening of the labia minora. The child was then quickly transferred to a specialized center. There was excellent clinical response after surgical drainage (Pfannenstiel incision) and the placement of a drain in the vaginal cavity. Fluid aspect and biochemical analysis were likely indicative of mixed vaginal secretions and urine. Vaginal opacification confirmed the presence of a type-IV HMC with vesico-vaginal fistula. Subsequent interventions, staggered over time, will allow for surgical repair of the fistula and lower vagina.

Conclusion

HMC is a rare condition requiring tight collaboration between paediatricians, radiologists and urologists. Future quality of life, such as continence or fertility, hinges on early diagnosis, which is key to efficient management.

PW 22.

Differential diagnosis of CNO/CRMO: a case report

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Background
Chronic non-infectious osteomyelitis (CNO) and chronic recurrent multifocal osteomyelitis (CRMO) are rare inflammatory bone disorders that most frequently affect children and adolescents. Currently, CNO/CRMO remain a diagnosis of exclusion as no widely accepted and prospectively tested diagnostic criteria are available.

Methods
Case description.

Results
An 8-year-old Caucasian boy with autism spectrum disorder (ASD) was seen in the paediatric rheumatology clinic with a 4-month history of bone pain, initiating in his knees, expanding to both ankles, sacroiliac joints and pelvic joints. There was a progressive limping gait and pronounced morning stiffness. The boy had an restrictive food intake disorder as part of his ASD for which he was admitted at Zeepreventorium De Haan. Physical exam showed a boy in general good health but wheelchair bound. There was a painful palpation over the proximal humerus, distal radius, proximal and distal tibia. MRI of the right knee showed bone edema of the distal femur metaphysis and proximal tibia metaphysis.

Based on history, clinical examination and MRI of the knee, the working diagnosis of CRMO was made and a whole-body MRI was performed which confirmed this diagnosis. He was treated with NSAID and bisphosphonates, but there was no significant clinical improvement. Three weeks later he developed acute gingival overgrowth with bleeding. Additional laboratory examinations revealed abnormally low levels of ascorbic acid. Vitamin C supplements were started and he improved rapidly, both mentally and clinically.

Discussion
CNO/CRMO are rare diseases with an often difficult and delayed diagnosis due to the lack of widely accepted diagnostic criteria or disease biomarkers, but it is important to consider it in the differential diagnosis of a child with persistent bone and/or joint pain. Whole-body MRI is the gold standard for the diagnosis and follow-up. Nevertheless, several differential diagnoses should be considered, such as lymphoma, Langerhans cell histiocytosis, hypophosphatasia or vitamin C deficiency.

Nowadays, vitamin C deficiency is rare in high-resource countries. Bone pain can develop after 1–3 months, but painful hemarthroses, petechiae and ecchymoses, gum disease, poor wound healing and emotional changes can also occur.

This case highlights that vitamin C deficiency should be considered in patients with chronic pain and/or aseptic osteitis, particularly in children with restrictive dietary habits.

PW 23.

A qualitative study on the knowledge and attitude of primary school students towards pediculosis capitis.

M. Daenen, J. Toelen

KU Leuven

Background and aims
Pediculosis capitis or headlice remains an important issue in school-aged children. Clinical consequences are mainly limited to itchiness and irritation, but the social impact of infestation is high. That impact is often sustained by a lack of knowledge and prejudice leading to the reluctance of children and parents to openly discuss the matter. Most of the past research focussed on topics like treatment and prevalence, but little work has been performed to evaluate knowledge, perceptions, and beliefs. In this study we investigated the knowledge and attitude of primary school students on headlice in Flanders.

Methods
We used a qualitative methodology with semi-structured. Ten primary schools in Flanders were included on a voluntary basis, representing the distribution of the three school networks. The opinions of 240 students from the fourth, fifth or sixth grade were obtained in a knowledge part (ten true/false questions) and a reflective part (to assess their perceptions, feelings and beliefs). Data-analysis was conducted using the QUAGOL method for qualitative data.

Results
In the knowledge part, a total mean score of 63% (SD +/-37%) covering six topics was detected. The topics lifecycle, symptoms and transmission routes of headlice scored the worst. The most prominent misunderstanding is the fact that a large majority of students believe headlice can jump, demonstrated by only 21% correct answers on that topic. In the reflective part of the interview three main themes occur: misconceptions, attitude (feelings, friendship and behaviour) and disclosure (towards parents, teachers and friends).

Conclusion
This study examined the knowledge and perceptions of primary school students in Flanders on the topic of headlice. Students scored well on some topics, however the headlice's transmission route scored poorly. The main concepts in their reasoning were identified. This study suggests that accurate health education could be useful in educating children on the topic of headlice, in reducing misconceptions and social stigma and in achieving better mental health in young children. Previous studies show that this might help in diminishing transmission rates as well.

PW 24.

Bilateral Pulmonary Embolism in a teenage girl

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Centre Hospitalier de Mouscron

Aim

Pulmonary embolism is a serious condition, often underestimated during childhood, with multifactorial ethiopathology and major complications, sometimes lethal. Diagnosis and treatment remain a challenge in current pediatric practice, which is why we present the present case. Precipitating risk factors can be hereditary or more often acquired. Severe thrombophilia highly increases the risk of pulmonary embolism and deep vein trombosis.

Methods

In pre pandemic february 2020 a 14-year-old child, previously follwed for asthma, presents in the Emergency Departement of CH Mouscron with lochalised pain in the right hemithoracic base. The debut was 24 hours ago, accentuated by movement and breathing and with a relatively good general condition (136/69 mmhg of blood pressure, 115/min heart rate, 98% saturation, 37,1 temperature, tachypnea). A minimal echymosis was noticed in the distal third of the inner face of the left leg, with a fine post-excoriation scar following a left ankle sprain, treated a month ago with the AIRCAST splint.

It should be noted that for 2 weeks she has been taking contraceptives as indicated by her Gynecologist. Body measurements were normal with 164 cm height and 65 kilograms of weight.

Results

Laboratory tests showed D dimeres at 6,14 mcg/mL (threshold value at 0,5 mcg/mL) , moderately positive C reactive protein of 34,1 mg/dL, normal chest X-ray. Pulmonary CT and angio CT were performed, with confirmation of a bilateral pulmonary condensation with bilateral embolism.

Treatment with Enoxaparin 1mg/kg body weight was debuted twice a day, blood gas measurement monitoring followed during hospitalisation in the Pediatric wards.

Further exploratory tests revealed protein C deficiency, which explains the predisposition to venous thrombosis and the risk of pulmonary embolism. Compared to plaster cast , the AIRCAST splint can be removed and can mobilize the leg. The patient was permanently monitored by repeated chest x-rays, cardiac ultrasound and normal venous Doppler. Intravenous Tradonal was used for pain control.

Conclusion

The multidisciplinary collaboration for a correct diagnosis and a precise therapeutic conduct are key elements in this rare pathology in children.

The particularity of the case is given by the presence of bilateral pulmonary infraction in a child with an unknown protein C deficiency, one month after after a spartial immobilisation.

PW 25.

Clinical decision support through mobile applications: a systematic assessment of pediatric fever management apps.

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UZ Leuven, KU Leuven, Spaarne Gasthuis

Introduction
Current development and implementation of mobile health interventions has become a field of interest within pediatric healthcare. Mobile applications with parental decision support system assist parents in decision- making activities, counting the promotion of disease management.

Objective
The aim of this study was to identify existing pediatric fever management applications and to compare their decision algorithm with current evidence based guidelines regarding fever in children.

Methods
Mobile applications were identified through a systematic search of the Apple App store for IOS and the Google Play store for Android from May to July 2022, using different search terms. The recruited applications were subject to four rounds of screening, identifying a final set of apps that matched prespecified selection criteria. All applications were reviewed in two ways. First, all applications were independently evaluated by a team of five reviewers using the MobileApplicationRatingScale. Second, the decision support algorithm of each app was mapped by exploration and adherence to existing fever management recommendations was appraised through comparison against the NICE guideline and the triage protocol of Schmitt- Thompson, using stratification of disease symptoms into a traffic light system.

Results
Out of the 878 apps retrieved from initial searches, 6 applications matched our prespecified selection criteria of which 3 applications were finally assessed. With regard to the total quality rating within the individual apps, the Kinsa app and the FeverApp app were equally the highest scoring mobile applications (4.4 out of 5), followed by the FeverFriend app (4.0 out of 5). When evaluating the decision algorithm of each application against the NICE guideline, the FeverFriend app showed highest adherence to the European guideline, followed by the Kinsa app and the FeverApp app respectively. When evaluating the decision support algorithm against the Schmitt-Thompson triage protocol, the Kinsa app showed highest adherence to this, followed by the FeverFriend app and the FeverApp app respectively.

Conclusion
The current availability of fever management applications with PDSS in the two leading app stores worldwide remains limited. Included applications matched specified EBM guidelines partially.

LO 2.

Isolated chronic fetal hypoxia results in delayed lung development and maturation using an extrauterine womb lamb model

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Background
The impact of isolated fetal hypoxia on lung development is unclear. Animal models have not been able to achieve fetal hypoxia without concurrent reductions in nutritional delivery or increased maternal stress. In this study, we aim to study lung development and maturation during isolated fetal hypoxia.

Method
Following cesarean section delivery, preterm lambs (105-110 days gestational age) were supported on an EXTra-uterine Environment for Neonatal Development (EXTEND) system under normoxic or hypoxic conditions for either 7 days (N=5 per group) or 17 days (N=4 per group). Hypoxia was achieved by decreasing oxygen delivery by 35% below normal levels. Lung structure was evaluated using light microscopy and computer-assisted stereology techniques. Surfactant-related gene expression were quantified by RT-PCR.

Results
Hypoxia for 7 days decreased (P=0.018) alveolar septum volume and increased (P=0.042) alveolar airspace volume. Alveolar septum and airspace volumes tended to decrease following 17 days of hypoxia. The mean linear intercept tended to increase in hypoxic animals. Surfactant protein expression and production machinery were impaired by hypoxia. SP-C, ABCA3, and LPCAT expression tended to decrease after 7 days and significantly decreased after 17 days of hypoxia (SP-C: P= 0.012, ABCA3: P= 0.01, and LPCAT: P= 0.049).

Conclusion
These preliminary data demonstrate that isolated fetal hypoxia impacts both structural and biochemical lung development which may contribute to the higher incidence of perinatal respiratory failure and bronchopulmonary dysplasia observed in IUGR infants.

SO 23.

Does the new Dutch norms of the Alberta Infant Motor Scale better predict motor outcome in a Belgian preterm population? A 2 years follow-up study.

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Background
Predicting motor outcome in preterm infants could improve infants orientation to intervention programs. However, early prediction of motor outcome remains difficult due the presence of multiple factors that influence motor development during early childhood. The Alberta Infant Motor Scales (AIMS) assess early gross motor development and is used worldwide in preterm infants. However, during the last decade, cross-cultural differences have been identified regarding the original AIMS norms. This study aims to compare the ability of the new Dutch AIMS norms with the one of the original Canadian norms, to predict motor developmental delay at 2 years in preterm infants.

Method
This retrospective cohort study included 74 very preterm infants (< 32 weeks of gestation and/or with a birthweight < 1500g), that were assessed on the Bayley Scales of Infant Toddler Development (Bayley-III) at 2 years of age. Among these, 52 were assessed on the AIMS at age 9-14 months, and 64 at age 3-6 months. Properties of both AIMS norms were compared based on their ability to predict a motor delay on the Bayley-III at 2 years of age (mild and significant motor delay were respectively defined as Bayley-III motor composite score < 85 and < 70).

Results
To predict mild motor delay at 2 years from the age of 3-6 months, the Canadian 10th centile showed best balance between sensitivity and specificity (Se 74% [95%CI 49-91%], Sp 56% [95%CI 40-70%]), while the Dutch 5th and 10th centiles showed sensitivities below 50%. Concerning significant delay, the Canadian 5th centile showed best properties (Se 80% [95%CI 28-99%]), Sp 69% [95%CI 56-81%]), while only the Dutch 10th centile seems to be sensitive enough (Se 60% [95%CI 15-95%], Sp 85% [95%CI 73-93%]). Surprisingly, to predict motor delay at 2 years from the age of 9-14 months, both norms showed poorer properties. Only the Canadian 10th centile showed a sensitivity higher than 50% (Se 57% [95%CI 29-82%], Sp 82% [95%CI 66-92%] to predict mild motor delay; and Se 60% [95%CI 15-95%], Sp 75% [95%CI 60-86%] for significant motor delay).

Conclusion
Although the Dutch population is geographically and culturally close to the Belgian one, our results show that the new Dutch AIMS norms does not better predict motor outcome at 2 years of age in preterm infants. Dutch norms are indeed less sensitive than the Canadian ones, thus increasing the risk of missing infants who could benefit from early intervention and appropriate follow-up.

SO 24.

Invasive Group A streptococcal disease in a Tertiary Centre Paediatric Intensive Care Unit: an 8-year prospective cohortstudy.

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Background

Group A streptococcal (GAS) infection often causes mild illness as tonsillopharyngitis, impetigo and scarlet fever. Rarely, invasive GAS (iGAS) disease may have a life-threatening character, most often presenting as streptococcal toxic shock syndrome (STSS), community-acquired pneumonia (CAP) or skin and soft tissue infections (SSTI). The World Health Organization (WHO) and European Centre for Disease Controll (ECDC) have spread an alert on an increased incidence of iGAS disease in children under 10 years of age since September 2022. There may be an association with high circulation of respiratory viruses, including seasonal influenza and respiratory syncytial virus, as viral coinfection may increase the risk of iGAS disease.

Methods

During an 8 year period (Jan. 2015 – Dec. 2022), we prospectively registered all paediatric patients with iGAS, admitted to the Paediatric Intensive Care Unit of a tertiary paediatric centre, and documented relevant infection-related data (demography, morbidity, treatment, microbiology, virology, outcome) using a computerized surveillance system integrating relevant data sources. We describe epidemiologic, clinical, microbiology and outcome data of this patient cohort.

Results

- Epidemiology: 58 cases were registered during the 8 year study period, of which 13 patients in Nov.-Dec. 2022, indicating a significant outbreak
- Most often (54/58) previously healthy children
- Clinical diagnosis: CAP 24/58, STSS 20/58, SSTI 16/58, 23/58 > 1 clinical diagnosis
- Frequent viral co-infections (18/58), 75% SSTI: co-infection Varicella Zoster Virus
- Outcome: median LOS PICU 5 days, low mortality 1/58

Conclusion

Our data confirm the WHO and ECDC reports on the increased incidence of iGAS infections in Europe among children. Healthcare providers should maintain a high degree of clinical suspicion for iGAS infection as a possible cause of severe illness, especially if persistent or worsening symptoms follow initial improvement of a viral illness. Early recognition of signs and symptoms and prompt initiation of specific and supportive therapy can be life-saving. It is essential to obtain blood and, as clinically indicated, wound or pleural fluid cultures in suspected iGAS infections. Ask laboratories to hold iGAS isolates and send them to the public health laboratory for emm-cluster typing. Notify appropriate public health departments as soon as possible about iGAS disease affecting children as secondary prophylaxis is indicated.

PW 11.

Asymmetric crying facies: writing on the wall?

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Background

Asymmetric crying facies (ACF) is a rare disorder caused by an agenesis or hypoplasia of the m. depressor anguli oris. The presence of ACF has been associated with other malformations.

Results

We describe a male infant born at 34 weeks and 6 days of gestation. The pregnancy was spontaneous, the mother had no previous history, while father received chemotherapy for testicular carcinoma three years before. During pregnancy, several fetal abnormalities were visualized on structural ultrasound: the fetus had a right-sided aortic branch, limited filling of the stomach and a micropenis. Following these findings, genetic counseling was offered. An array CGH was performed but revealed no abnormalities.

The pregnancy was further complicated by preterm premature rupture of the membranes at 34 weeks and loss of meconium-stained amniotic fluid at 34 weeks and six days, after which delivery was induced. The neonate had Apgar scores of 5, 7 and 8 at respectively 1, 5 and 10 minutes after birth. He was cyanotic and required insufflations, followed by positive end expiratory pressure. Afterwards, the child had a continued need for respiratory support by Continuous Positive Airway Pressure (CPAP), consistent with hyaline membrane disease grade II. Clinically, the child had a micropenis with cryptorchidia. When crying, the right corner of the mouth did not move, suggestive of an ACF. Umbilical catheters and a gastric tube were placed shortly after birth. Radiography of the thorax revealed a gastric tube curled up in the esophagus, suggestive of esophageal atresia. No vertebral abnormalities were observed. Echocardiography revealed an atrial septum defect with a vascular ring. Kidneys were normal on ultrasound. Biochemical analysis showed a low LH and FSH. The child was referred to a specialist center for surgery and genetic analysis is being performed.

Conclusion

Although several malformations were already defined on structural ultrasound during the pregnancy, ACF should always warrant further investigations for underlying malformations. Furthermore, more studies are needed on the gonadotoxic effects of chemotherapy and possible effects in the offspring; and patients should be counseled accordingly.

PW 12.

Case report: Severe Neonatal Methylmalonic Acidemia associated with a heterozygous 5-Deoxyadenosylcobalamin A gene mutation

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Methylmalonic Acidemia (MMA) is an autosomal recessive disorder consisting of an inborn error of branched-chain organic acids metabolism. It occurs when there is an accumulation of Methylmalonic Acid due to deficiency of Methylmalonyl-CoA mutase (MCM) or to its cofactor 5-deoxyadenisylcobalamin (AdoCbl). Symptoms can present in the first days of life, and include acute deterioration, metabolic acidosis and hyperammonemia. Treatment includes promotion of anabolism by protein restriction, caloric support, ammonia scavengers, and dialysis. N-carbamoyl-L-glutamic acid (NCGA) is a synthetic analogue of N-Acetylglutamate (NAG), that activates the urea cycle. It is not only used in NAG Synthase deficiency treatment, but also to decrease ammonia levels in branched-chain organic acidemias. MMA clinical outcomes remain poor and the prognosis is influenced by the duration, peak and number of metabolic decompensation episodes.

This is the case of a term male newborn with severe hyperammonemia (ammonia levels at 1357 µmol/L) on his third day of life. He presented with severe encephalopathy, confirmed by a pathologic electroencephalogram (EEG) and Brainstem Auditory Evoked Response. Adequate treatment was initiated, and included empiric administration of NCGA, leading to a twelve-fold ammonia decrease 16 hours after the first dose; and recovery of consciousness 48 hours after admission. Ultimately, dry blood spot analysis revealed increased levels of C3 Propionylcarnitine and Methylmalonate, suggesting the diagnosis of MMA and explaining the adequate response to NCGA. A neurological follow-up at the second week of life included an EEG and a brain magnetic resonance imaging, both showing no abnormalities. At 12 months old, the patient's motor neurodevelopment is below the norm, but surprisingly good considering his medical history.

Nevertheless, a whole genomic trio sequencing merely detected a heterozygous mutation paternally-inherited on the MMAA gene, responsible for the production of AdoClb-A, which is usually associated with less severe forms of MMA. On the other hand, postnatal maternal serum dosage levels revealed moderate deficiency of vitamin B12, also a MCM's cofactor, which could explain the early marked hyperammonemia. However, the chronic presentation can neither be explained by MMAA mutation's heterozygosity, nor by gestational vitamin B12 deficiency. Therefore, genetic analysis is still on-going with RNA sequencing on the lymphoblastoid cell lines.

LO 3.

Serum cytokines differentiate among patients with multiple inflammatory diseases: proof-of-concept data for FEBRIS, a multi-centric prospective study

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Background
Fever is a cardinal but nonspecific symptom of systemic inflammation. Patients with acute, chronic or relapsing systemic inflammation may suffer from one of many diseases, including systemic infection, autoimmunity (AI), autoinflammatory disorders (AID), and hyperinflammation (HI).

Despite their clinical overlap, the underlying pathophysiology and subsequent patient management are different, making it challenging to diagnose and treat individuals.

We aimed to discover blood protein signatures for systemic infection, AI, AID and HI. Envisioning a prospective study, we favored maximal accuracy with the smallest possible number of biomarkers.

Methods
We included patients with known clinical and/or genetic systemic inflammatory diseases. Serum samples were collected. By Mesoscale Discovery, 55 proteins were quantified and normalized for age. Unbiased variable selection was performed by random forest regression, MUVR and Boruta.

Results
Fifty-five patients (median age 6y [IQR 3-13]; 19/28 M/F) with active inflammatory disease (5 systemic infections, 8 AI, 26 AID, 8 HI patients) and 16 healthy controls (HCs) were analyzed. Among patient groups and/or with HCs, 38 proteins were significantly up- or downregulated.

Combining results from three machine learning methods, we identified 9 proteins (Eotaxin-3, ICAM-1, IL-10, IL17A/F, IL-27, Tie-2, IL-1Ra, IP-10 and SAA) that maximally separated patient groups. Principal component analysis and unsupervised hierarchical clustering confirmed separate clustering of diseases, besides some HI and infections overlapping.

High serum Tie-2 and ICAM-1 were found in HI. High SAA with relatively low ICAM-1 characterize AID. AI patients show low SAA and Tie-2 but high IP-10. Also in infections, the Tie-2/IP-10 ratio is low, but also Eotaxin-3 is characteristically low.

Multinomial regression modeling revealed high significance for AI and AID ($P<0.0001$) and HI ($P=0.0003$), but less for infection ($P=0.08$). Predictive accuracy was excellent for AI (AUC 0.99) and AID (AUC 0.89), good for HI (AUC 0.82) and poor for infection (0.64).

Conclusion
We identified a 9-plex serum protein signature capable of separating patients with AI, AID, HI and infection with adequate accuracy. In FEBRIS, a multi-centric cohort study, we are now prospectively validating findings.

These results may contribute to a better understanding of pathophysiology and improve early diagnosis and management of patients with systemic inflammation.

LO 4.

Does air pollution affect the airways of early-career elite athletes?

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Background/Aims
Although physical exercise improves overall health, increased physical activity, in a polluted area as Belgium, might act as stressor to airway barrier. The aim was to study the exposure and impact of air pollutants in early-career indoor and outdoor elite athletes.

Methods
Early-career elite athletes attending “Flemish-Elite-Sports-Schools” (12-18 years) of different in- and outdoor sport disciplines: basketball (n=24), football (n=38), volleyball (n=14) and swimming (n=14) and controls subjects (n=25) were recruited. To test for exercise-induced bronchoconstriction (EIB), the eucapnic voluntary hyperventilation (EVH) test EucapSys® (SMTEC SA, Switzerland). Air pollution data, more specifically particulate matter <10 µm (PM10) and <2.5 µm (PM2.5) were obtained from Belgian Interregional Environment Agency (IRCEL). Markers at mRNA and carbon load in airway macrophages (AMs) were studied on induced sputum samples.

Results
Sputum samples of athletes contained significantly more carbon loaded AMs compared to controls (P<0.0001). Similarly, the number of particles in macrophages and percentage area occupied by black carbon were significantly increased in athletes compared to controls (P<0.0001). No significant difference was observed between in- and outdoor athletes. Eight elite athletes tested positive for EIB. By performing multiple linear regression analysis adjusted for humidity, temperature, age-squared, gender, BMI and atopic state, PM10 and PM2.5 were found to be independent predictors of drop in FEV1(%) post EVH test. The maximal fall in FEV1 was 10.45% lower for each 1 µg/m3 increment in average PM2.5 and 10.42% lower for each 1 µg/m3 increase in PM10, indicating a reduction in maximal fall in FEV1 with increasing air pollution exposure. In the multi-pollutant model, considering PM2.5 and PM10, the association with PM10 appeared to be the most robust. In addition, significantly lower mRNA levels of OCLN and ZO-1 in athletes exposed to higher levels of PM10 (>20 µg/m3, n=22) compared to athletes exposed to lower levels (<20 µg/m3, n=23) are observed (p=0.0114, p=0.0147).

Conclusion
Early-career athletes showed increased uptake of black carbon by AMs, likely the result of their high ventilatory demands during exercise. Remarkably, the airway response to EVH testing in athletes was associated to prior air pollution exposure, indicating that exposure to increased air pollution may induce short term increased airway hyperreactivity.

SO 25.

Outbreak of diphtheria among asylum seekers in Belgium in 2022

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Background
Diphtheria is a rare disease in high income countries but since 2022, Europe including Belgium, has been facing an epidemic of cutaneous diphtheria among Applicants for International Protection (AIP). Cases of respiratory diphtheria have also been reported, including one fatal case. Belgium lacks reception places and many AIP are without shelter (around 2050 persons in October 2022) greatly complicating vaccination, diagnosis and case management.

Method
Vaccination and case management including contact tracing were performed by Fedasil for AIP in reception centers. For AIP without shelter, Commission communautaire commune of Brussels facilitated the management of the outbreak in Brussels and a fix vaccination line for all AIP, alongside Non-governmental organizations such as Doctors Without Borders organized a test and treat center as well as mobile vaccination teams. Microbiology analysis (PCR and Elek test) was performed by the National Reference Center (NRC, UZ Brussels).

Results
In Belgium, the first case of diphtheria related to this outbreak was diagnosed in March 2022. Up to 15 December, 24 cases were confirmed by the NRC. All but one were male (3 unknown), with a median age of 17 (15-39), 19 coming from Afghanistan, 3 from Syria and 2 with unknown origin country. All were cutaneous cases caused by toxin-producing Corynebacterium diphtheria but one was a very severe respiratory diphtheria case treated with diphtheria antitoxin. No deaths have been reported. Preliminary molecular typing shows that most strains belong to MLST 574 or 377, types that also represent a large part of the cases in other European countries at the moment. For positive cases of AIP residing in reception centers, the treatment and prophylaxis guidelines developed in 2019 by the Superior Health Council were followed. For AIP supported by Non-governmental organizations, a swab was taken in case of ulcerations and antibiotic therapy was systematically administered without waiting for the laboratory results. Chemoprophylaxis and swabs of close contacts was not possible in this case.

Conclusion
This outbreak is difficult to manage given the lack of capacity of screening people at arrival due to a reception crisis. AIP must be vaccinated quickly, especially children. Health practitioners should be aware of the possibility diphtheria in unvaccinated or incompletely vaccinated AIP and particularly children who are more at risk of developing a respiratory form of diphtheria

SO 26.

Distinct Phenotypes of Multisystem Inflammatory Syndrome in Children: a Cohort Study.

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Background
Multisystem inflammatory syndrome in children (MIS-C) is a severe disease with an unpredictable course and a substantial risk of cardiogenic shock. Our objectives were to (a) compare MIS-C phenotypes across the COVID-19 pandemic, (b) identify features associated with intensive care need and treatment with biologic agents.
Methods
Youth aged 0-18 years, fulfilling the World Health Organization case definition of MIS-C, and admitted to the Alberta Children's Hospital during the first four waves of the COVID-19 pandemic (May 2020-December 2021) were included in this cohort study. Demographic, clinical, biochemical, imaging, and treatment data were captured.

Results
Fifty-seven MIS-C patients (median age 6 years) were included. Thirty patients (53%) required intensive care. Patients in the third or fourth wave (indicated as phase 2 of the pandemic) presented with higher peak ferritin (µg/l, median (IQR) = 1134 (409-1806) vs 370 (249-629), P=0.001), NT-proBNP (ng/l, median (IQR) = 12217 (3013-27161) vs 3213 (1216-8483), P=0.02) and D-dimer (mg/l, median (IQR) = 4.81 (2.24-5.37) vs 2.01 (1.27-3.34), P=0.004) levels, and higher prevalence of liver enzyme abnormalities (n(%) = 17 (68) vs 11 (34), P=0.02), hypoalbuminemia (n(%) = 24 (100) vs 25 (81), P=0.03) and thrombocytopenia (n(%) 18 (72) vs 11 (34), P=0.007). These patients had a higher need of non-invasive/mechanical ventilation (n(%) 4 (16) vs 0 (0), P=0.03). Unsupervised clustering analyses classified 47% of the patients in the correct wave and 74% in the correct phase of the pandemic. NT-proBNP was the only significant contributor to the need for intensive care in all applied multivariate regression models. Treatment with biologic agents was significantly associated with peak CRP (mg/l (median, IQR = 240.9 (132.9-319.4) vs 155.8 (101.0-200.7), P=0.02) and ferritin levels (µg/l, median (IQR) = 1380 (509-1753) vs 473 (280-296)).

Conclusions
MIS-C patients in a later stage of the pandemic displayed a more severe phenotype, reflecting the impact of distinct SARS-CoV-2 variants. NT-proBNP emerged as the most crucial feature associated with intensive care need, underscoring the importance of monitoring.

SO 27.

ETI (Elexacaftor / Tezacaftor / Ivacaftor) - a closer look at the first 14 days of treatment using a telehealth platform

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Objective
In Belgium, ETI reimbursement for eligible patients with cystic fibrosis was very late (September 2022). Under ETI treatment, substantial improvement is well documented after 2 weeks. Yet, little is known about what more precisely happens during these 14 days. We decided to monitor this period closely.

Methods
In this prospective observational study (NCT05599230), the first 20 patients meeting the following criteria were recruited: 12 y of age, medical and psychological stability, owning a smartphone, Grade A acceptability of spirometry and FEV1 repeatability at the baseline visit preceding the Monday on which treatment was started. Home spirometry (Spirobank) was recorded on the 3 days prior to the start of treatment and then daily for 14 days, as was a respiratory symptoms score (RRS) and a diary of events experienced by each patient. Baseline data and those collected at the next visit, after 6 weeks of treatment, were also compared.

Results
Mean age (± SD) of the 20 patients (8M) was 29.4 (± 11.1) years, mean FEV1 84.2 (± 17.7) pr, mean BMI z-score: 0.18 (± 0.82). Except for 7 patients carrying a F508del/min F genotype, all were already on modulators (I: 2, T/I: 11 of whom 4 F508del/res F). After 6 weeks under ETI, FEV1 increased on average by 10.3% VA ($p<0.0001$). Compared with the average of the 3 days before the start of treatment, the RSS deteriorated significantly on D1 ($p<0.05$), then improved from D6 onwards. The quality of FEV1 measurements at home was high (grade A: 82%). FEV1 improvement became significant from D6 onwards too. In one patient, a 25% decrease in FEV1 was observed at D4, which quickly responded to a three-day course of oral steroids.

Conclusion
Providing detailed information to patients before starting the treatment proved to be valuable. Respiratory benefit was significant from day 6. The most troublesome events occurred during the first 4 days of treatment. Starting treatment on a Monday seems to be advisable.

SO 28.

Effects of climate and airborne pollutants on children's health in Belgium within the RetroPollen project.

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Background
Air pollution has tremendous effects on mortality and quality of life, and imposes additional distress on people suffering from respiratory diseases (1,2,3). Likewise, biogenic aerosols such as airborne pollen affect public health with an estimated quarter of the adult population and a third of all children in Europe suffering from pollinosis (3,4).
In light of the ongoing climate change, the RetroPollen project aims at reconstructing four decades of spatio-temporal airborne pollen levels for Belgium to assess the health impact of the combined exposure to airborne pollen, air pollution, and meteorological conditions. The study population consists of 1085 participants from five patient groups with different underlying health conditions and severity of symptoms, ranging from acute asthmatic exacerbations to cystic fibrosis. Currently, the data sets are evaluated and pre-processed, and in the next step, the health impact will be investigated.

Methods
Longitudinal clinical data was obtained from the ULB-ERASME hospital in Brussels, and from the Zeepreventorium, De Haan, Belgium, including lung function measurements and relevant covariates. For the exposure assessment, the spatio-temporal distribution of birch and grass pollen between 1987-2020 was reconstructed. Surface observations of anthropogenic air pollution were calculated with a spatiotemporal interpolation model and meteorological variables collected from monitoring stations. Distributed lag non-linear models (DLNM) were applied for a first assessment of the associations between air pollution, pollen levels, and climate factors on forced expiratory volume in one second (FEV1) in the pediatric patients, considering a 7-day lag of the exposures, seasonality, long-term trends and random effects.

Results
The mean (SD) age of the 126 patients from the asthma pediatric population during the longitudinal trajectory was 10 years (2.46) and seven lung function measurements were performed on average per child with an average FEV1(L/min) of 1.94 (0.59). The preliminary analysis by DLNM, adjusted for various covariates suggests an inverse association between PM2.5 and FEV1 at lag 0 (β= -0.036 (95% CI: -0.072 - -0.00059).

Conclusion
This preliminary analysis, based on historical datasets of the pediatric patient population of the RetroPollen project, shows promising outcomes and warrants further in-depth evaluation of the health effects of air pollution. Full data set analysis is expected by march

SO 29.

PK, SNA, and Efficacy Against RSV MALRI From a Phase 1b/2a Study of the Monoclonal Antibody Clesrovimab (MK-1654) in Infants

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Merck & Co., Certara

Background
MK-1654 is an investigational RSV-neutralizing monoclonal antibody targeting site IV of the RSV F protein currently in phase 3 development for the prevention of RSV medically attended lower respiratory tract infection (MALRI) in infants.
Methods
This phase 1b/2a double-blind, randomized, placebo-controlled study evaluated the safety, tolerability, pharmacokinetics (PK), and serum neutralizing antibody (SNA) titers of MK-1654 in pre-term (born 29-35 weeks gestational age) and full-term infants. Participants (n=181; aged 2 weeks to 8 months) were randomized in a 4:1 ratio within five separate panels (pre-term: 20, 50, 75, or 100 mg; full term: 100 mg) to receive a single intramuscular dose of MK-1654 or placebo. Blood samples were collected to quantify MK-1654 serum concentrations and SNA titers. A preliminary population PK (popPK) model was developed to describe PK of MK-1654 in infants. The efficacy of MK-1654 was predicted using clinical trial simulations which were based on the popPK model and a published model-based meta-analysis. An exploratory efficacy analysis of observed RSV MALRI through day 150 was conducted.

Results
Concentration data from 111 pre-term infants and 32 full-term infants through at least 150 days post-administration were available. The PK of MK-1654 was best characterized by a linear two-compartment popPK model with first-order absorption and elimination. Clearance and volume of distribution (Vd) scaled allometrically with time-varying body weight. The half-life of MK-1654 was approximately 42 days. A linear relationship was observed between increasing concentrations of MK-1654 and increasing SNA. Clinical trial simulations predict that a single 100-mg dose of MK-1654 will provide >76% efficacy for the prevention of RSV MALRI for a duration of 5 months in infants. Exploratory analysis of the phase 1b/2a study data yielded an observed efficacy of 74.2% (95% CI: -92.9%, 96.5%) for all dose groups (20-100 mg) vs. placebo and 80.6% (95% CI: -141.2%, 99.6%) for the 100-mg dose group vs. placebo.

Conclusions
Model-based efficacy predictions aligned with the observed MK-1654 efficacy to prevent RSV MALRI in the phase 1b/2a study. The data support the continued evaluation of MK-1654 in ongoing phase 3 studies.

SO 30.

Monitoring of varicella trends in Belgium between 2017 and 2022 through Google Trends

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Sciensano

Introduction
Varicella is a common infectious disease whose diagnosis is essentially clinical. In European countries, an annual epidemic occurs in March-May. Few data sources exist in Belgium to track trends of this disease over time, but several studies have validated the use of search queries for syndromic surveillance or trend monitoring for diseases such as varicella. We examined Varicella trends in the recent years to assess a possible influence of the covid-19 pandemic and the measures to limit its spread.

Methods
Google Trends reflects the proportion of searches for a given keyword in a region and for a specific period, compared to the region where the rate of use of this keyword is the highest (value of 100). The numbers are standardized within each country such that values range from 0 to 100. We data-mined varicella information-seeking behavior using Google queries for the terms “varicelle”, “windpokken” and “waterpokken” for Belgium and for the 3 Belgian regions, per month, for 2017 to 2022, lockdown periods included.

Results
We detected, as expected, significant seasonality of the Google Trends data for 2017 and 2018 (peak between March and June). Varicella seems to have been more intense in 2019 compared to previous years with an increase of queries as of February and a higher number of queries during the epidemic season. A drop in the number of queries is observed in March 2020 until June 2021 (61-81% drop in absolute search volume between April and July 2020 in comparison to the average of April to July 2017-2019) when a slight increase is visualized. The year 2022 was intense in terms of the circulation of the virus with a record number of total queries, particularly in July and Augustus with an increase of respectively 125% and 150% compared to the average absolute search volume of July and Augustus 2017-2019. Very similar trends are observed for Flanders and Wallonia. In Brussels, the trends are more variable, especially from March 2020.

Conclusion
The circulation of the varicella zoster virus has been strongly impacted by the covid-19 pandemic related measures. Already validated tools such as Google trends represent an interesting alternative to conventional surveillance systems and have the advantage of being inexpensive, accessible to all, and of monitoring in real time certain diseases whose symptoms are easily recognizable by the population.

SO 31.

Group A Streptococcal Alert

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Background
Early December 2022 an alert was published by different countries in the European Early Warning and Response System on the surge of invasive Group A Streptococcal infections (iGAS) and associated fatalities in children less than 10 years. GAS usually cause mild infections like scarlet fever or pharyngitis but can occasionally cause life-threatening infections.

In Belgium, iGAS is a mandatory notifiable disease and circulating strains of iGAS are monitored by the national reference centre (NRC). All GAS infections (including iGAS) are monitored by a network of sentinel laboratories.

Methods
Data on GAS infections in 2022 collected by the NRC and the sentinel labs were analysed and compared with prior years.

Results
Sentinel labs showed an increase in 2022 for GAS infections, particularly in the age groups 0-4y and 5-9y. Those labs reported 282 cases in the 0-4y old in 2022, compared to an average of 41 cases during the pandemic years 2020-2021 and an average of 116 cases for 2015-2019. In the 5-9y old 122 cases have been reported in 2022, compared to an average of 11 in 2020-2021 and an average of 38 cases for 2015-2019. In line with this, NRC data show an increase in iGAS infections, above the trend preceding COVID years, particularly in 0-4y (131 cases in 2022 compared to an average of 57 cases for 2015-2019). Both sources show a markedly high monthly peak value this year: 54 cases in sentinel labs and 25 cases in NRC compared to an average peak of respectively 19 and 10 cases for 2015-2019 in 0-4y. In previous years incidence peaked in winter or early spring, whereas 2022 incidence peaked in June and October-December.

Typing of the strain by the NRC of iGAS in 0-4 year shows a diverse range of emm gene sequences with emm1 and emm12 being the most frequent (proportions of 36% and 24% respectively). So far, the occurrence does not appear to be linked to new circulating genotypes or increased antibiotic resistance. A hypothesis for this change in epidemiology could be the decreasing hygienic COVID-19 measures after a period of reduced exposure to GAS and viral infections, and a subsequent reduction in built-up immunity. The additional probable increased circulation of varicella in 2022 observed through other sources could be contributing to increased risk of iGAS, where coinfection occurs.

Conclusion
Increased awareness of iGAS infections is needed in physicians and caretakers of young children.

SO 32.

Does analysis of ventilator's built-in software data predict abnormal transcutaneous CO2-measurements in children on chronic non-invasive ventilation?

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Background/Aim
Follow-up of children on chronic non-invasive ventilation (NIV) at home could be improved by telemonitoring, using the ventilator's built-in software (BIS) parameters. This study investigates whether analysis of BIS parameters could predict abnormal transcutaneous CO2 (TcCO2) and saturation (SaO2) measurements. This alternative for in-hospital sleep studies could reduce costs and time, improve patient independence and contribute to early detection of infections.

Methods
Children on chronic NIV followed up at the Antwerp University Hospital were retrospectively included. TcCO2 and SaO2 measurements from overnight sleep studies were collected together with BIS parameters from three different time points: at the same night as the sleep study (t1), the mean values from 48 hours (t2) and from 72 hours (t3) before the sleep study. Predictions were calculated for following outcome measures: % recorded sleep time TcCO2 > 46.9 mmHg (%RT TcCO2; abnormal if >2%), recorded sleep time SaO2 < 93% (RT SaO2; abnormal if > 1 hour), abnormal TcCO2 or SaO2, mean TcCO2, mean SaO2.

Results
A total of 69 measurements was included. %RT TcCO2 was separately predicted by reached tidal volume t2 (OR 0.97; p = 0.05; AUC = 30%) and reached IPAP t1 (OR 1.05; p = 0.05; AUC = 66%). Secondly, leakage t1 predicted RT SaO2 (OR 1.21; p = 0.03; AUC = 84%). For mean TcCO2, linear regression analysis showed a significant model with reached tidal volume t2 (rs = -0.31; p = 0.03). Analysis for other outcome measures did not provide additional significant models.

Conclusion
Abnormal values of TcCO2 and SaO2 can be predicted by certain BIS parameters. Future studies with larger sample sizes are warranted to further investigate the predictive value of the BIS parameters identified in this study (reached IPAP t1, reached tidal volume t2 and leakage t1).

SO 33.

Whole blood TCR Vβ21.3 staining as a diagnostic test for multisystem inflammatory syndrome in children: a proof-of-concept study

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Background/aims

Multisystem inflammatory syndrome in children (MIS-C) is a rare inflammatory condition, occurring 1-2 months after SARS-CoV-2 infection in children.

The clinical features of MIS-C are nonspecific. Since early treatment is of prognostic value, clinicians are faced with the challenge to recognize patients timely. However, lacking a specific test, diagnosing MIS-C remains largely based on clinical expertise.

Enrichment of Vβ21.3+ T-cell receptors is a frequent finding in MIS-C. We aimed to assess the value of whole blood (WB) Vβ21.3 staining as a diagnostic test for MIS-C.

Methods

EDTA blood was obtained in healthy controls (HCs) and patients fulfilling the WHO MIS-C case definition (before immunomodulatory treatment). WB was stained, lysed and fixed within 2h of sampling. By flow cytometry, the relative frequency of Vβ21.3+ T-cells (CD3/CD4/CD8) was assessed as well as activation markers (HLA-DR).

Results

Four patients and five healthy controls were included. The proportion of Vβ21.3+ T-cells were increased in one case (3.6-5.6% of T-cells), a 12yo girl presenting typical MIS-C and responding rapidly with first-line treatment. Although all other patients fulfilled the MIS-C case definition at inclusion, their further disease course led to alternative diagnoses, including Streptococcus pyogenes sepsis, haemophagocytic lymphohistiocytosis and metabolic cardiomyopathy. These non-MIS-C patients and HCs showed only 1.0-2.6% Vβ21.3+ T-cells. Additionally, in MIS-C 37.7% of Vβ21.3+ lymphocytes were HLA-DR+, while only 0.1-11% in HCs and non-MIS-C patients.

Conclusion

We provide proof-of-concept that WB Vβ21.3 staining can be used as a rapid diagnostic test to distinguish MIS-C from other severe inflammatory diseases. Its sensitivity and specificity should be assessed in larger prospective studies.

PW 1.

Group A Streptococcus meningitis: report of a case

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HUDERF

Background

Group A Streptococcus (*GAS*) is a rare agent of meningitis. The World Health Organisation recently alerted on the rise in paediatric invasive *GAS* infections. We present the case of a child with *GAS* pharyngtitis and cellulitis, which evolved to *GAS* meningitis (GASM).

Aims: Share clinical features of a child with GASM, discuss treatement and sequelae.

Methods: We reviewed a patient's data.

Case description
An 11-year-old child presented with fever, headache, myalgia and signs of ankle inflammation. No trauma or insect bite was reported. She had no medical history and was fully immunized. She was febrile and tachycardic, but blood pressure was normal. Physical exam revealed inflammation of the ankle and the pharynx.
Blood analysis showed an inflammatory syndrome with increased CRP and normal, predominantly neutrophilic leukocytosis. An ankle ultrasound revealed cellulitis. In the forenoon petechiae and an abdominal rash appeared. Fever rose, she was painful and an increase of the biological inflammatory syndrome was evidenced. Toxic shock syndrome (TSS) being suspected, Ceftriaxone and Clindamycin were started. Blood cultures and a throat swab identified *GAS*, and signs of meningeal irritation were observed. Lumbar puncture confirmed meningitis, and immunoglobulins (IVIG) were given. She presented an encephalopathic clinical and electrical pattern. Head CT showed filling of sinuses. Intracranial hypertension was treated medically. MRI revealed a non-drainable frontal empyema with right cochlear damage, reducing auditory transmission. No cardio-respiratory support was required. Pyrexia was persistent.

Discussion
Clinical deterioration and the severity of the suspected disease, led to combined use of a Beta-Lactame and Clindamycin which has been shown more effective in invasive *GAS* infections. IVIG is recommended in TSS.
Pharyngeal gateway is frequent in children with GASM, and few have antecedents.
We only found one paediatric description of post-GASM cophosis and no literature on prevention by corticosteroids.

Conclusion
In case of deterioration with suspicion of TSS, Ceftriaxone, Clindamycin and IVIG should be started. Most children with GASM are healthy, and the gateway is usually an otitis or pharyngitis. *GAS* can rapidly spread via the blood. There is no literature on prevention of post GASM cophosis.

PW 2.

Pleural empyema at 1 month of age: important considerations and pitfalls, a case report

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A 45-day old boy was admitted with a pneumonia of the left lower lobe, for wich treatment was started with Amoxicillin and Cefotaxim intravenously. After 24 hours he needed oxygen-supplementation via low flow nasal canula, for which a chest X-ray was repeated which showed pleural effusion on the left side. An ultrasound and chest CT confirmed a necrotising pneumonia with empyema of <1 cm.The antibiotics were changed to amoxicillin + clavulanic acid. Vancomycin was added a day later because the parents had a recent history of recurrent MRSA furuncles, treated locally a few months before the boy was born. Initially, fever resolved and inflammatory blood parameters improved, but he needed more respiratory support (high flow nasal canula). After 48 hours of apyrexia fever returned and there was no further improvement of chest X-ray or inflammatory blood parameters. A thoracoscopic surgery and bronchoscopy was performed and a chest tube was left in place. Within 24 hours he was apyretic. After 5 days, the respiratory support was stopped and the drain was removed. Immunologic testing results are pending. Superficial skin cultures were positive for methicillin-resistant S. aureus (MRSA), as was the bronchoalveolar lavage. The empyema culture showed a methicillin-sensitive S. aureus (MSSA). Antibiotics were changed to Vancomycin monotherapy. Father turned out to still be carrier of an MRSA as the parents had never received eradication therapy.

Necrotising pneumonia with pleural empyema is rare in young infants. Almost no cases are reported. Immunodeficiency should be considered, although some pathogens can cause invasive disease in immunocompetent hosts. S. aureus is notorious for invasive infections.

MRSA in the environment is at the basis of this condition. This case shows how important a thorough anamnesis is: ask for risk factors such as skin infection, health care profession or contact with (farm)animals. Decolonization is always needed when there is invasive infection requiring hospitalization, when the patient needs surgery as there is high risk for invasive infection, when working in health care, when recurrent infections arise or when there is a predisposing medical condition. Decolonization of all household contacts simultaneously is adviced. As this patient was treated for 3 weeks with vancomycin intraveneously and subsequent cultures were negative for MRSA, only family members were started with decolonization treatment.

PW 3.

Complication of chickenpox: osteitis and venous thrombosis in immunocompetent children

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Uliege

Summary
Male, 3 years old, 4 days of chickenpox, fever up to 40°C with no response to antipyretics and loss of appetite. Extreme pain in the right leg and foot with loss of mobility. Pharyngitis with odynophagia.

Complementary exam
leukocytosis (23060/mm3) with inflammatory syndrome (125mg/L). VS: 20mm/h. Buccal swab: Strepto A + and COVID-19 +. Hemoculture: strept. A pyogenes +. Echography of the right foot: minimal joint effusion with superficial thrombosis of the saphenous vein. Bone scan: suspicion of osteitis in the distal cartilage of the tibial bone.

Result
Chickenpox with osteitis of the distal cartilage of the tibial bone and superficial thrombosis of the saphenous vein.

Conclusion
Chickenpox is a very common disease in children. Complications are rare (2%) but can be life-threatening in certain case and practitioners must therefore quickly recognize their signs. Infectious complications have been reported predominantly in younger children up to 4 years of age whereas neurologic complications occur more frequently in an older age range. By order of frequency, the most common complications are: infectious, neurological, Reye's syndrome and coagulation's problem. In this case, superficial thrombosis was multifactorial. Chickenpox can temporary cause a protein S and/or C deficiency but COVID-19 infection can also lead to an increase in veinous thrombosis. Osteitis and/or septic arthritis are mostly caused by K. Kingae under 36-month. Staph. aureus and S. Pyogenes are more common after 2 years of age, which was the case here. In regular forms of chickenpox, no treatement is indicated except cleaning and desinfection of the cutaneous lesions. When a complication is suspected, antibiotic treatment is essential. Streptococcus pyogenes or staphylococcus aureus are generally the leading cause of bacterial infections. The association of amoxicilline and clavulanic acid is generally recommended. The addition of clindamycine is justified when a severe infection such as necrosant fasciitis is suspected, as it is known to significantly reduce the early release of streptococcus pyogene's toxines. Antiviral medication, e.g. acyclovir, is effective at early stages of varicella but has shown no apparent influence on complications. Superficial thrombosis ordinarily do not require any medication. In this case, the immobilization caused by the pain was a treatment factor and an anti-thrombosis medication at prophylactic doses was administrated.

PW 5.

Immune dysregulation syndrome due to cytotoxic T-lymphocyte antigen 4 (CTLA-4) deficiency responsive to Abatacept therapy

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Background

Regulatory T-cells are major mediators of self-tolerance via CTLA-4 signaling pathways. Heterozygous germline mutations in CTLA-4, inherited through an autosomal dominant way, are associated with immune dysregulation syndrome. Clinical manifestations include on one side primary immunodeficient disease (PID), with hypogammaglobulinemia and recurrent infections, and on the other side auto-immune manifestations such as systemic lymphadenopathy and severe and relapsing auto-immune cytopenia. An increased frequency of malignancies is also described.

Methods

A 10-year old girl with significant familial history of immunodeficiency and severe auto-immunity was admitted to our department with auto-immune hemolytic anemia (AIHA). She had a personal history of recurrent infections and hypogammaglobulinemia. She was first treated with high dose corticosteroids and rituximab because of cortico-dependance. Her clinical status went worse as she developped auto-immune thrombopenia, mediastinal and retroperitoneal adenomegaly and granulomatous lymphoid interstitial lung disease. CTLA-4 deficiency was genetically diagnosed and allowed the compassionate use of Abatacept, a CTLA-4 fusion protein. Results were conclusive with normalization of blood count in 4 months, disappearance of lymphadenopathy in 6 months and normalization of respiratory function in 8 months after treatment initiation.

Results

CTLA-4 deficiency is responsible for severe immune dysregulation. So far, first line treatment consisted in corticosteroid and immunospuressive therapy (such as rituximab, sirolimus) in addition to immunoglobulin substitution.

Abatacept, a CTLA-4 fusion protein, is a targeted option. Several studies show that an initial dose of 20mg/kg every 15 to 21 days administrated intraveinously until complete response of all target organs seems to be well tolerated up to 5-years follow-up without sever adverse effect, and especially without appearance of malignancies. However, the risk of relapse after discontinuation is still unknown and makes hematopoietic stemcells transplant (HSCT) the only long-term cure for CTLA-4 insufficiency. Abatacept treatment would also improve organ function before HSCT.

Conclusion

Children with auto immune cytopenia and personal or familial history of dysimmune disease sould be screened for underlying PID / dysimmune syndrome. In patients with CTLA-4 deficiency, abatacept seems to be a safe and effective targeted treatment.

PW 6.

Recurrent tracheoesophageal fistula after repair of a congenital esophageal atresia. A challenging therapeutic and diagnostic journey: A case report

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Case report of a newborn with esophageal atresia (EA) type C. Flexible bronchoscopy (FB) revealed one tracheoesophageal fistula (TEF), cranial from the carina. Primary correction of the EA was performed via right-sided thoracotomy with extrapleural approach. First postoperative week was uneventful. Enteral feeding started at postoperative day (POD) 3 through the transanastomotic tube (TAT). At POD 10 feeding intolerance led to a contrast esophagogram, showing no anastomotic stricture but persistent fistula. A new esophagogram 2 weeks later showed no fistula. However, FB with instillation of methylene blue (MB) through the TAT, pulled upwards during the procedure, showed a small persistent TEF, located just cranial from the original TEF, suggesting the development of a new TEF.

A brushing technique and instillation of 50% trichloroacetic acid (TCA) in the TEF through rigid bronchoscopy (RB) was performed. Three weeks later, FB demonstrated an important reduction in the flow of MB through the previously brushed TEF, but not a complete closure. A second brushing procedure with application of tissue glue has just been performed.

Literature search

Recurrent TEF after surgical EA repair has an incidence of 7%. Recurrence typically occurs in the early postoperative period, up to 18 months after initial repair.

Contrast esophagogram and FB/RB are the first line investigations in suspicion of a recurrent TEF. A bronchoscopic approach, while pulling back the esophageal tube during instillation of MB, can demonstrate a TEF, which has a higher sensitivity in detecting small TEF than a pull-back tube esophagogram by radiography.

Endoscopic management of recurrent TFE with trichloroacetic acid is a safe and effective procedure, mainly when performed in small fistulas. Combining brushing followed by injection of TCA improves success rates. However, repeated procedures may be needed in order to close the TEF completely. This low-invasive technique avoids a second more invasive thoracoscopy/thoracotomy. Other therapeutic endoscopic modalities are described (laser, tissue glue, endoclips/stitch).

Take home message

Despite complete surgical closure of the initial TEF, recurrence can occur.

FB, with the use of MB, is the most sensitive diagnostic test for first line investigation and follow-up in these conditions.

Recurrent TEF can be managed with less invasive techniques, such as a fistula brushing combined with the instillation of TCA through rigid bronchoscopy.

PW 7.

Post-Infections bronchiolitis obliterans: 3 cases reports

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Background

Bronchiolitis obliterans is a rare chronic form of obstructive pulmonary disease, the incidence ranges from 0.5 to 17.8/100,000 worldwide. BO leads to a progressive airway fibrosis and bronchiolar obstruction. 3 main forms are described: post-infectious, post-lung transplant and post-marrow transplantation.
PIBO disease progression is divided in 3 stages: acute infectious stage (adenovirus), inflammatory stage, peri-bronchiolar fibrosis stage.

Case reports

Case 1
Acute infection at 7 months: severe adenovirus+rhinovirus bronchiolitis, non-invasive ventilation

Diagnosis at 8 months: reduced oxygen saturation (day and night), tachypnea, cough

Diagnostic test: Alveolar hypoventilation. HRCT: mosaic pattern. BAL: neutrophilia, increased CD8 T lymphocytes

6 months post diagnosis: reduced oxygen saturation (night only), decreased tachypnea, no cough

Case 2
Acute infection at 10 months: severe respiratory infection, non-invasive ventilation (no germe)

Diagnosis at 4 years: chronic productive cough, shortness of breath (exertion), respiratory crackles

Diagnostic tests: HRCT mosaic pattern, upper right atelectasis. BAL: neutrophilia, bacterial culture: M. Catarrhalis, H. Influenzae

10 months post diagnosis: Normal air saturation, no chronic cough, no tachypnea. Respiratory crackles

Case 3
Acute infection at 3 years 5 months: Severe respiratory infection, non-invasive ventilation

Diagnosis at 4 years: Chronic productive cough, dyspnea (exertion+rest), respiratory crackles

Diagnosis test: BAL: positive culture (pneumococcus + H. Influenza). HRCT: hypoventilation zones

2.5 years post-diagnosis: auscultatory abnormalities, proximal and distal obstruction, pulmonary overdistension

Conclusion

PIBO is severe complication of bronchiolitis, rare, probably underdiagnosed. PIBO sould be suspected in any patient with bronchiolitis whose symptoms persist up to 4-6 weeks after the acute episode. A clinical scoring system (BO-score) was recently validated. Rapid diagnosis and treatment may minimize bronchiolar fibrosis and improve the prognosis. There's no clear consensus on therapeutic management and the prognosis of BOPI is generally pool due to irreversible pulmonary fibrosis and airway obstruction. A better understanding of the physiopathology of the disease might improve the treatment and prognosis.

PW 8.

When the parasite travels with the man!

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Background

Echinococcosis is a zoonosis caused by parasites, tapeworms of the genus Echinococcus. There are several species of them which determine the form of the disease. Two of these forms are predominant in humans: Alveolar echinococcosis and Cystic echinococcosis.

This latter is also known as “Hydatid cyst” and is caused by the species Echinococcus granulosus. The disease is responsible for the formation of cysts whose location is most often the liver and lungs. In the latter case, the rupture of the cysts can be responsible for hemoptysis or even dyspnea. At other times, the patient can be completely asymptomatic.

The treatment of these cysts can either be medical or surgical and is discussed between the various intervenors.

Case presentation

As part of the tuberculosis screening offered to all migrants returning from a country with a high incidence of the disease, a teenager arriving from the caucasian region is sent for a chest X-ray.

The radiological exam shows a round mass in the upper lobe of the left lung. The child is then 12 years old and is totally asymptomatic. He has no notable medical history and practices sport regularly without experiencing any discomfort such as shortness of breath or dyspnea.

No previous radiological imaging is available. General blood tests don’t demonstrate any anomaly and the tuberculosis screening tests are all negative.

A chest scan is then performed to clarify the borders and content of the lump and confirms the presence of a voluminous cystic lesion of 5x5,5x6,5cm in the upper lobe of the left lung, more likely to be a hydatid cyst.

Western blot is also coherent with the presence of Ecchinococcus granulosus.

In order to exclude the presence of other cysts, an abdominal ultrasound is executed and doesn’t reveal any other cysts. A cerebral IRM is also negative.

A surgery is performed to resect the cyst. PCR on the shell of the cyst and on its liquid are both positive for Echinococcus granulosus.

Conclusion

Cystic echinococcus is rare in our countries. However, it is considered endemic in different areas such as Central Asia, East Africa, Western China, Chile, Argentina, Peru. The symptoms are often tardive and vary depending on the location of the cysts. Several modalities of treatment exist.

PW 9.

Infectious Bronchiolitis, foreign body aspiration or both ? A case report

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Background

A case presentation of a toddler with signs of bronchiolitis in combination with late reaction on foreign body aspiration

Clinical History

A 17 month old girl presented at the general pediatric consultation , during the RSV season,with coughing, wheezing and fever. The siblings, aged 4 and 5 year are also coughing with low degree fever.

A week before the toddler , already coughing , has been choking on a walnut peel while sitting in a car. The peel was removed by an accompanying adult. She was examined at an emergency ward but no Chest Xray was taken. Dismissed with diagnosis of bronchitis and treatment with oral amoxicilline, budesonide and salbutamol in aerosol.

At presentation temperature is 37° C , with normal auscultation and no respiratory distress. Installed treatment is continued. Two days later patient shows again with high fever, coughing and a coarse voice. Taking in account the walnut incident she is referred to Pediatric Pneumology for further evaluation.

Results

Chest ray shows pneumonia of the left lower pulmonary lobe. Inpatient treatment with Augmentin IV and respiratory physiotherapy is started. Rigid bronchoscopy does not reveal presence of a foreign body, but important granulation and inflammation of the left main stem bronchus.

COVID 19 and RSV PCR remain negative. Viral and bacterial culture also.

Discussion

Even if no viruses or bacteria were found , and a foreign body was not retrieved from the bronchi, clinical and complementary evaluation suggests that the patient had infectious bronchitis (suggestive for RSV) and an aspiration of foreign body (walnut peel) Infectious bronchitis in patient and siblings does not rule out possible foreign body aspiration.

PW 10.

Wheezing episodes in children before and after the start of the COVID-19 pandemic in Brussels

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Background/aims
Studies have demonstrated important changes in the seasonality of pediatric respiratory illnesses since the onset of the COVID-19 pandemic. The aim of this study was to describe the epidemiology of childhood wheezing episodes before and after the start of the COVID-19 pandemic and to study their potentially associated environmental triggers.

Methods
Files of children treated with salbutamol for a wheezing episode at the CHU Saint-Pierre hospital in Brussels in the time period September-October of the years 2019, 2020 and 2021 were retrospectively reviewed. Daily concentrations of gaseous (NO2, O3) and particulate (PM10, PM2.5) air pollutants and airborne Basidiospores, Alternaria and Cladosporium spores were collected over the same time period.

Results
298 episodes of wheezing were observed in 2021 compared to 111 in 2020 and 86 in 2019 ($p<0.001$). The most common diagnosis was viral induced wheezing followed by asthma and bronchiolitis. Compared to 2019, children with wheezing in 2021 were older (mean age 4.6 years in 2021 and 3.6 years in 2019, $p<0.001$) less likely to be hospitalized (21% in 2021 and 32% in 2019, $p=0.034$) and less likely to have a history of recurrent wheezing (43% in 2021 and 64% in 2019, $p<0.001$). The concentration of air pollutants PM10, PM2.5 and O3 was higher in 2021, as compared to both 2019 and 2020 ($p<0.001$). There was no change in the concentration of airborne spores.

Conclusion
Wheezing episodes were observed three times more often in autumn 2021 as compared to 2019 in Brussels, especially in children without antecedent of recurrent wheezing. An increase in air pollution and exposure to SARS-CoV-2 may have contributed to this observation.

PW 41. Case report: Intracranial complications of acute sinusitis in children

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Introduction

Intracranial complications of sinusitis (ICS) are rare but dangerous and call for early, aggressive treatment. We report the story of a girl that, though banal in the beginning, reminds us of the risk of complications.

Case report

A 14-year-old girl without significant medical history was brought to our ER with headaches and confusion. She'd been diagnosed with acute sinusitis 12 days earlier; symptoms faded after 72h, without antibiotics.

Patient was tachycardic and febrile, with GCS of 12 (E3V3M6). She had left peri-orbital edema, exophthalmia, neck stiffness and photophobia. Laboratory tests showed raised CRP (366 mg/L) and leukocytosis (25900/mm^3, 92% neutrophils). Two hemocultures isolated *Streptococcus intermedius*.

CT-scans showed maxillary, ethmoidal and sphenoidal sinusitis with osteolysis, bitemporal edema and pachymeningeal enhancement, as well as extensive veinous thrombosis of cavernous and transverse sinuses, left ophthalmic and internal jugular veins. In the absence of intracranial hypertension signs, lumbar puncture was allowed and showed CSF pleocytosis (1034/mm^3, 91% neutrophils), slightly elevated proteins and normal glucose levels, with negative PCR panel and CSF culture.

Treatment was quickly initiated with IV dexamethasone, heparin and broad-spectrum antibiotics (cefotaxime, vancomycin, metronidazole). Sinuses were surgically drained. 24h later, MRI imaging showed left temporal empyema, pre-suppurative bitemporal encephalitis and intra-orbital abscess. Due to persistence of the collected lesion and intense headaches, ethmoidal trepanation was performed 3 weeks later with antibiotic instillation. After 6 weeks of antibiotics and 3 months of LMWH, patients presents no sequelae except for intermittent headaches.

ICS are rare but possible, especially in adolescents. In that case, the most described patterns of growth are *Streptococcus* species, most commonly *S. milleri*. Infection can spread directly through bony defects and osteolysis or indirectly via retrograde thrombophlebitis of diploic veins. Patients often lack nasal symptoms or focal neurological signs. Orbital complications are frequent. Medical management requires aggressive, culture-directed IV antibiotics during 2-6 weeks. Neurosurgical interventions and endoscopic sinus surgery are often indicated. Long term neurological deficits such as epilepsy, vision loss and focal paresis can occur in up to 35%.

Conclusion

Though rare, ICS can cause significant long-term morbidity and mortality. The best chance to improve patient outcome is through early and aggressive treatment.

LO 5. H

Higher drug exposure to infliximab correlates with rate of anti-TNF induced skin lesions in paediatric IBD patients

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Background
Although infliximab (IFX) therapy has revolutionised treatment of inflammatory bowel disease (IBD) patients, there is still high variability in response necessitating drug optimisation. While higher IFX trough levels (TLs) are associated with better outcomes, this could serve as a risk for more adverse events (AEs), including IFX-induced skin lesions. Therefore, we studied the correlations of IFX exposure with the occurrence of AEs in paediatric patients with IBD.

Methods
In this single-centre study, all children with Crohn's disease (CD) and ulcerative colitis (UC) receiving maintenance IFX therapy who underwent pro-active drug monitoring between March 2015 and August 2022 were included. IFX doses/intervals and patient characteristics were prospectively registered, including appearance of AEs or skin lesions. IFX TLs were analysed using apDia IFX ELISA kit. Data are presented as median with interquartile ranges [IQR] and hazard ratio (HR) with 95 % confidence intervals [95% CI].

Results
A total of 109 patients (72 CD and 37 UC; 48% male; median age at IFX start of 12.9 [11.5-15.0] years) contributed 2913 IFX TLs (median 23.0 [11.0-39.0] per patient) at 3042 infusion visits. During a median follow-up of 3.0 [1.5-4.5] years, we observed 684 AEs in 101 patients and 49 skin lesions in 35 patients. AEs were mainly represented by upper respiratory tract infections (n=333, 48.7%), gastroenteritis (n=130, 19.0%), and pharyngitis or tonsillitis (n=84, 12.3%). Thirty-eight confirmed COVID-19 cases were reported (23 patients were fully vaccinated), all with a mild course.

There was no significant difference (p=0.467) in median TLs between patients with (8.1 [5.8-9.2] µg/mL) and without (8.1 [6.2-10.0] µg/mL) skin lesions. However, Cox proportional hazard modelling showed that higher median IFX doses [HR 1.084 (1.024-1.148), p=0.005] were associated with increased risk of skin lesions, additionally to female sex [2.210 (1.187-5.310), p=0.016] and CD [1.695 (1.241-1.877), p=0.011]. Considering IFX therapeutic TL cut-offs of <5.0 and >9.0 µg/mL, there was no significant difference in AEs rate/year (p=0.749 and p=0.833, respectively). Also, no significant correlation was observed between IFX doses and AEs rate/year (p=0.159).

Conclusions
Increasing the IFX dose to achieve therapeutic TLs will not increase the risk of AEs in paediatric IBD patients. However, concerns may arise regarding the risk of skin lesions, especially in female CD patients.

SO 20.

Missed diagnoses of seasonal eosinophilic esophagitis?

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UZ Gent

Background/ Aims

Guidelines on eosinophilic esophagitis (EoE) from Espghan (2014) and BSPGHAN (2022) mention seasonal distribution. But how to diagnose seasonal EoE?

A 12 year-old boy had in 2014 an endoscopic diagnosis of EoE with 100 Eosinophils per high power field (HPF). Esophageal eosinophils dropped to 25/HPF with a cow's milk free diet and secondly adding local budesonide. Thereafter, he was evaluated every 6 months using the validated PEESS (paediatric eosinophilic esophagitis symptom score), and yearly endoscopically. In 2017 he developed hay fever symptoms based on a grass pollen allergy (RAST >100 kU/L). The EoE flared clinically and endoscopically (>100 eosinophils/HPF) while still treated with diet and budesonide. During the winter, symptoms disappeared (PEESS 8/100) and the diet and budesonide were gradually downgraded and stopped. An endoscopy in January showed no eosinophils. In July 2022 the PEESS increased to 35/100 and the endoscopy revealed > 100 eosinophils/HPF. This pattern of symptoms suggested a seasonal EoE. Currently, this boy is treated with local budesonide during grass pollen season.

The aim for the future study based on this case is to evaluate potential missed diagnoses of seasonal EoE.

Methods

In the future EoE patients will be evaluated for complaints of allergic rhinitis with the Sino-Nasal Outcome test-22 Questionnaire in the winter and the summer period. Allergic rhinitis patients will be evaluated for symptoms of EoE with the paediatric eosinophilic esophagitis symptom score.

Results and discussion

Several studies proved seasonal distribution in EoE. Ram et al. (2015) described the presence of seasonal exacerbations in 2.7% (32/1180) (1/40) of children diagnosed with EoE. These children had a concomitant diagnosis of allergic rhinitis. Reed et al. (2020) describe a seasonal EoE frequency of 2% (13/782) (1/50).

The results of the questionnaires will be merged into a database. So far ethical committee is pending.

Conclusion

Seasonal distribution by aero-allergens is accepted as a potential role in EoE. We present a case of seasonal EoE. Diagnosis should be made by performing an endoscopy during different aero-allergen seasons with at least a two-fold increase in eosinophils while not changing treatment. The frequency of seasonal EoE is rather low (1/40 to 1/50). Future research will be started coming spring to identify missing cases of seasonal EoE.

SO 21.

Self-reported prescribing behaviour of vitamin d prophylaxis in healthy children by belgian paediatricians

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UZ Gent, UZ Brussel, ZNA

Objectives and Study
There is currently no consensus on the guidelines for vitamin D prophylaxis in healthy children. The purpose of this study was to investigate the prescribing behaviour of vitamin D prophylaxis among Belgian paediatricians.

Methods
Between June and September 2022, a questionnaire was distributed by e-mail to all Belgian paediatricians who are members of scientific or professional organizations, as well as to the heads of every Belgian paediatric hospital ward.

Results
We analysed 426 completed questionnaires. All regions, age categories and subspecialties were represented. Vitamin D prophylaxis is always or frequently recommended by 98% of paediatricians. However, only 58% of paediatricians advise vitamin D prophylaxis up to the age of 6 and 66% of paediatricians advise a daily dose of 400 IU. The dosage and/or duration of vitamin D prophylaxis is adjusted based on skin colour by 72% of paediatricians. Approximately 40% of paediatricians adjust the dosage by seasonality and the amount of sun exposure. In nearly every hospital in Belgium (96%), there is a specific protocol for vitamin D prophylaxis for infants on the maternity ward. In contrast, only 30% of all heads of departments confirmed the existence of a protocol for vitamin D prophylaxis on the paediatric ward. When blood sampling is indicated, 56% of paediatricians frequently to always request 25-OH vitamin D.

Conclusions
Belgian paediatricians uniformly prescribe vitamin D prophylaxis to infants. Reported practices regarding duration and dosing of vitamin D prophylaxis show large variability. Most paediatric wards do not have a protocol. To our knowledge, this is the first study investigating the prescribing behaviour of vitamin D prophylaxis of Belgian paediatricians in healthy children.

SO 22.

Handgrip strength as a parameter of health outcome in hospitalized children or children with chronic disease

A. Larue, L. Verbrugghe, K. Huysentruyt

UZ Brussel

Background and aims
The measurement of handgrip strength (HGS) had been advocated as a useful indicator of functional status during hospitalisation or in the setting of a chronic disease. HGS is influenced by nutritional status, hand preference, gender, weight and height. The aim of our systematic review is to analyse the evidence about using HGS as a parameter of different health outcomes in hospitalized children or children with chronic disease.

Methods
A systematic search was performed in PubMed, Embase, Lilacs and the Cochrane Library from inception until 16/02/2022 without language restrictions (Prospero ID: CRD42022291558).

Results
8475 unique references were screened, 17 studies included. Paediatric HGS studies focused on cystic fibrosis (CF) (4 studies, 227 patients), chronic kidney disease (CKD) (2 studies, 484 patients), type 1 diabetes mellitus (DM1) (2 studies, 282 patients), asthma (2 studies, 245 patients), congenital heart disease (1 study, 569 patients), juvenile idiopathic arthritis (JIA) (1 study, 23 patients), surgical patients (1 study, 175 patients), hospitalised patients (3 studies, 904 patients). In the included studies correlation between HGS and different functional and biochemical health outcomes was investigated. HGS was positively correlated with pulmonary function in CF and asthma (4 studies, 352 patients) and quality of life in CF, asthma, JIA and CKD (4 studies, 619 patients). No association was found with HbA1c in DM1 (2 studies, 282 patients).Two studies (770 patients) showed correlation between HGS and nutritional status, however one study showed no correlation (220 patients). HGS was lower in patients with non-glomerular causes of CKD than in glomerular causes, these findings were only significant is 1 of the 2 included studies (2 studies, 187 patients).

Conclusions
Several studies showed a significant correlation of HGS with health outcomes in different paediatric diseases. HGS can serve as a biomarker in CF or other chronic paediatric conditions. Future trials should determine feasibility of using this parameter in clinical practice.

PW 26.

Neonatal appendicitis : A diagnostic pitfall in a preterm neonate

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Introduction

Neonatal appendicitis (NA) is an extremely rare surgical emergency. Because of its non-specific symptomatology, the diagnosis is frequently missed or delayed, leading to increased rates of peritonitis and mortality. We report a case of perforated NA in a preterm neonate.

Case report

The patient is a female neonate, born by C-section at 34 weeks of gestation due to maternal pre-eclampsia, with a birth weight of 1335g. Apgar score was 8/8/9. Enteral feeding was started on day 0 and gradually increased with good tolerance. On day 7, she presented abdominal distention and bloody stools. Blood analysis showed a white blood cell count of 3.9x10^3/mm³ and a CRP of 32mg/L. Intestinal pneumatosis was suspected on X-ray, suggesting the diagnosis of necrotizing enterocolitis (NEC). As a result, she was fasted and triple intravenous antibiotic therapy was started. On day 8, abdominal ultrasound revealed the presence of a digestive perforation, requiring an urgent laparotomy. This showed a perforated appendix in its middle portion without intestinal involvement, making the diagnosis of NA. Successful appendectomy was performed. Enteral feeding was reintroduced on day 16 and exclusive enteral nutrition was reached on day 25. She was discharged on day 35, with good clinical evolution.

Discussion

NA is an extremely rare condition. Protective factors have been reported in neonates, such as a funnel-shaped appendix, soft diet, recumbent position and rarity of neonatal intestinal infections. Prematurity is the major risk factor, but obstructive diseases such as Hirschsprung's disease, cystic fibrosis and meconium plug have been described in term neonates. The thin appendiceal wall, the undistensible caecum, the poorly developed omentum and the lower resistance to infections contribute to higher incidence of perforated NA, resulting in peritonitis and higher mortality. However, the main pejorative factor appears to be the delay in diagnosis and treatment due to non-specific symptoms. The diagnosis can be radiologically suspected but is often made during laparotomy. The treatment involves antibiotic therapy and surgical appendectomy.

Conclusion

Association of abdominal distention and bloody stools in preterm infants usually evoke the diagnosis of NEC. However, NA is part of the differential diagnosis of these non-specific features. With this report, we highlight the importance of recognizing this rare condition, since the prognosis is time-dependent.

PW 27.

Blenderized tube feeding for children: a systematic review of the impact on upper gastro-intestinal symptoms

L. De Belder, H. Delcourt, R. Van den Eynde, K. Huysentruyt

UZ Brussel

Background/Aims
Blenderized tube feeding (BTF) is on the rise among children who require enteral nutrition but the impact on health benefits is not clearly defined. Therefore, we aimed to perform a systematic review on the evidence of BTF on health outcomes. The primary aim was to determine the effect of BTF on upper gastro-intestinal (UGI) symptoms in pediatric patients.

Methods
A systematic review was performed by searching 4 databases (MEDLINE, EMBASE, Cochrane trials and LILACS) for randomised controlled trials (RCT), prospective and retrospective cohort studies and cross-sectional studies reporting on health outcomes in children on BTF (PROSPERO CRD42022306237). No language restrictions were used. Quality assessment was done using the ROBINS-I tool.

Results
A total of 2573 studies were screened on title and abstract. In total, 8 studies (422 patients) fulfilled the inclusion criteria and reported on health outcomes while on BTF. Assessment of the outcome was at high risk for bias in all, four studies have a moderate risk of bias, three studies have a serious risk of bias and one study has a critical risk of bias. No RCT met the inclusion criteria. All cohort studies reported an improvement in UGI symptoms (quantified in four studies, ranging from 42,4% to 95%). An increased oral intake was observed in four studies (40 patients). Three studies (75 patients) reported a decline in the use of acid reduction medication.

Conclusions
There is a lack of high quality research on the health outcomes of BTF. The current available evidence shows that BTF might improve GI symptoms and oral intake.

PW 28.

Exploring parental thoughts and clinical experiences on blended food in a pediatric population, a qualitative study

R. Verheije, F. Carbone, T. Bosmans, K. van Hoeve, I. Hoffman

UZ Leuven

Introduction
There is an increased interest of blended food (BF) as an alternative to Commercial Food in tube fed children.

Aim
The aim of this study was to explore parental experiences and evaluate whether BF is an appropriate alternative in children, assessed by anthropometric evolution, dietary alterations, biochemical nutritional status and medication changes.

Methods
In this cross-sectional study, we included all children who were on BF at University Hospital Leuven in March 2022 and where parents were willing to complete a patients satisfaction questionnaire. Patient's charts were retrospective analysed. Parent satisfaction score was calculated by using cumulative scores on 17 questions (scale from one to five). A score of 51 points, indicating an average score of more than 3 per question, was considered significant.

Results
Nine children receiving BF were identified (median age 4.7 [2-13] years, median weight 14 [8,6 - 35,3] kg, and 66% male). All parents were satisfied using BF based on the parent satisfaction score (> 51 points).

Main reason to switch to BF according to parents were less food processing discomforts. Additional results showed no clinically relevant weight changes (no drop ≥ 1 SD line in weight-for-age growth chart).

No patients needed to discontinue BF, although in five patients alterations in BF were made by the dietician. Nutritional deficiencies (iron ± zinc deficiency) were present in four patients, although timing of onset of deficiency was unsure due to retrospective study design.

Conclusions
Based on parental and clinical experiences BF was well tolerated. A standard follow-up scheme is proposed, in addition to the guidance by an experienced medical team to ensure successful outcomes.

PW 27.

Blenderized tube feeding for children: a systematic review of the impact on upper gastro-intestinal symptoms

L. De Belder, H. Delcourt, R. Van den Eynde, K. Huysentruyt

UZ Brussel

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Conclusions
There is a lack of high quality research on the health outcomes of BTF. The current available evidence shows that BTF might improve GI symptoms and oral intake.

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Main reason to switch to BF according to parents were less food processing discomforts. Additional results showed no clinically relevant weight changes (no drop ≥ 1 SD line in weight-for-age growth chart).

No patients needed to discontinue BF, although in five patients alterations in BF were made by the dietician. Nutritional deficiencies (iron ± zinc deficiency) were present in four patients, although timing of onset of deficiency was unsure due to retrospective study design.

Conclusions
Based on parental and clinical experiences BF was well tolerated. A standard follow-up scheme is proposed, in addition to the guidance by an experienced medical team to ensure successful outcomes.

SO 15.

Inotuzumab ozogamicin as a bridge to hematopoietic stem cell transplantation in relapsed pediatric BCP-ALL after CD19-targeted CAR T-cell therapy

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Aims

CD19-directed chimeric antigen receptor T cells (anti-CD19 CAR T cells) are promising in the treatment of refractory or relapsed B-cell precursor acute lymphoblastic leukemia (R/R BCP-ALL). However, 30-50% of patients relapse after CAR T-cell therapy. After second or later relapse, prognosis is dismal, with only limited treatment options and no existing therapeutic consensus. Here, we report on four children with a relapse after anti-CD19 CAR T-cell therapy treated with inotuzumab ozogamicin (InO).

Methods and results

All patients were initially diagnosed with BCP-ALL and treated according to EORTC 58081 guidelines. After second relapse (three patients) or refractory disease at first relapse (one patient), they all received anti-CD19 CAR T-cell therapy (tisagenlecleucel). Three patients relapsed with a CD19-/CD22+ BCP-ALL after a mean of 16,3 months (range 4-36 months). One patient relapsed with a CD19+/CD22+ BCP-ALL after 16 months. Following relapse, they all received two cycles of InO. After first cycle of InO, all patients achieved complete remission (CR) and three patients had no detectable minimal residual disease (MRD). The last patient still had detectable MRD (PCR <1E-04) after two cycles. After two InO cycles, they all underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT), after conditioning with total body irradiation and etoposide. One patient developed a sinusoidal obstruction syndrome (SOS) after allo-HSCT, but recovered after two weeks of treatment with defibrotide. Seven months after allo-HSCT, one patient developed an isolated extramedullary relapse in the anterior eye chamber (MRD in bone marrow and cerebrospinal fluid was negative), for which palliative radiotherapy was given. Three patients were still in remission during last follow-up (mean 5,3 months; range 1-9 months).

Conclusion

InO can be successfully and safely used for the treatment of CD22+ relapse of BCP-ALL after anti-CD19 CAR T-cell therapy as a bridge to allo-HSCT in heavily pretreated pediatric patients.

SO 16.

Retrospective study on the epidemiology of vincristine-induced peripheral neuropathy in patients with pediatric solid tumors

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Background

Vincristin (VCR) is a cytotoxic drug, used in the treatment of different tumor types. One of its major side effects is peripheral neuropathy, more especially sensory, motor, sensorimotor, autonomic and cranial neuropathy. In patients with vincristin induced peripheral neuropathy (VIPN), the dose of VCR often needs to be reduced.

As not many data are available on the epidemiology of VIPN in children with solid tumors and on the impact of VCR reduction on the outcome of the tumor, a retrospective study was set up.

Methodology

All children with solid tumors treated with VCR between 2010 and 2020 in the Ghent University Hospital were included in the study. Approval of the local Ethics Committee was obtained. Data including demographics, occurrence of VIPN as well as dose reductions were retrieved from the electronic patient files and chemotherapeutic prescription orders. Data were anonymized and analyzed via SPSS, version 2.8.

Results

A total of 123 patients treated for neuroblastoma, medulloblastoma, nephroblastoma, low grade glioma and Hodgkin or Burkitt lymphoma were included in the dataset. The majority of them (102/123; 82.9%) developed VIPN, of which autonomous and sensory neuropathies were most frequently observed.

Overall, females had a significant higher risk for developing motor neuropathies (p=0.014). Age of patients was found to be significant only for patients with neuroblastoma (p=0.016) , with the older patients being more vulnerable to develop sensorimotor neuropathies in this group.

A higher cumulative dose was correlated with more motor, sensory and sensorimotor neuropathies and severity of symptoms.

VCR dose reductions were performed in 22 patients (17,9%) ranging from 25-100% reduction. The occurrence of different types of neuropathies was strongly correlated with reductions. Patients with VCR dose reductions suffered significantly more frequently of progressive disease (p = 0.040).

Conclusion

VIPN is a commonly observed side effect of VCR treatment, with a cumulative VCR dose being a risk factor. In our study population, dose reductions were often performed and were correlated with a significant worse outcome. The impact of sex and age on VIPN development was not statistically significant in this study. Because of the low number of patient populations, these data have to be interpreted with caution. A future study, including more patients, could give more reliable data.

SO 17.

Chronic myeloid leukemia in children and adolescents – clinicopathological results of a monocentric retrospective study

L. Nevejan, V. Labarque, N. Boeckx

UZ Leuven

Background
Barely two per million Belgian children and adolescents are diagnosed with chronic myeloid leukemia (CML) annually. In this retrospective, monocentric study, we aimed to investigate the main diagnostic features, clinical and laboratory characteristics, and treatment outcome of this rare entity.

Methods
Medical records of all pediatric CML patients (age ≤17 years) diagnosed at the University Hospitals Leuven between 1986 and 2021 (n=35 years) were reviewed.

Results
Fourteen patients (8 female, 6 male, median age at diagnosis 12.5 years) were included, all presenting in chronic phase (diagnostic data not available in one patient). Median white blood cell count at diagnosis was 295 000/mL (range 66 000 - 578 000/mL), with four patients (29%) requiring leukapheresis. Hydroxyurea (HU) was initiated at diagnosis in nine patients (64%). Two out of these 9 patients subsequently underwent an allogeneic hematopoietic stem cell transplantation (allo-Tx), but both deceased (10 months and 23 years post allo-Tx, respectively transplant-related and due to a metastatic adenocarcinoma). Three other patients on HU were subsequently treated with interferon; two of them accelerated to acute leukemia and deceased (21 and 42 months after diagnosis), the third underwent an allo-Tx and was alive at last follow-up (FU). The remaining 4 out of 9 patients on HU were additionally and/or subsequently treated with a first generation tyrosine kinase inhibitor (1°G TKI). Two of them also underwent an allo-Tx and were alive at last FU. The remaining 5 patients not treated with HU (36%) were treated with 1°G TKI. One of them subsequently underwent an allo-Tx and was alive at last FU. Eventually, 4 out of 9 patients treated with 1°G TKI were switched to 2°G TKI (due to response failure (n=1), due to toxicity/incompliance (n=3)), one patient was additionally switched to 3°G TKI (due to failure of TKI cessation). Median time to major molecular response (MMR) in the 9 TKI treated patients was 15 months (not achieved in 1 patient). All non-transplanted patients treated with TKI (n=6) were alive at last FU (overall survival (OS) TKI 100%), while 4 out 6 transplanted patients survived (OS allo-Tx 67%). However, 3 of the 6 (50%) non-transplanted patients treated with TKI had lost MMR at last FU, all related to compliance issues.

Conclusion
Our study confirmed that TKI significantly improved the prognosis of pediatric CML. However, drug compliance poses a considerable challenge.

SO 18.

Retrospective study of children with chronic myeloid leukemia treated in Belgium between 2000 and 2021

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Introduction
Chronic myeloid leukemia (CML) in children and adolescents is a rare disease with an annual incidence of one case per million. The condition is characterized by the translocation t(9;22)(q34;q11.2) resulting in a BCR-ABL1 fusion oncoprotein localized on the newly formed Philadelphia (Ph) chromosome. With the current retrospective study, we aim to identify the clinical and biological characteristics of Belgian CML patients up to 18 years treated in Belgium between 2000 and 2021, as well as to evaluate the response to treatment, potential long-term side effects, and prognosis.

Methodology
Children and adolescents up to 18 years of age treated for CML in eight Belgian pediatric hemato-oncology centers between 2000 and 2021 were included in the present study as part of an international registry study (I-CML-Ped Study). The data of the pediatric CML patients were collected in a Belgian CML registry on case report forms (CRFs) after which they were inserted into a database. IBM SPSS Statistics was used for statistical analysis of the data. Survival curves were made using the Kaplan-Meier method.

Results
A total of 30 pediatric CML patients treated between 2000 and 2021 in Belgium were included for data analysis. The population consisted of 10 boys and 20 girls with a mean age of 9 years (range 1-16 years). The mean follow-up time was 99 months with a range of 8 to 247 months. The first symptoms of CML were from most to least common: asthenia, weight loss, abdominal pain, fever, and bleeding. The spleen was palpable in 22 patients with a mean of 10 cm below the costal margin (range 1-20 cm). Twenty-nine patients were in the chronic phase (CML-CP) at diagnosis, while one patient was in the blast phase (CML-BC). In the pre-TKI era (before 2004), the majority of the patients were treated with an HSCT preceded by Hydrea. After 2004, the standard first treatment was imatinib. The overall survival (OS) of all included patients was 96.7%.

Conclusion
In general, the clinical and biological characteristics of the Belgian pediatric CML population are in line with the literature. Although the outcome is excellent, it is essential to consider the long-term side effects of TKI treatment and a hematopoietic stem cell transplantation (HSCT) and weigh the advantages and disadvantages of both treatments.

SO 19.

Poorly differentiated thyroid carcinoma in children and adolescents: a very rare type of thyroid tumor related to DICER1 mutation.

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Introduction

Thyroid cancer is rare in the pediatric population. It typically occurs during the second decade with an incidence 4-6 times higher in girls compared to boys. The most frequent tumor type is papillary tumor carcinoma (80-85%) followed by follicular (10%) and medullary (3-5%) thyroid carcinomas. Anaplastic and poorly differentiated thyroid carcinomas (PDTC) are exceptional in children and adolescent. However, in young individuals, this latter subtype seems to have different clinical features and genetic mechanisms than in adults.

Case report

We report the case of a 14-year-old girl presenting with a palpable thyroid nodule. Ultrasound confirmed a 3 cm heterogeneous macro-nodule of the right thyroid lobe (classified Eu-Tirads 4) that appeared as "cold" on scintigraphy. Cytologic examination of fine-needle aspiration revealed follicular cells without major nucleocytoplasmic atypia (category III according to Bethesda classification). A right hemi-thyroidectomy was initially performed. Histological analysis demonstrated a poorly differentiated component of 25 mm with a high mitotic index and a pT2NxR0 staging. The genetic workup identified a somatic DICER 1 pathogenic variant (E1813K) on tumor tissue but no germline DICER 1 mutation. Postoperative PET-Scan, ultrasound and CT scan excluded the presence of pathological cervical adenopathy and distant metastasis. Based on the aggressive behavior of PDTC in children and adolescents, a total thyroidectomy with left cervical lymph node dissection was performed and a radioiodine therapy is scheduled.

Discussion

PDTC are extremely rare in children and adolescents. On very limited reported series, they are characterized by poor prognosis and have a specific genetic signature. Pediatric PDTC are associated with DICER1 mutation either in tumor tissue or as constitutional abnormality. Patients with constitutional DICER1 syndrome may develop pleuropulmonary blastoma, cystic nephroma, nasal hamartoma, embryonal rhabdomyosarcoma and ovarian sex-cord stromal tumors often at young age.

Conclusion

This report illustrates the impact of genetic profiling in thyroid tumors. At the individual level, it allows to orientate the diagnosis, prognosis and therapeutic approach. At a broader level, it improves the understanding of specific mechanisms of oncogenesis and may contribute to the identification of potential therapeutic targets.

PW 13.

Late metastatic relapse of an initially bifocal intracranial germ cell tumor in a 12-year-old child with modestly elevated tumor markers

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Introduction

Primary intracranial germ cell tumors (GCTs) are rare, often affecting children and young patients. There are two main types of intracranial GCT: non-secreting germinomas and secreting GCTs. We present the case of a 12-year-old child, who was admitted with polyuro-polydipsic syndrome. His biological assessment showed a diabetes insipidus (DI).

Case report

A 12-years-old boy presented to hospital for polyuria and polydipsia, following which a diagnosis of DI was made. The cerebral MRI showed a bifocal lesion of the pituitary and the pineal glands. Tumor markers in the cerebrospinal fluid (CSF) showed an an HCG level of 92 IU/l. According to European guidelines, the thresholds of AFP and HCG in both serum and CSF have been sat at 25 ng/ml and 50 IU/l respectively. Tumors markers had to be below or equal to these values to consider these tumors as non-secreting tumors. Based on the existence of an HCG level in the CSF higher than the norm, this local disease was defined as CNS-NGGCT. The patient was treated by chemotherapy, followed by focal radiotherapy. 14 years after the end of the treatment and his remission, the patient came back with periventricular relapse. The diagnosis retained, because of the periventricular relapse of an initially bifocal tumor and borderline HCG level, was finally a metastatic relapse of a germinoma.

Discussion

Primary intracranial GCTs generally occur in the pineal or neuropituitary region, in the midline structures. Some patients have synchronous lesions in both regions defined as bifocal tumors. These tumors are not considered metastases, and are most often germinomas.

Levels of HCG and AFP in serum and CSF are necessary for diagnosis and for planning the treatment. The positivity of AFP or HCG in serum or CSF confirms the germinal and secreting nature of the tumor, histological proof with biopsy is not necessary. For non-secreting tumors, histological evidence by biopsy is essential, except in case of bifocal lesions because the vast majority are germinomas. In this case report, the initial level of total HCG in the CSF is increased (>50 IU/l). This classifies the tumor, according to European guidelines, as a malignant NGGCT. However, this threshold of 50 IU/l is artificial and questionable. Depending on the country, different guidelines are used and the thresholds of the tumor markers may change.

Finally, the type of relapse, late and ventricular, evokes much more a germinoma.

PW 14.

A Rare Case of Congenital Sideroblastic Anemia in an Infant

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Background

Pearson Syndrome (PS) is an extremely rare cause of congenital, sideroblastic anemia resulting from mitochondrial DNA deletion. The mutation causes pleiotropic multisystem disorders including lactic acidosis, exocrine pancreatic dysfunction, failure to thrive and renal tubulopathy. Hematological symptoms may be palliated by regular blood transfusions. Surprisingly, in certain cases, anemia resolves spontaneously. Most patients die before the age of five and survivors develop Kearns–Sayre syndrome.

Clinical Case and Discussion

We herein report a case of PS in an infant born full-term to non-consanguineous, caucasian parents. Pregnancy was marked by intrauterine growth restriction, for which biological work-up was performed at birth. Control blood analyses at seven weeks of age showed severe, aregenerative, macrocytic anemia associated with leukopenia (Hb 5.2 g/dl, mean corpuscular volume 109 fL, platelets 159 G/L, white blood cells 3.75 G/L of which neutrophils 0.39 G/L, reticulocytes 30 G/L), in an asymptomatic infant. Clinical examination was unremarkable, with absence of hepatosplenomegaly. Neonatal alloimmune and hemolytic anemia were excluded. Iron tests were normal. A bone marrow aspiration (BMA) was required. The BMA excluded Diamond-Blackfan anemia and showed vacuolisation of a significant proportion of erythrocyte precursors, containing pathological ringed sideroblasts (revealed by Perls procedure). Aetiologies for acquired macrocytic and sideroblastic anemia were excluded, including myelodysplastic syndromes, hypocupremia, drug-induced (notably certain antibiotics), alcohol-related and folic acid or cobalamin deficiencies. The association of sideroblastic anemia with vacuolisation of erythrocyte precursors were highly indicative of PS. Genetic and metabolic tests were performed. Homocysteine dosage was normal, and serum amino acids and urinary organic acids tests were inconclusive. Whilst awaiting genetic results, the patient received thiamine and riboflavin supplements, failing to yield clinical benefits.

Four months later, next generation sequencing panel was negative for the SCL19A2 and SLC25A19 gene mutation but revealed a de novo, large, heteroplasmic mitochondrial DNA deletion ((NC_012920.1):m8483-13459del), confirming the diagnosis of PS.

Conclusion

PS is a rare metabolic cause of neonatal anemia that should be considered in the differential diagnosis of congenital sideroblastic anemia.

PW 15.

Granulocytic sarcoma of the pancreas: a very rare manifestation of acute myeloid leukemia in children

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Introduction

Myeloid or granulocytic sarcoma (GS), also called chloroma, is an extramedullary mass composed of immature myeloid cells. It is described in 2,5-10% of patients with acute myeloid leukemia (AML), sometimes as the first manifestation of the disease. It occurs mainly in lymph nodes, skin and soft tissue, testis, bone, peritoneum, and gastrointestinal tract. GS of the pancreas is extremely rare and, so far, has only been reported in adults. We report the clinical history of girl presenting with abdominal pain, vomiting and a slight increase of pancreatic enzyme that led to the diagnoses of GS and AML.

Clinical case

A 9-years-old girl presented with abdominal pain, vomiting, anorexia, fatigue, sudation, and weight loss lasting for 7 weeks despite symptomatic treatment. At the onset of symptoms, an initial blood test and abdominal ultrasound were unconclusive. The second biological workup showed a moderate hyperleukocytosis with elevation of blasts (16 110 WBC/µL, 41,3% of blasts) and a slight increase of lipase levels (117 UI/L). At that time, the abdominal ultrasound revealed two pancreatic nodules (35 and 25mm large) resulting in moderate dilatation of the Wirsung duct. An abdominal MRI confirmed expansive infiltrations into the caudal pancreas and cephalic pancreas with retrograde dilatation of the Wirsung duct and interlobular ducts. There was no hepatosplenomegaly or other adenopathy. The diagnosis of M1-AML was confirmed by bone marrow examination. The child was treated according to the NOPHO-DBL AML 2012 protocol. After one course of chemotherapy, radiological examinations showed a dramatic hematological and digestive response.

Discussion and conclusion

This case illustrates that pediatric leukemia may present with extramedullary infiltration leading to various symptoms sometimes predominating over hematological manifestations. It also underlines the importance of exploring the pancreas when facing persistent abdominal pain or digestive symptoms. This report is the first description of pancreatic infiltration by AML in pediatrics. Rare cases of pancreatic infiltration have been reported in children with acute lymphoblastic leukemia or lymphoma. Therefore, in pediatrics, pancreatic mass should always be investigated to exclude infiltration by a hematologic malignancy.

PW 16.

A genetic syndrome unknown to practitioners

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Constitutional mismatch repair deficiency (CMMRD) syndrome is a rare childhood cancer predisposition syndrome caused by biallelic pathogenic variants in one of the four mismatch repair genes: MLH1, MSH2, MSH6 and PMS2. Mismatch repair deficiency facilitates replication errors resulting in a mutator phenotype and as a consequence, cancers development. The mono-allelic gene mutation is responsible of Lynch syndrome, an adulthood cancer predisposition syndrome.

Nearly all CMMRD patients develop a malignancy within the first decade; especially haematological malignancies, malignant brain tumours and Lynch syndrome associated malignancies. Non-malignant clinical manifestations are also described: café-au-lait spots, freckling, plexiform neurofibroma, optic glioma and hypopigmented spots. Most of these are suggestive of neurofibromatosis 1 (NF1).

Identification of mismatch repair gene homozygous mutation is the most reliable method to confirm the diagnosis. Immunohistochemistry and the analysis of microsatellite instability in tumor tissue (or on skin biopsies) is included in the classical approach, aim to represent the phenotypic evidence that mismatch repair genes are dysfunctional. These are less sensitive and less specific methods.

A very poor prognosis is described in this population with a high risk of multiple cancers, much worse than patients with Lynch syndrome. Prognosis impact of an early diagnosis is still discussed: the European and International consortiums surveillance protocols are considered as restrictive and effectiveness is not yet proven.

We reported a rare case of CMMRD syndrome in a young child with a high-grade glioma. In addition to neurological symptoms, the physical examination revealed skin anomalies as café-au-lait spots, hypopigmented spots and inguinal freckling. The phenotype overlap with NF1 in his young age, in addition to a cerebral tumour in a child permitted the genetic suspicion. Unspecific consanguinity was an added argument for a genetic disorder.

It is regularly described clinical manifestations reminiscent of NF1 with lacked germline NF1-mutation in the first years of life, and a few years later, a malignant diagnosis that suggests a CMMRD syndrome. Therefore, the negative NF1 genetic test should always lead to more genetics researches. Early and definite diagnosis is required to enable family screening given the high risk of CMMRD and Lynch syndromes in relatives.

PW 17.

A case of LRBA deficiency with persistent immune dysregulation posttransplant

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Introduction

Lipopolysaccharide-responsive beige-like anchor protein (LRBA) deficiency, first reported in 2012, is an inborn error of immunity caused by biallelic mutations in LRBA. It is characterized by a broad clinical and immunological spectrum. Most patients suffer from severe immune dysregulation and autoimmunity. Additional manifestations include hypogammaglobulinemia, recurrent infections and lymphoproliferative disease with increased risk of lymphoma.

We report a patient with LRBA deficiency who underwent hematopoietic stem cell transplantation (HSCT).

Results

The patient is a girl born to consanguineous parents of North-African origin. She presented at the age of 9 with refractory immune thrombocytopenia (ITP) for which she received multiple lines of treatment. In the next years, she also developed severe interstitial lung disease, recurrent pulmonary infections, diffuse lymphadenopathies and T2-FLAIR-hyperintense lesions on brain MRI. Genetic testing confirmed LRBA deficiency. She was treated with steroids, sirolimus and abatacept. Despite initial improvement, she continued to suffer from chronic ITP and severe progressive interstitial lung disease. In 2021, at 14 years of age, she underwent HSCT with a matched sibling donor (heterozygous carrier of LRBA mutation). Myeloablative conditioning (Bu-Flu-ATG) was given. The immediate posttransplant period was uncomplicated. Engraftment was seen at D+25. A stable donor chimerism of 89-91% was reached. There were no signs of GVHD. Lung and brain imaging showed regression of the lesions. However, 3 months posttransplant she developed dyspnea with a recurrence of lung lesions. Because a fungal infection was suspected, cyclosporine was stopped and voriconazole started. One month later, she presented with a immune-mediated hemolytic crisis, splenomegaly and a further increase of granulomatous lung lesions under voriconazole. Treatment with high-dose steroids and sirolimus was initiated after exclusion of infection. Because of insufficient effect of sirolimus, mycophenolate mofetil and eltrombopag were associated leading to gradual resolution of the disease manifestations. Currently, 20 months posttransplant, she is clinically stable under sirolimus and mycophenolate mofetil, but has extensive avascular necrosis of lower limbs and had an episode of pulmonary aspergillosis.

Conclusion

Posttransplant recurrence of severe immune dysregulation in LRBA-deficient patients remains a significant complication.

LO 7.

Child with intractable hiccups and vomiting: The gut or the brain?

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A 7 year-old boy of African orgin was referred to our hospital with a 10-day history of intractable hiccups and vomiting. Unable to drink or eat, TPN was initiated. Medical history was unremarkeble, except for a benign ptosis which was regulary checked by an oftalmologist. Blood and urine testing were unremarkeble (incl. urinary catecholamines). CT-scan of the brain and abdomen showed no abnormalities except for constipation and mild mesenteric adenitis. ENT and oftalmologic evaluation were also normal. Ultimately, the brain MRI showed medullary lesions at the area postrema (AP), pathognomonic for the area postrema syndrome (APS). The AP is located at the bottom of the fourth ventricle and is known as the “chemoreceptor trigger zone” or vomiting centre. APS is part of the neuromyelitis optica spectrum disorder (NMOSD), these are rare inflammatory disorders of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage predominantly targeting optic nerves and the spinal cord. As subclass of NMOSD, APS (with an incidence of 16-43% in NMOSD) is associated with typical medullary brain stem lesions with associated nausea, vomiting and/or hiccups. NMOSD, including APS, are rare disorders with an incidence of 0.37-10 per 100,000. The median age of onset for is 32 to 41 years, but pediatric cases are described. The diagnostic marker for NMOSD (in CSF) is Anti-aquaporin-4-immunoglobulin G (AQP4-IgG) and returned negative in our case. In literature, the seropositivity rate is then times higher in females compared to male patients. Although the medullary MRI lesions are a core criterion of NMOSD, as a lone standing fact they aren't strong enough to confirm the diagnosis of APS. Pulse corticoids were initiated and the hiccups and vomiting disappeared over the following days. Until today the patient is symptom-free, but NMOSD and APS may have a relapsing course over the years. With this case report we would like to highlight thinking of neurological causes in patients with nausea and vomiting, even without headache.

PW 18.

A case of SETD2 mutation : a new clinically recognizable syndrome ?

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Introduction

SETD 2 gene appears to be crucial on neurodevelopmental disorders. Mutations on these gene are extremely rare but can lead to extremely severe disabilities.

Clinical Case

The patient girl was born at 346/7 weeks gestational age in the context of pre-eclampsia. She presented with multiple malformations including cleft palate, micrognathia, microcephaly, hypertelorism, anterior located anus, as well as global hypotonia along with poor spontaneous motor skills. Complementary examinations followed, allowing to assess the poly-malformation and thus steer the genetic testing. The latter revealed multiple IVCs and partial abnormal pulmonary venous return, mega ureters and cortical renal cysts, dilatation of the cerebral ventricles and subarachnoid spaces, and fundus abnormalities. After 6 weeks, following a normal karyotype and CGH-array, Whole exome sequencing revealed a pathogenic variant (p.Arg1740Trp; c.5218 C>T) of the SEDT2 gene. The patient's evolution was characterised by chronic respiratory failure, cardiac failure, transient hyponatremia, sepsis, exclusive enteral feeding, and extremely poor psychomotor development.

Discussion

The SETD2 gene codes for a methyltransferase that acts on histones and microtubules. It plays an important role in the regulation of transcription. About thirty variants of the SETD2 gene have been described in literature, half of which concern exon 1740. Two pathogenic heterozygous variants of the same exon have been described [1], however, giving diverging phenotypic characteristics. The phenotype of the heterozygous Arg1740Gln variant results in a moderate to severe intellectual disability, without associated congenital anomalies. However, the heterozygous Arg1740Trp variant, as described in the present patient, clinically results in microcephaly, a characteristic facies, profound intellectual deficit and multiple congenital anomalies. Gain of function of the SETD2 has been postulated to be one of the different mechanisms found in patients with variants affecting codon 1740.

Conclusion

This present patient ads more clinical evidence to the phenotypic characteristics that appear to be related to the non conservative Arginine-Tryptophane substitution. Adding values to this recognizable pattern of malformation could better describe this new clinically recognizable syndrome.

LO 8.

Success rate of percutaneous balloon dilatation as first treatment option in children with Pulmonary Stenosis associated with Noonan syndrome

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Background and aim
Noonan syndrome (NS) can be associated with a number of congenital heart defects (CHD) of which a (supra-)pulmonary valve stenosis ((SV)PS) is the most frequent. Possible treatment options are percutaneous balloon pulmonary valvuloplasty (BVP) or surgical intervention. However, anatomical location of the PS may help predict BVP failure.

We aimed to evaluate the outcome of treatment with BVP of PS in children with Noonan syndrome.

Methods
All medical records of children with a clinical diagnosis of Noonan syndrome and in follow-up at the Antwerp- and the Ghent University Hospitals were retrospectively reviewed. The study was approved by the medical ethical committee of both institutions (EC2022/0141)

Results
50 children (median age 6months, IQR 1.7-54, 54% female) were included in the study (28 PTPN11, 8 SOS1, 5 RIT1, 1 LZTR1, 1 RAF1, 1 KRAS, 1 BRAF, 1 SHOC2, 4 unknown). Of these children 39 (78%) had a congenital heart disease (CHD) of which 32 (64%) a (SV)PS, either isolated or in combination with other CHD. 69% of the children with PS had a SVPS. The prevalence of PS and SVPS was similar for all genes.

A surgical or percutaneous intervention was necessary in 17/32 patients with PS (53%). Except for 2 children with pulmonary valve stenosis, all had SVPS. Only 2 of these 17 children had a surgical repair as first option. The remaining 15 (13 SVPS) underwent a percutaneous balloon dilatation. 10 of these 15 patients (66%) needed a second balloon dilatation, all of them ultimately converted to surgical repair due to persistent stenosis. Except for one patient, all had SVPS. Median time to reintervention was 1 month. The global success rate of percutaneous intervention in children with Noonan and SVPS was (30,7%).

Conclusion
(SV)PS is the most frequent CHD in children with NS. In our cohort, the prevalence of (SV)PS was similar for all genes. The success rate of BVP in patients with NS is low. The most determinant factor of treatment failure seems to be the presence of SVPS. However, BVP might still be useful in selected cases and might be considered to clarify the anatomical location of PS.

Key words: Noonan syndrome, (supra) pulmonary valve stenosis, balloon pulmonary valvuloplasty

SO 13.

Decompensated vasoreactive pulmonary arterial hypertension following erroneous calcium channel antagonist magistral preparation

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Vasoreactive pulmonary arterial hypertension (PAH) in children is a form of idiopathic PAH. In that case, vasoreactivity, that means significant decrease of pulmonary vascular resistances upon vasoreactive testing with oxygen (O2) and nitric oxide (NO) is confirmed during heart catheterization. The treatment of choice of vasoreactive PAH is calcium channel antagonists (CCA) that allow to nearly normalize pulmonary arterial pressure. However, its short lasting effect makes the patient dependent on regular and adequate drug intake.

In growing children, drug dose must be adapted to weight. The absence of available low-dose preparation makes the use of officinal formulations mandatory. From prescription to administration, including transcription and preparation, a multitude of errors, involving different actors, can occur.

To illustrate this, we report a case of a compounding error with underdosage of CCA, leading to acute decompensation of vasoreactive PAH in an adolescent.

Case presentation
A 12-year-old girl diagnosed with vasoreactive PAH at the age of 5 years is successfully treated by diltiazem (3x100 mg/d). On holidays, she experienced several short episodes of palpitations with generalized weakness and brief loss of consciousness alternating with prolonged periods of normal condition. Urgent cardiac examination showed impaired right ventricular (RV) function with estimated RV pressure at a systemic level. NT-Pro-BNP blood levels were increased. The patient was monitored on the intensive care and treated by inhaled O2 and NO. CCA brought from home was continued. She was weaned from her inhaled treatment and showed asystole which led to an ECMO support.

Parents indicated that a new drug preparation had been performed by the pharmacist. This prompted us to investigate the exact dosage of the capsules. Toxicological analysis revealed that the capsules present in the box contained 10 mg of diltiazem instead of 100 mg. After treatment adaptation, patient could be weaned from ECMO and have a good evolution.

Conclusion
This case illustrates acute decompensation of a chronic disease in a child due to erroneous magistral preparation of a life saving drug. The lack of availability of adapted industrial preparations for children renders magistral preparations necessary. One must be aware of the source of errors related to such preparations and make professionals sensitive to the dependency patient's survival may have upon particular drugs.

SO 14.

Evaluation of Late Cardiac Effects After Multisystem Inflammatory Syndrome in Children.

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Background and aim
Multi Inflammatory Syndrome in Children (MIS-C) is associated with important cardiovascular morbidity. On short-term follow-up most patients recover. However, a small portion of patients has persistent cardiac sequelae at mid-term, but data are scarce. The goal of our study was to assess cardiac outcomes of MIS-C at mid-term by echocardiography, cardiac MRI (CMR), NT-proBNP and 24-hour Holter monitoring.

Methods
A prospective observational multicenter study was performed in children admitted with MIS-C and cardiac involvement between April 2020 and March 2022. Follow-up by echocardiography, 24-Hour Holter monitoring, NT-proBNP measurement and CMR was performed at least 6 months after MIS-C diagnosis.

Results
We included 36 children with a median age of 10.0 (8.0-11.0) years who could undergo CMR without sedation. At diagnosis, all patients had an elevated NT-proBNP and 40% had a decreased left ventricular ejection fraction (LVEF; < 55%). Follow-up visit was done at a mean time of 12.1 (± 1.0) months after diagnosis. One patient kept a severely reduced LVEF and myocardial fibrosis on CMR requiring heart transplantation. He was our first pediatric patient with MIS-C of the SARS-CoV-2 pandemic and he did not receive immunoglobulins nor corticosteroids. All other patients had normal NT-proBNP and normal echocardiographic LVEF at follow-up. LV global longitudinal strain, as marker of subclinical myocardial dysfunction, was decreased (z < -2) in 35%. CMR identified one patient with borderline LVEF, another patient had moderate MI and no patients showed signs of myocardial fibrosis. 24-Hour Holter monitoring was normal in all except one patient showing supraventricular tachycardia.

Conclusion
The majority of MIS-C patients have no clinically significant cardiac sequelae at mid-term follow-up, however a subgroup has persistent subclinical myocardial dysfunction and a small minority shows clinically relevant residual lesions.

PW 19.

Growing-up with a complex congenital cardiac disease

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Due to the progress in the care of children with congenital cardiac disease (CCD) 85% of the patients reach adulthood.Half of them and most of those with complex CCD will require re-intervention of their residual lesions.

We report the case of a 33 years old woman

The diagnosis of a right-sided isomerism with asplenia and mixed form of total anomalous pulmonary venous return (TAPVR),complete atrio-ventricular septum defect,severe sub-pulmonary stenosis,transposition of the great arteries and right aortic arch was made after birth.

Since she was in equilibrated hemodynamic condition,the cardio-surgical medical staff decision supported by the parents was to not intervene.The surgical alternative palliations for such complex CCD (total cavo-pulmonary connection (TCPC)or systemic-to-pulmonary shunt)were extensively discussed based on the international experience 3 decades ago.

At the age of 5,she showed significant hypoxemia.The complex form of TAPVR was considered to render the TCPC preparation technically difficult therefore a modified left-sided Blalock-Taussig anastomosis (BTA)was done.

11 years later,as hypoxemia increased,a second BTA was performed on the right side after exhaustive international expert discussions excluding the possibility of a bi-ventricular repair and considering again TCPC a too risky palliation.

The patient developed well with good quality of life and an oxygen saturation above 85%,achieved university master level and had a job.

She developed however supraventricular arrhythmia treated by propafenon and metroprolol.

At the age of 32,she acutely showed a cerebral insult due to a thrombus of the right-sided BTA with left-sided cerebellum emboli.Expert consensus was in favor of a new BTA that was realized with initial good hemodynamic results.

Postoperative outcome was complicated with an unusual systemic inflammatory reaction syndrome leading to renal failure,sustained supra-ventricular arrhythmias and cardiac arrest.

Resuscitation was successful but the patient developed pleural-pericardial effusions

Currently,the patient is convalescent.

This case illustrates how difficult decision making can be to propose the best therapeutic choice for children with complex CCD and how this choice,that in our case must be understood in the historical context,impacts long-life the grown-up patient outcome. Its suggests also that adults may experience unexpected complicated postoperative outcome after so-called simple surgical procedures

PW 20.

The efficacy of the use of atropine in children with pallid breath holding spells: can cardiac pacemaker implantation be avoided?

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Background
Pallid breath holding spells (BHS) or reflex anoxic seizures (RAS) are a manifest overreaction of the vagal system. This leads to hypotension and a bradycardia or brief cardiac arrest. Because of the usually benign character of the spells with no complications on short or long term, treatment is seldom required. Moreover, breath holding spells are self-limiting in time, with complete resolution of the symptoms before the age of eight years. However, in case of frequent spells or severe clinical presentation, treatment can be necessary. Treatment options are medication such as atropine or the implantation of a cardiac pacemaker, with the latter being invasive and entailing risk for important complications. We investigated atropine treatment and aimed to examine if pacemaker placement can be avoided.

Methods
We reviewed literature on breath holding spells, pharmacological treatment options and pacemaker placement, regarding definition and outcome. Medline (accessed by Pubmed) and Embase were used as data sources. We retrospectively reviewed patients treated in our center for reflex anoxic seizures with atropine sulphate from January 2017 until May 2022, and compared our results to those in the literature. Statistical analysis was performed by SPSS.

Results
In our population, 100% of the patients reported symptom management after atropine treatment, with complete resolution in 14%. After pacemaker placement, up to 20% patients reported incomplete symptom management. Minor side effects were reported in 57%, with need for change of treatment in one patient (14%). Severe complications were not reported, unlike 40% permanent or severe complications in pacemaker placement.

Conclusion
Atropine is a safe and efficient treatment to manage the symptoms, with similar success rate to pacemaker implantation. However, pacemaker implantation entails a substantial risk for complications and is accompanied with morbidity such as scar formation. This might be considered redundant for a benign and temporary condition, certainly given the possibility of other efficient treatment option.

Given the benign nature of the spells and the good long-term prognosis, coupled with the success and complication rates as described, we recommend atropine treatment as alternative option to implantation of a cardiac pacemaker in children with severe RAS.

LO 9.

New consensus in Belgium regarding febrile urinary tract infections in children: diagnosis and treatment

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Background
The kidneys and the urinary tract are a common source of infection in children of all ages, especially infants and young children. The evidence for the diagnosis and treatment of urinary tract infections (UTI) in children has changed the last decades. New guidelines recommend a more conservative approach in terms of investigations, treatment and follow-up and prophylaxis. Our aim is to write a Belgian consensus paper regarding UTI.

Methods
This is an initiative of national collaboration initiated by a group of paediatric nephrologists working in university and general paediatric centres in Belgium. Based on literature review, a questionnaire was formulated and according to a Delphi procedure, validated by an expert panel regarding UTI. Statements were reformulated when they didn't reach consensus. Consensus was defined if at least 70% of the members agreed on the opinion stated.

Results
We present Belgian recommendations for the diagnosis and treatment of a first febrile UTI in infants and young children, more than three months old. UTI can have specific symptoms, but should be considered in every child with fever without a source. Patients with increased risk warrant another approach. Urine collection methods should be based on age and risk factors with the lowest possible contamination rate. A “negative” collection bag, rules out a UTI, avoiding unnecessary invasive investigations. The diagnosis requires urinalysis and significant growth of a uropathogen in monoculture. Empirical treatment of UTI should be based on local sensitivity patterns. The standard of care is oral antibiotics in children more than 1 year old if treatment can be started within 6 hours after diagnosis. Increased risk patients need hospitalisation and parenteral therapy should be considered. Duration of treatment is 7 to 10 days. Additional investigations, follow-up and prophylaxis is reserved for a second part of the recommendations.

Conclusion
In line with new international guidelines, a Belgian consensus about febrile UTI in children is formulated for diagnosis and treatment, with the aim of achieving more consistent clinical practice.

SO 9.

The impact of chronic kidney disease on the renal circadian rhythms in children

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Background/Aims
The kidneys follow a circadian rhythm, which has an essential role in maintaining the homeostatic balance. Adult chronic kidney disease (CKD) patients exhibit altered renal circadian rhythms an impact their health and quality of life. Little is known if the same is true in children. However, due to differences in physiology, CKD pathophysiology and comorbidities between adults and children, it seems plausible that (disturbances in) circadian rhythms aren't comparable and should be studied. The aim is to evaluate which renal circadian rhythms exist in healthy children and whether these are disturbed in children with CKD. And if so, what are the prevalence, pathophysiology and potential impact?

Methods
These questions are answered through a narrative review based on literature research in PubMed, Embase, Web of Science and Google Scholar. 807 articles were found and screened based on title and abstract. Next, 56 full texts were evaluated based on inclusion and exclusion criteria. Age was limited to 18 years and studies on renal replacement therapy were excluded. Also reviews, case reports and articles not in English were excluded. Finally, a total of 11 articles were included.

Results
In healthy children, circadian rhythms were noted for glomerular filtration rate, urinary electrolyte excretion, diuresis and blood pressure. Values were higher during the day than at night. Circadian rhythms were also seen in the endocrine system. Children with CKD exhibit altered renal circadian rhythms. As a result, complications such as nocturnal polyuria and blood pressure non-dipping occurred. Risk factors for non-dipping are discussed, e.g. sodium intake, proteinuria and female gender. The rhythms aren't affected by age, but sleep deprivation leads to significant changes.

Conclusion
Renal processes follow a circadian rhythm in healthy children and this may be altered in children with CKD. Future prospective studies are needed to document abnormalities and gain knowledge about pathophysiology, impact, prevalence and risk factors. Researchers should consider the heterogeneity of the patient population and interactions between renal processes. For clinicians, it is advisable to monitor circadian rhythms in CKD patients, especially in those who exhibit blood pressure non-dipping and/or nocturnal polyuria. Finally, extra attention to sleep quality and cardiovascular morbidity is recommended.

SO 10.

Copeptin as a predictive biomarker for desmopressin response in children with enuresis

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Background/aims
Enuresis is a common disorder, affecting up to 10% of 6-year-old children, with an important impact on a child and its environment. Nocturnal polyuria, caused by a lack of arginine-vasopressin (AVP) increase overnight is an important pathophysiological factor. Administration of desmopressin (dDAVP), an AVP-analogue, is the most used pharmacological approach in children with enuresis. However, this therapy is not effective in all children with nocturnal polyuria. Therefore, a predictive biomarker could identify which children would benefit from dDAVP. One of the suggested biomarkers is copeptin. The objective is to investigate whether copeptin, a part of the AVP precursor, could predict response to dDAVP in children with enuresis.

Methods
Children that needed a renal concentration test were included in a PK/PD study of dDAVP. Copeptin analysis was a subanalysis in the original study design. In total 25 children aged 6 months to 8 years were included, of which 4 children had desmopressin-resistant enuresis and 21 children had polyuria. All children received a water load (15ml water/kg body weight) 1 hour before dDAVP administration. Patients were monitored, blood and urine samples were taken to evaluate urinary osmolality and copeptin. The latter was analysed 1 hour before dDAVP administration representing overnight AVP and 2 hours after administration, representing daytime AVP. Variation of copeptin was evaluated by calculating the difference and a day/night ratio. An adequate response to dDAVP was defined by reaching urinary osmolality of 800mOsm/kg.

Results
No differences in copeptin were found when comparing patients responding well to the concentration test versus patients not sufficiently responding. Early morning copeptin showed a median value of 4.70pmol/l while daytime copeptin averaged 2.90pmol/l. Variation in copeptin values showed a median difference of 1.90pmol/l with higher values overnight, and an average day/night ratio of 0.60.

Conclusion
We were able to define day/nighttime values of copeptin in children with polyuria. However, earlier findings reported a potential role for copeptin as a predictive biomarker for dDAVP response in enuresis, which could not be confirmed. This might be explained by the main limitations of this study, namely a small study population and only 2 samples of copeptin. Therefore, more research is necessary to evaluate the value of copeptin as a predictive biomarker in enuresis.

SO 11.

Risk and management of an acute aminoglycoside overdose: case report and literature review

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Background
Aminoglycosides have a narrow therapeutic range and therapeutic drug monitoring (TDM) is widely used to prevent nephro- and ototoxicity during prolonged therapy. However, the risks and management of an acute overdose of aminoglycosides are less well-known. We describe the case of a young child who received an amikacin overdose together with an overview of management strategies, based on a literature review.

Methods
A literature search for cases of aminoglycoside overdoses was performed in PubMed.

Results
An amikacin dose of 125 mg/kg (recommended dose: 15 mg/kg q24h) was accidentally administered to a girl of five months old with pyelonephritis and normal renal function. On the advice of the Belgian Poison Center and the pediatric nephrologists, she was started on acute hemodialysis. Hemodialysis was initiated seven hours after administration and continued for four hours until subtherapeutic trough plasma levels were reached. Amikacin levels showed a rapid decline before the start of and during hemodialysis. Nephro- or ototoxicity was not observed during follow-up (now almost one year after the event).

Literature review. A number of case reports on acute overdoses (3 to 20 times the recommended dose) have been published for amikacin (6), gentamicin (6) and kanamycin (3). Two-thirds of these cases concern young children. Various treatment strategies have been applied: supportive therapy (intravenous hydration, monitoring of the vital signs and renal function, and aminoglycoside TDM), hemodialysis, peritoneal dialysis, and exchange transfusion. From these interventions, hemodialysis is most effective at removing aminoglycosides from the body. This was clearly demonstrated in one adult patient with end-stage renal disease. Four out of the fifteen patients (~25%) experienced nephro- or oto-toxic effects. The incidence of toxicity did not differ between patients on supportive therapy and those treated with hemodialysis.

Discussion
Because of their low molecular mass, small volume of distribution, and low protein binding, aminoglycosides are efficiently removed from the body by extracorporeal treatments. However, scientific evidence on the added value of hemodialysis above supportive therapy for intoxications with aminoglycosides is scarce and mainly based on expert opinion, except in patients with pre-existing renal impairment. When hemodialysis is preferred, it is advisable to start as fast as possible with high-flux intermittent hemodialysis.

PW 32.

When hypercalcemia reveals an unusual diagnosis

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Background
Congenital or acquired hypercalcemia may be harmful for children. Hypercalcemia manifests with unpathognomic symptoms such as constipation, anorexia, vomiting, polyuria, and dehydration. Severe hypercalcemia may lead to organ damage such as nephrocalcinosis, neuropsychiatric symptoms and heart rhythm disorders. Hypercalcemia should always be investigated including the exploration of the phosphocalcic and Vitamin D pathways.

Methods
We report a 10-month-old girl who has been admitted in pediatric unit care for failure to thrive, intractable vomiting and inappetence. She is the first child of a non-consanguineous Tunisian couple. Episodes of recurrent vomiting began when she was 4-month-old and were attributed to gastroenteritis. Initial blood test revealed a severe hypercalcemia (3,16mmol/L) associated with a hypervitaminosis 25(OH)D (>150ng/ml), a depleted parathyroid hormone level (<4ng/L) and hypercalciuria (UCa/UCreat=1.2mmol/mmol). Kidney ultrasound found severe nephrocalcinosis. Vitamin D intoxication was first suspected, but the vitamin D pathway exploration showed an increase 1,25-(OH)2-vitamin D level (109pg/ml) and a low level of 24,25-(OH)2-vitamin D (1.4ng/ml), the inactive vitamin D metabolite. 25(OH)D-to-24,25(OH)2D ratio was higher than 80 and suggests a defect in vitamine D catabolism. Genetic analysis revealed a homozygous class 4 mutation in CYP24A1 gene, responsible for infantile hypercalcemia type 1.

Results
Infantile hypercalcemia type 1 is a rare autosomal recessive disorder characterized by a homozygous mutation in the CYP24A1 gene leading to the non-expression of the 24-hydroxylase enzyme. The 24-hydroxylase catabolizes the active 1,25-(OH)2-vitamin D into its inactive form. The lack of 24-hydroxylase leads to high 1,25-(OH)2-vitamin D and all its precursors' levels, resulting in severe hypercalcemia responsible for severe complications such as nephrocalcinosis, kidney chronic damage, bone damage and heart rhythm disorders. Initial treatment consists of stopping oral intake of vitamin D and reducing oral intake of calcium.

Conclusion
Hypercalcemia in children particularly in infants could be life-threatening and may reveal rare diseases. Hypercalcemia in infant should never be ignored and calcemia should always be part of the initial assessment.

PW 33.

Familial Renal Glucosuria Due to Mutations in the SLC5A2 Gene in a Male Adolescent. M.K.F. Docx,

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Independent research-Praktijk Care in Balance Eetstoornissen bij kinderen en jongeren,

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Introduction

Familial renal glucosuria (FRG) is an inherited disorder mostly caused by mutations in the SLC5A2 gene, mapped to 16p11.2 and coding for the sodiumglucose co-transporter 2 (SGLT2) in the proximal tubule.

Material and methods

A 17-year old Macedonian male presented since the age of 1.5 years with an isolated renal glucosuria in the absence of hyperglycemia. Renal function was normal. No bedwetting, polyuria-polydipsia or polyphagia and no intellectual disability. Renal glucosuria varies from 8 g/L (1.5 years) until now 41.2 g/L (17 years). Genetic analysis was performed. He was heterozygous for two variants of the SLC5A2 gene:(1)c571A>C p(Thr191Pro) and (2) c1405G>A p (Ala469Thr). The familial mutations have been looked for by Sanger Sequencing.The mother has a heterozygosity for mutation 1 and absent for mutation 2. The father has a heterozygosity for mutation 2 and absent for mutation 1. Both parents have a normal renal function and no glucosuria.

Results

The variant c1405G>A p(Ala469Thr) of the SLC5A2 gene was reported by Calado et al. (2008 NDT 23:3874-3879) in the index case (Family 15). The index case is a 2 year old Macedonian girl with also a compound heterozygosity. She had a glucosuria of 14.2 g/L.

Conclusions

Our patient have similar characteristics with the index case in the literature. These are: ethnicity, compound heterozygosity, mild-moderate glucosuria and the young age of onset. FRG is mostly a benign disorder with no longterm effects on renal function. Exceptional failure-to thrive, postprandial hypoglycemia as well as chronic urinary and genital infections are described.

PW 34.

An unusual severe acute kidney injury requiring prolonged dialysis in a 5 months old girl with a thrombotic thrombocytopenic purpura

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Introduction

Child-onset thrombotic thrombocytopenic purpura (TTP) is a very rare disorder causing thrombotic microangiopathies (TMA). The diagnosis of TTP is confirmed by a severe deficiency of ADAMTS13 activity (<10% of normal). It may be congenital or immune.

The most frequent TMA in children is hemolytic uremic syndrome (HUS). 90% of HUS in children will be caused by Shiga toxin-producing Escherichia Coli (STEC) infection. Diagnosis of STEC-HUS is made by the association of signs of TMA and the presence of STEC in stools.

Case report

We report the case of a 5-month-old girl who presented with gastroenteritis symptoms and a febrile complex seizure. At admission, the typical biological triad of TMA was present with mechanical hemolytic anemia, thrombocytopenia and acute renal failure. Complementary analysis demonstrated a deficient ADAMTS13 activity at 3% but also presence of STEC in stools. Treatment consisted of plasma exchanges, corticotherapy and supportive management. The evolution was slow with prolonged biological signs of TMA and the need in dialysis during 2 weeks.

Discussion

The diagnosis of TTP is confirm with low ADAMTS13 activity. The presence or not of ADAMTS13 auto-antibodies direct us towards an immune or congenital origin, but the prevalence of congenital TTP is higher in very young children. Early childhood onset of cTTP is frequent but not inevitable. Indeed, ADAMTS13 deficiency can exists without any disease development and triggering factors of acute episodes are well described. The typical clinical presentation of TTP combines signs of hemolysis and neurological impairments. Severe kidney failure is very rare. The treatment consists in plasma exchange providing a source of ADAMTS13 and permitting a rapid improvement. In our case, we suppose that the STEC infection was a possible trigger of the acute episode of the TTP, and that the combination with the STEC-HUS can explain the severity of the acute kidney injury, rarely seen in adequate treated TTP. Indeed, prolonged anuria is more common in STEC-HUS and only supportive management is possible. After treating adequately the TTP, we suppose that the tardy improvement was linked to the spontaneous evolution of the STEC-HUS.

Conclusion

Severe acute kidney injury leading to renal replacement therapy is very rare in congenital TTP. The association with a STEC-HUS probably explains this atypical presentation. The systematic research for STEC in stools seems relevant in case of TMA.

LO 10.

Genetic etiology, histology and outcome of bilateral testicular regression: a large Belgian series

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Background
The etiology of bilateral testicular regression (BTR) remains largely unknown. A vascular origin is suspected, however, some have been attributed to missense mutations in DHX37. In addition, long-term outcome is understudied.

Methods
Thirty-three phenotypical males with BTR were recruited in five Belgian centers (mean age: 14.2±5.2 years). We performed exome-based testing of genes (n=241) involved in gonadal development and spermatogenesis, retrospective analysis of initial presentation and management, cross-sectional clinical and genital exam in all and histological analysis of gonadal rests in 12 cases.

Results
Median age at presentation was 1.2 years [0-14 years]. Pregnancy complications, in particular monozygotic twin pregnancy, were common (35.5% and 9.7% respectively). Heterozygous (likely) pathogenic variants in DHX37 (p.Arg334Trp and p.Arg308Gln) were confirmed in three. All three presented with a small phallic structure, versus five out 29 (17.2%) patients without DHX37 variant. One child with a DHX37 variant had partial labioscrotal fusion, was raised female and received estrogen replacement during puberty (only patient in this cohort). The other two patients with DHX37 variants had limited or no phallic growth following testosterone therapy during infancy, in contrast to a “good” response in 4 patients without DHX37 variants where response to testosterone during infancy was documented. No other (likely) pathogenic variants were found in this cohort. Hormone replacement therapy (HRT) in incremental doses was initiated in 22 patients (median age 12.4 years), leading to normal pubertal development and growth with a final height within target height range in all. Penile growth was satisfactory in all but one (1/9; 11.1%; stretched penile length <7cm). Histological analysis of 2/3 patients with DHX37 variants revealed early disruption of gonadal development (presence of Müllerian remnants and undifferentiated gonadal tissue). In ten analyzed patients with BTR, no gonadal remnants were found.

Conclusion
Although presenting with a similar phenotype, analysis of pregnancy details and clinical data revealed subtle differences between those with a suspected environmental (e.g. pregnancy complications) and a genetic cause (i.e. DHX37) of BTR. Histological analysis confirms DHX37 as a gonadal development rather than BTR-related gene. Regardless of etiology, physical outcome of BTR is good with adequate HRT.

LO 11.

Validity of TSH newborn screening as early as 48 h of life and before maternity discharge

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Background
Screening programs may be affected by earlier discharge of newborns. Initially dried blood spot sampling was performed between 72 and 120 hours of life. Due to change in newborn healthcare policy, Newborn Screening (NBS) in South Belgium evolved, allowing from November 2019, a sampling as soon as 48 hours of life, with the objective to accelerate the NBS process and to allow more sampling during hospital stay. Our objective was to confirm the validity of this early screening by comparing neonatal TSH results on dried blood spot (DBS) collected before 72 hours of life with later sampling and by comparing the efficiency of dried blood spot collection before discharge or at home.

Methods
This retrospective study includes live births ≥ 37 weeks of gestation, screened by the ULB Newborn Screening Center between January 2019 and December 2021. We compared TSH results for screening < 72 h and screening ≥ 72 h. We also compared TSH results of newborn screening occurring at home with that performed in the maternity.

Results
A total of 54,746 newborns were included. The results of 24,816 healthy newborns screened before 72 h of life and of 28,978 healthy newborns screened between 72 and 144 hours of life were compared. The median TSH level (1.50 mU/L and 1.20 mU/L respectively) and the percentage of false positives were similar (0.08% and 0.07% respectively, NS). Earlier sampling, before 72 h, allows treatment of positive cases at 6 days rather than 8.5 days. Blood spot sampling at home results in longer delay for transferring the sample to the laboratory (a median of 3.0 days for hospital sampling vs 5.0 days for home sampling). A poorer quality of home blood sampling is observed, with 0.27% unusable samples compared with 0.06 % unusable samples for hospital sampling ($p < 0.001$).

Conclusions
In term newborns, TSH screening before discharge, as early as 48 h of life is a valid strategy. It allows earlier treatment of positive cases, does not increase the percentage of false positives and results in fewer unusable samples.

SO 5.

Solving the puzzle of MEN2B syndrome in an adolescent girl

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Background
MEN2B is a rare genetic tumor syndrome that causes medullary thyroid cancer at a young age and may lead to pheochromocytoma later in life. Early diagnosis is crucial for thyroidectomy before metastasis. This case report aims to increase awareness of MEN2B signs and symptoms and the need for early referral and treatment.

Case
A 10-year-old girl was referred for ultrasound imaging of a swollen submandibular gland that had been present for several months. In the past, she had been seen by an ENT specialist for a thickened upper lip present since birth, undergone surgery for a clubfoot, and consulted several times for chronic constipation and poor weight gain.

Ultrasound showed calcifications within the swollen submandibular gland and a nodule with calcifications in the right thyroid lobe, strongly suggestive of a thyroid neoplasm. In addition to the swollen left cervical gland, the patient's examination revealed thickened lips and mucosal neuromas on the tongue. Her thyroid gland appeared normal on palpation. She had an elongated face and thin body habitus. Thyroid hormone and serum thyroglobulin levels were normal, but serum calcitonin was markedly elevated at 11290 ng/L (ref. <7.2ng/L). Urinary catecholamines were within normal limits.

Ultrasound-guided thyroid biopsies confirmed medullary thyroid cancer. A computed tomography scan of the lungs revealed two small nodules (< 1 cm) in the right lung. A positron emission tomography (PET) scan with Ga-DOTANOC showed heterogenous uptake in the thyroid and some cervical lymph nodes but not in the pulmonary lesions. The patient underwent a total thyroidectomy with cervical lymph node dissection. The tumor had invaded several adjacent structures. Genetic analysis of lymphocytes and thyroid tissue revealed a pathogenic missense variant in the RET proto-oncogene in exon 16 (M918T), which is found in >95% of MEN2B patients. Calcitonin levels decreased after surgery but remained elevated at 5981 ng/L.

Conclusion
Medullary thyroid cancer in MEN2B is a highly aggressive disease. Clinical guidelines consistently recommend prophylactic thyroidectomy within the first few months of life. In this case, several diagnostic opportunities were missed despite the classic presentation of the disease. Early diagnosis and treatment could have resulted in a better prognosis, but this can only be achieved through increased awareness of this rare syndrome.

SO 6.

A monoallelic AIRE gene mutation in a female adolescent with " isolated " hypoparathyroidism and high levels of anti-IFNα auto-antibodies

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Background
Heritable forms of hypoparathyroidism (HYP) may present as an isolated form or be part of a more complex genetic syndrome, such as auto-immune polyendocrine syndrome type 1 (APS-1).APS-1 is clinically characterized by a triad of chronic mucocutaneous candidiasis, adrenal insufficiency and hypoparathyroidism caused by biallelic mutations in the autoimmune regulator (AIRE) gene. Recently, monoallelic AIRE mutations with a dominant mode of heritance were found to increase the susceptibility for isolated autoimmune diseases

Methods
Molecular analysis of 23 candidate gene for hypoparathyroidism was done by next generations sequencing analysis at the Genetics Laboratory of the Erasme Hospital (Brussels). Antibodies against IFNα were measured by ELISA at PID research lab (Ghent)

Case report
A 14-year-old girl presented with lingering fatigue and tingling in the arms and legs for several years. She had suffered from recurrent respiratory infections during infancy and had been hospitalized for a severe varicella.Recurrent vaginal candidiasis, one episode of onychomycosis and chronic urticaria during the last years were noticed. At physical examination height was 160 cm(-0.5 SDS) and BMI 18.83 kg/m²(-0.4 SDS). Nail, skin and hair examination was normal. Serum calcium was decreased(1,68 mmol/l), serum phosphorus increased(2,99 mmol/l) and urinary calcium/creatinine was low normal.Serum PTH was unmeasurable(<5 ng/L), confirming the diagnosis of HYP. A computed tomography of the brain showed multiple intracranial parenchymatous calcifications in the basal ganglia. Molecular karyotyping was normal. Candidate gene analysis for hypoparathyroidism documented an heterozygous class 5 variant c967_979del (p.Leu323fs*51) in the PHD1 domain of AIRE gene,which was confirmed by Sanger sequencing. Anti-IFNα auto-antibodies(1674 ng/ml) were significantly increased, whereas anti-TPO, anti-adrenal and anti-parietal cell auto antibodies were unmeasurable. In addition, dosage of serum cortisol, ACTH, TSH and FT4 was normal.No autoimmune diseases were present in relatives.AIRE gene mutation analysis in the parents is pending

Conclusion
This case confirms that monoallelic dominant negative AIRE mutations, located at the PHD1 domain,can present with isolated hypoparathyroidism during adolescence in combination with very mild chronic mucocutaneous candidiasis.High levels of anti-IFNα auto-antibodies, pathognomonic for biallelic APS-1,can used as an additional diagnostic marker

SO 7.

Monitoring quality of rehabilitation using a new evaluation instrument: Patient Reported Experience Measures (PREMs).

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Zeepreventorium

Background

Zeepreventorium is an inpatient centre financed by a convention with RIZIV/INAMI. The centre helps children with a chronic disease and their family to work on specific rehabilitation needs such as adherence to therapy, physical condition, psychosocial balance, social functioning and school attendance. Considering the high cost of an inpatient care program, RIZIV requested a biannual report using objective parameters to evaluate the effectiveness of such program for children and adolescents with a severe chronic disease.

Methods

In collaboration between all disciplines working in Zeepreventorium, an evaluation tool with evidence-based indicators has been developed using the Castor's electronic data capture (EDC) platform. The normal values have been determined for each parameter together with what, if abnormal, can be considered as a significant improvement. In addition to the use of patient-related outcome measures such as BMI, psychosocial wellbeing,…(PROMs), patient experience-related measures (PREMs) have been included. This data collection has been performed with informed consent of parents and patients.

Results

On 289 admissions in 2021, 190 patients have completed the PREMs survey at discharge. The overall mean score of satisfaction is 8/10. At the question "would you recommend the centre to a friend, patients have scored 'probably yes'. On the items 'caring', 'safe care' and 'preparation for discharge', patients have given the centre the maximum score. Additional results from patients admitted in 2022 will be available in March 2023.The survey has also showed that there is still room for improvement on the items: information before and during admission, peers, participation, customised care and way of dealing with parents and children.

Despite the corona period (all parent contacts were digital), the PREMs survey at discharge has also been completed by 105 parents. The parents' overall score is 9/10, just slightly higher than that of the patients. As their child, parents have indicated that information before and during admission, involvement and participation can still be improved.

Conclusion

the use of an evaluation instrument allows therapists and policy makers of the centre to adjust and improve the care pathways and daily work of the rehabilitation centre. This quality monitoring helps Zeepreventorium to further guarantee its excellent and specialized care for children and adolescents with chronic diseases.

SO 8.

Three families with TSH resistance and different clinical presentations

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Background
TSH resistance is a rare genetic disorder most commonly due to biallelic loss-of-function (LOF) variants in the TSH receptor gene (TSHR). We describe patients from four different families with a phenotype of TSH resistance ranging from severe congenital hypothyroidism to slightly elevated serum TSH concentrations during childhood.

Methods
Patients from families with hypothyroidism, neither goiter nor autoimmunity, harboring biallelic variants in TSHR were included.

Results
Eight affected children from four consanguineous families (family 1 with three affected children has already been published (JCI 1997)) were found to harbor biallelic TSHR variants. We report an additional three families with five affected children. In family 2, the proband (born in 2008) harbors a known inactivating homozygous pathogenic variant: c.1657G>A (p.Ala553Thr) in the TSHR transmembrane domain. At neonatal screening (NBS), dry blood spot TSH was >200 mU/L (cut-off 25 mU/L). A severe congenital hypothyroidism was confirmed: serum TSH was 658 mU/L (N 0.51-4.30), free T4 3.9 pmol/L (N 12.5 - 21.5 pmol/L); the thyroid was orthotopic but hypoplastic. In family 3, the proband (born in 2016) harbors a homozygous deep intronic variant (c.242+6T>C); NBS TSH was 16.6 mU/l; cut-off :15). Hypothyroidism was confirmed: serum TSH was 54.3 mU/L, free T4 13.8 pmol/L. The thyroid was orthotopic and of normal size. In family 4, the proband (born in 2011) was diagnosed at 3.9 years with isolated non autoimmune hyperthyrotropinemia (TSH: 27.3 mU/l, normal free T4 at 12.9 pmol/L) and was found to have an orthotopic normal-sized thyroid gland. Genetic analysis of TSHR revealed the known inactivating homozygous variant c.1349G>A (p.Arg450His), affecting one intracellular loop of TSHR; patients 7 and 8 are the siblings of patient 6 (proband of family 4) and were diagnosed after family screening. Their TSH values on DBS were in the normal range using the cut-offs in use when they were born (18.1; 13.4 and <20 mU/l respectively).

Conclusion
Genetic analysis of TSHR should be considered in consanguineous families with non-goitrous congenital hypothyroidism or isolated hyperthyrotropinemia, without autoimmunity and with orthotopic normal-sized thyroids, particularly if family history suggests an autosomal recessive inheritance.

PW 35.

Congenital hyperinsulinism due to a new mutation in the gene ABCC8

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We report the case of a newborn with neonatal hypoglycemia due to congenital hyperinsulinism (CHI) caused by a new variant in the ABCC8 gene.

A 11-day-old newborn boy was referred to our Neonatal Intensive Care Unit for repetitive symptomatic hypoglycemia. His gestational age was 37 weeks 5/7. He presented intra- uterine growth restriction (IUGR) with a birth weight of 2160 g (-2.45SD), length 44 cm, (-2.56SD) and head circumference 33 cm (-0.74SD). IUGR was related to drug use during pregnancy. Clinical examination was normal. No dysmorphic feature was noted.

Parents were non-consanguineous. Familial history was without particularity.

At day 11, he presented drowsiness and tremors. Blood sugar measurement revealed hypoglycemia (38 mg/dl). Insulin blood level measured at the time of hypoglycemia was not suppressed (insulin 3.4 mUI/L; n:3-25 mUI/L). Cortisol (22.1 µg/dL) and GH (5.4 µg/L) responses were satisfactory. Ketonuria was negative. A second sample showed glycemia at 34 mg/dl with insulin measurable at 5 mUI/L. Glucagon test was positive with a rise in glycemia of 40 mg/dl. Cardiac and abdominal ultrasounds were normal.

Those biological values led to a diagnosis of HI. Despite a very high glucose infusion rate (20 g/kg/d) through continuous enteral feeding and intravenous infusion of glucose 10%, he repeated hypoglycemia. Treatment with diazoxide was started (from 10 to 20 mg/kg/d). Because hypoglycemia persisted, octreotide was added with a dose increased up to 35µg/ kg/day (initially subcutaneous infusion every 6 hours and then continuous subcutaneous infusion with insulin pump). In parallel, intravenous infusion was stopped and enteral continuous feeding was gradually decreased.

Genetic analysis revealed a new mutation in the ABCC8 gene. Maternal genetic study was normal. Paternal DNA was not available. Fluorine 18-L-3,4 Dihydroxyphenylalanine Positron Emission Tomography (18F-DOPA-PET/CT scan) reported a focal lesion at the isthmus of the pancreas which has been removed by laparoscopic surgery leading to complete recovery.

CHI represents the most frequent cause of persistent hypoglycemia in newborn. Management of those patients remains a challenge. Genetic analysis and 18F-DOPA-PET/CT scan help differentiate focal and diffuse forms, and select patients for which a curative surgical management can be proposed. Before that, the goal of the treatment is to achieve normal glycemia to prevent neurological damages secondary to hypoglycemia.

PW 36.

The relationship between HbA1c and Time in Range during the preceding 2, 4 and 12 weeks in a paediatric population

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Introduction
Recently, the proportion of time in range (TIR), measured by continuous glucose monitoring (CGM) using a target glucose range of 70 to 180 mg/dL, is often proposed as a suitable alternative to the use of HbA1c. Studies in adults revealed a strong correlation between TIR and HbA1c. However, this correlation has been insufficiently investigated in a paediatric population. Therefore, this retrospective monocentric cohort study aimed to determine the correlation between HbA1c and TIR during the preceding 2, 4 and 12 weeks (TIR_{2w}, TIR_{4w} and TIR_{12w}) in a paediatric population diagnosed with type 1 diabetes mellitus (T1DM).

Materials and methods
168 children and adolescents (0-18 years old) with T1DM were included in this retrospective study at the University Hospital of Leuven. CGM data, HbA1c and multiple demographic variables were collected from the patient files.

Results
A strong negative linear correlation was found between HbA1c and TIR_{2w} ($R = -0.571$), TIR_{4w} ($R = -0.603$) and TIR_{12w} ($R = -0.624$). Secondary outcomes revealed even stronger correlations between HbA1c and time above range (TAR) during the preceding 2, 4 and 12 weeks, TIR_{2w} and TIR_{12w} as well as TIR and TAR at the different time points.

Conclusion
A strong correlation was found between HbA1c and TIR in a paediatric population, which makes TIR a potential alternative to HbA1c for assessing individual glycaemic control. TIR_{2w} seems a viable alternative to TIR_{12w}. Furthermore, TAR also appears promising in assessing this glycaemic control.

PW 37.

A diabetes can hide another: always think about type 1 diabetes in children

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Introduction

Monogenic diabetes account for 1 to 6 % of pediatric diabetes while type 1 diabetes for over 90 % . We report the story of a family where monogenic and type 1 diabetes coexist.

Case report

A sixteen year old boy presented for glycosuria detected to the school medical visit, without weight loss, polyuria or polydipsia. He is the eldest of three children. The parents are of Moroccan origin, not consanguineous. The mother has autoimmune hypothyroidism, the father is in good health. Medical history revealed a simple pubertal delay, having received testosterone injections. Laboratory investigations showed HbA1c at 6.8 % (51 mmol/l) and C peptide level at 0.6 µg/l (N 0.5-3.0 µg/l). There were no ketosis. We performed an oral glucose tolerance test showing a fasting glucose level at 155 mg/dl and after two hours at 310 mg/dl with an insufficient insulin level at 134 pmol/l. The diagnosis of diabetes is confirmed. The teenager is hospitalized and, while awaiting the results of immunological and genetic markers, insulin therapy is started. IAA, ICA, GADA and IA2A were negative. The genetic analysis showed an heterozygote c.236A>T p.(Glu79Val) variant in the HNF-1-alpha gene. The current meaning of this variant is unclear. Following this result, we empirically introduced repaglinide and the insulin was quickly weaned based on blood glucose monitoring. Metabolic control remained optimal (HbA1c 5.3 % - 35 mmol/l) with repaglinide 120 mg/d and Novorapid injections in case of dietary deviations. We proposed genetic research of this variant in the parents. The mother has the same variant, without diabetes. The variant is then looked for in the brothers, who do not have it. However, one year later, the second brother, at the age of 13, presented with polyuria, urinary urgency, polydipsia and a 5% weight loss. In consultation, glucose level was measured at 433 mg/dl, HbA1c at 10.9% (95 mmol/l) and C peptide diminished to 0.314 nmol/l. There were no ketosis. The teenager is hospitalized to start subcutaneous insulin therapy. IAA (1.1 %), ICA (50 U JDF) and GADA (52.6 U/ml) were positive, confirming the diagnosis of type 1 diabetes.

Conclusion

The most common form of diabetes in children is type 1 diabetes. Therefore, a family history of monogenic diabetes does not exclude the development of type 1 diabetes. Establishing a correct diagnosis has important implications for guiding appropriate treatment, prognosis and genetic counselling.

PW 38.

Ectopic adrenocortical adenoma : a rare cause of hirsutism and hyperandrogenism

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Background
Excessive hair growth or hirsutism is a common complaint in adolescent girls. The most common causes are idiopathic hyperandrogenism and polycystic ovarian syndrome (PCOS). Less common causes are nonclassic adrenal hyperplasia and androgen-secreting tumours. We present a girl with an ectopic adrenocortical adenoma causing hirsutism.

Case-report
A 14 10/12 yrs old girl (height: 160.5 cm (-0.6 SDS); weight: 53.3 kg (-0.1 SDS)) was referred for the evaluation of hyperandrogenism causing hirsutism. The excessive hair growth started at the age 10 yrs. Breast development started at 11 yrs. The patient did not yet had her menarche but she had growth arrest. Referred blood results showed elevated serum levels of androgens (testosterone 0.68 ng/mL (norm: 0.10–0.40), androstenedione 363 ng/dl (30–200), DHEA-sulphate 20.00 µmol/L (0.92–7.60). Pelvic ultrasound showed normal ovaries (no signs of PCOS). After ACTH administration high levels of 17OHpregnenolone (6700 ng/dL (< 274)) were found with a normal increase of cortisol and a slight increase of 17OHprogesterone (1,67 ng/mL (< 0.76)). Suspicion for a nonclassic 3-beta-OH-steroid dehydrogenase deficiency was raised. Treatment with prednisone was started without any effect on androgen levels. Subsequently, MRI of the abdomen revealed a large mass (11x7.7x 8.0 cm) in the right hypochondrium. The adrenal glands were normal. The patient was referred to the department of oncology of U.Z. Leuven. A biopsy showed an adrenocortical tumour. Resection of the mass revealed a 207 gram tumour, histologically an adrenocortical adenoma. Postoperatively the androgen and 17OHpregnenolone levels normalised quickly and the hirsutism disappeared completely. Menstruation started 1 month postoperatively.

Discussion
This is a rare case of an ectopic virilising adrenocortical tumour. Ectopic adrenocortical tumours are a very rare entity in paediatrics. They are usually found along the gonadal descent paths. The majority of paediatric adrenocortical tumours occur in children less than five years, with a female predominance prior to adolescence. They most commonly present with virilisation, followed by hypercortisolism and hyperaldosteronism. It is difficult to separate benign from malignant tumours. Histopathological classification may not be reliable.

Conclusion
In girls with hirsutism due to hyperandrogenism a meticulous hormonal evaluation has to be done before starting treatment with contraceptives or spironolactone.

PW 39.

Pendred syndrome: a rare cause of hypothyroidism with goiter and sensorineural hearing impairment

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Background
Pendred syndrome (PS) is a rare autosomal recessive disease, classically defined by the combination of sensorineural deafness, presence of a goiter and an abnormal thyroidal organification of iodide with or without hypothyroidism.

Methods
A 7 year old girl with bilateral congenital profound hearing loss of unknown etiology is diagnosed at the pediatric endocrinology department with hypothyroidism and a goiter. Ultrasound portrays a multinodular deformation with nodules containing solid as well as cystic components and peripheral micro-calcifications. Urinary iodide excretion is normal. Thyroglobulin levels are elevated. Genetic examination identifies a mutation in the SLC26A4 gene.

Results
Prevalence of PS is estimated between 7.5 and 10 per 100,000. PS accounts 10% of all hereditary deafness cases. PS is caused by a defect in the Pendrin protein, located in the follicular thyroid cells – which causes partial impairment of thyroid iodide organification – and in the cochlea, where it influences endolymphatic fluid resorption and acid-base balance. Hearing impairment is congenital or prelingual, bilateral and profound. Goitrous enlargement and presence of hypothyroidism are variable and influenced by iodine intake. The risk of follicular thyroid carcinoma is elevated. Laboratory thyroid function tests are not conclusive in identifying nor excluding PS. A Perchlorate test is also inconclusive. Genetic testing for mutations in the SCL26A4 gene serves as the standard confirmatory diagnostic tool. Thyroxine substitution is the primary treatment option but total thyroidectomy is warranted is some cases. Early audiology support is pivotal in assuring social development and quality of life.

Conclusion
Thyroid phenotype in PS is highly variable. Hypothyroidism occurs in about 30-50% and can be congenital. Perchlorate testing should not be considered the “gold standard” test for confirming nor excluding PS diagnosis.

PW 40.

Extreme short stature with microcephaly after intra-uterine growth retardation : a challenging diagnosis.

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Background

Several genetic syndromes present with postnatal growth failure and microcephaly after intra-uterine growth retardation. Clinical diagnosis might be challenging at birth or during infancy since not all symptoms might be present. Microcephalic osteodysplastic primordial dwarfism type II (MOPD II) is one of these syndromes to be diagnosed timely, given the very high-risk of life-threatening neurovascular diseases, such as moyamoya vasculopathy and intracranial aneurysms. We recently diagnosed MOPD II in a toddler with severe short stature and microcephaly, who had been falsely diagnosed with congenital hypopituitarism.

Case

A nineteen months old boy was seen at the endocrine department for growth hormone (GH) treatment because of a very short stature post intra-uterine growth retardation. He is the sixth child of a consanguineous Syrian couple. He was born prematurely (at 24-28 weeks of gestation) with a birth weight of 820 gr, length of 33 cm and head circumference of 25 cm. From the age of seven months, he was taking thyroxine and prednisolone for a suspected congenital hypopituitarism (hormonal data not available). His motor development was normal. At clinical examination, syndactyly of the second and third toes, a large right inguinal hernia, a high-pitched voice, small teeth and a broad nose base and root were observed. His body length was 56 cm (-9.64 SDS), weight 4.190 kg (-10.44 SDS) and head circumference 38 cm (-6.62 SDS).

Results

Hormonal testing after gradual stopping of hormonal therapy, showed an elevated TSH (11.9 uIU/ml, normal range 0.7-6.0) with normal FT4, normal cortisol, low IGF-1 (23.8ng/ml, normal range 27-157), normal IGF-BP3 and basal fasting insulin. Standard laboratory tests including liver/kidney function, electrolytes, calcium, phosphorus were normal. Candidate gene panel analysis for short stature showed a homozygote pathogenic c.2407C>T p.(Gln803*) mutation in the PCNT gene, which was inherited from his healthy heterozygous parents. Yearly hematological, ophthalmologic, orthopedic, neurological, endocrine and neurosurgical follow-up has been set up.

Conclusion

MOPD II should be suspected in short children born small for gestational age with microcephaly in combination with a prominent nose, high-pitched voice and small teeth. Although a very short adult height (<120 cm) is expected, GH treatment should not be instituted given the risk of insulin resistance and the development of severe neurovascular disorders

LO 12.

Poliomyelitis Surveillance in Belgium

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Sciensano

Background
Global targets aim to eradicate polio by 2026.

No cases of poliomyelitis have been reported in Belgium since 1999 and Belgium has been polio-free since 2002. However, Belgium is classified as an intermediate-risk of transmission for poliomyelitis according to WHO because of insufficiencies in surveillance systems.

Globally, there is a risk of reintroduction of polio into polio-free areas. In 2022, new cases of polio derived Acute Flaccid Paralysis (AFP) have being identified in areas previously believed to be polio-free (USA and Indonesia). Poliovirus has also been identified in environmental surveillance in countries which are classified as polio-free (UK and Israel).

Although vaccination coverage in Belgium is generally high, there may be susceptible populations where coverage is lacking.

AFP surveillance is considered the gold-standard for polio surveillance and is the primary surveillance system in Belgium. Notification of all AFP cases, regardless of cause, is mandatory across Belgium. To be considered a sufficiently sensitive surveillance system, it should be able to capture 1/100 000 cases of non-polio AFP in <15 year olds (19 cases/year in Belgium).

We evaluated current poliomyelitis surveillance systems in Belgium in relation to WHO standards.

Methods
All reported AFP cases in <15 year olds from 2003 to 2021 were analysed. Cases were either reported via mandatory notification and/or by a network of clinicians and paediatricians (PediSurv). Additionally, PediSurv includes monthly voluntary registration of zero-cases.

Results
82 AFP cases in children <15 years old were reported from 2003–2021, averaging 4 cases/year (~0.2/100 000). In 2019–2021, only 5 cases (~0.1/100 000) were reported, demonstrating a declining trend in reported cases.
Only 2 cases (2003-2021) underwent the required microbiological workup (2 stool samples collected 24-48h apart, within 14 days of disease onset).

Conclusion
In 2018, AFP surveillance in Belgium was 5 times too low for WHO quality indicators. This has worsened to 10 times too low from 2019 to 2021.
Greater awareness of AFP surveillance is required, as is optimisation of registration systems.
Options for improvements include enterovirus and environmental surveillance (wastewater testing). To maximize effectiveness, these need to be supplementary to current systems.
To reduce the risk of polio being reintroduced into Belgium it is necessary to improve the current surveillance systems.

SO 1.

The European Paediatric Clinical Trials Network conect4children (c4c): 5-year report of activities within Belgium

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Background/Aims
Currently, over 60% of clinical trials in children are unsuccessful due to insufficient recruitment, administrative burden, inadequate methodology, among other reasons. Sponsors experience difficulties identifying adequate and developed sites to conduct pediatric trials. To optimize and facilitate clinical trials, (inter)national networks have been developed by (academic) investigators such as the I-ACT for Children network (U.S.A.), Innovative Medicines Initiative 2 conect4children (IMI-c4c) grouped network (Europe), and MICRYN (Canada). For Belgium, the Paediatric Clinical Trial Network within BPCRN Belgian Paediatric Clinical Research Network), was developed in 2009 and included in c4c in 2018, managed by the Ghent University (Hospital).

Method
This report describes an update on the progress of c4c over the past 5 years. The Belgian Paediatric Clinical Trial Network has 15 hospitals connected. The network has been involved in 2 academic trials, 10 industry trials and over 35 preliminary feasibility requests.

Results
The Belgium national network (BPCRN) was selected in 2/4 academic trials, and 5/5 industry trials within c4c. Constructive communication with the sponsor increased the number of sites from 2 to 8 for the academic studies. The added value of the BPCRN in the academic trials was help by the national hub in regulatory submission and budget plan. For the industry studies, the administrative requests have been centrally buffered, with over 66% of the feasibility questionnaires being pre-filled. Moreover, an additional 32% new sites were identified for the industry sponsors.

The network is also involved in i) data standardization, inclusion of real-world data and rare disease data-dictionary development, ii) expert panels and iii) teaching pan-European courses for site and investigator development. Moreover, the Belgian network has been the liaison for the totality of European national networks with the US-based network I-ACT for Children, for clinical trials running outside of the c4c project scope.

Conclusion
Over the past 5 years, substantial developments and progress have been made with the Belgium network activity by BPCRN. Central optimalisation of site identification, site development and trial start-up have been prioritized. To achieve a sustainable network after IMI2 funding, a longitudinal commitment of both sites and sponsors is needed.

SO 2.

The Challenges in performing Pediatric Clinical Trials: an update after 15-years of EMA Regulation

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Background/Aims
Still 60% of drugs used in children are off label. Although the EMA regulation, increased largely the timely submission of Pediatric Investigational plans (PIP) and initiation of clinical trials (CT), the majority of these CT's remained unsuccessful due to insufficient recruitment, administrative burden, inadequate methodology, among others. Historically, the concept was largely developed for blockbuster drugs where the adult indication and design, was translated into the pediatric population.

Method
This report describes the core principles of conducting trials in a pediatric setting, gathered through literature and a collected global expertise of over 30 years of clinical trials in children.

Results
The main principles include adapting trial study teams for pediatric needs, limiting sampling and optimizing imaging, communication between trial site and sponsor (with or without network aid), as well as placing child and/or parent centrally within the trial design, targeting the pediatric indication of the drug. The increasing number of orphan drugs, with often major only indication in children, demands specific expertise. Alternative solution to sampling, such as sparse sampling and dry blood sampling are recommended. Novel anesthesiology and play therapy are highly encouraged and more widespread available. US-based and European networks have been developed (IMI2 conect4children (c4c), I-Act for Children) with increasing connectivity with rare diseases consortia (ERN, EJPRD, ERICA, EPTRI) and patient/parent organizations- Regarding patient engagement, a special focus on patient-reported outcomes is mandatory. Moreover, a national and continental budgeting plan for a pediatric setting has been developed, to speed up the initiation of the trials

Conclusion
In efforts to making the utopian completely on-label prescription of drugs in children a reality, learnings and expertise needs to be grouped and widely distributed. A dedicated expert or course in the conduct of pediatric clinical trials for young investigators could be beneficial.

SO 3.

Elimination of rubella in Belgium

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Background
In 2004, WHO Europe set forth to eliminate congenital rubella from the region by 2010. All member states, including Belgium, supported this objective. The milestone was however missed and timelines were adapted. We describe the evolution in Belgium.

Methods
Data from all available sources is combined. From 2002-2009, the only data source was PediSurv, a network of clinicians that perform monthly voluntary reporting of cases or 'zero-cases'. Since 2009, cases of (congenital) rubella are notifiable to regional health authorities in Brussels and Wallonia, but not Flanders. Since 2011, data from the National Reference Centre (NRC) for Measles, Mumps and Rubella and the NRC for Congenital Infections were systematically linked to other data sources. From 2018, suspected cases with fever and rash are additionally tested for rubella after a negative measles test. In 2020, retrospective active case-finding was done, using mortality statistics, minimal clinical hospital data, surveillance of congenital malformations and birth statistics (available with a delay of several years only).

Results
The last case of CRS was notified in Belgium in 2012 through PediSurv and was imported from Morocco. In 2018, additional testing of a measles-negative specimen identified rubella in a man who had travelled to Algeria. A possible rubella infection during pregnancy occurred in 2019. A seronegative woman developed itchy rash in the 3rd trimester, diagnosed by a dermatologist as pruritic urticarial papules and plaques of pregnancy (PUPPP). However, routine rubella serology one week later showed seroconversion. Clinical examination and rubella testing of the newborn were unremarkable. Despite the absence of reported CRS, WHO considered Belgium 'endemic' for rubella until 2018, due to 'insufficient surveillance'. Efforts to improve surveillance quality included active retrospective case-finding, sequential testing for measles and rubella in suspected cases and encouraging correct use of rubella serology in pregnancy. The PediSurv network, with its unique design confirming 'absence' of disease, played also an important role. For instance, in 2021, PediSurv received 3,211 zero-case reportings from 387 users. Thanks to these combined efforts, the Regional Verification Committee of WHO awarded Belgium the label 'rubella eliminated' since 2019.

Conclusion
Absence of disease is insufficient to reach elimination targets; sensitive surveillance systems are equally required.

SO 4.

Qualitative research to increase participation and quality of surveillance networks

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Sciensano

Background
The surveillance network 'PediSurv' collects clinical information in children <15 years on measles, mumps, acute flaccid paralysis, invasive pneumococcal disease, congenital rubella syndrome, haemolytic uremic syndrome and pertussis in hospitalized infants (< 3 months). Belgian pediatricians (and General Practitioners (GPs) in Brussels) voluntarily perform monthly registrations of 'cases' or 'zero-cases'. This active zero-case notification is key in surveillance of rare diseases and essential to track elimination/eradication goals of the World Health Organisation.

To optimise registrations we assess the physicians' needs and clarify what adjustments could make 'PediSurv' more valuable for them.

Methods
All registered physicians in October 2022 received an email with the invitation to complete a survey within 2 weeks. A reminder was sent after 1 week. In November 2022 the results were presented and discussed by a focus group discussion (FGD) at the 'PediSurv' steering committee in which 12 stakeholders from different federated entities in Belgium participated (clinicians, academics and policy makers).

Results
The survey was completed by 88 pediatricians and 43 GPs (response rate 35%). All respondents agreed that 'PediSurv' is important for public health and this seemed the most important motivation for participation: 82% would not be extra motivated by a financial incentive. Many participating physicians are in older age groups, 66% between 50-69 years and 10% >69years. The FGD attributed this to a lack of awareness regarding 'PediSurv' in young pediatricians and proposed active communication and diffusion of 'PediSurv' results through strategic channels as options for improvement. Indeed, 62% of respondents indicated that improved feedback would increase their motivation. A more user-friendly registration system would encourage 39% of current participants to report more regularly. The FGD specifically identified the current logging-in procedure as burdensome.

Conclusion
A quantitative survey complemented by a qualitative FGD identified clear actions for improvement. Participants acknowledge the importance of the surveillance network for public health and this is the main motivator. Regular feedback and easy reporting procedures are paramount, where financial incentives were not considered so. These findings are likely valuable for other surveillance networks too.

PW 29.

Rehabilitation for pediatric patients with chronic functional complaints

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Zeepreventorium

Background
Zeepreventorium is a residential center for children aged 0-18 years with chronic diseases. Also children with chronic functional complaints like muscle and joint pain, abdominal pain, headache, dizziness, pseudo-epilepsy, and/or fatigue are treated. Symptoms last for at least 3 months and single attributable diagnoses are missing. These complaints result in major distress for patients and their families, reinforcing the pathophysiological mechanism. Moreover, social isolation and absence from school ensue frequently. For most, ambulatory therapy by physicians, physiotherapists and psychologists helps sufficiently but, for a small group, an inpatient program is indicated.

Methods
In Zeepreventorium, children between 9-19 year are treated in a bio-psycho-social model following a time-contingent graded exposure program over a period of 6 months. Multidisciplinary therapy is given by a physician and nurse, physiotherapist, psychologist and dietician, within a living group. Cognitive behavioural therapy is provided, focussing on phasing out inappropriate coping strategies . This implies active participation of parents in gaining insight and changing behaviour. In the last 2 months, therapy focuses on taking responsibility by the patient and on the re integration at home. We also provide a follow-up by keeping contact with patients, families and their ambulatory caregivers for a period up to 3 years after the revalidation.

We give an overview of qualitative and quantitative results of the residency program, including long time follow-up after discharge.

Results
Between march 2019 and march 2022, 37 patients were included, following a treatment of minimally 6 months. As focusing on complaints enhances the circle of avoidance, we principally don't collect data of symptom scores.

On discharge, 34/37 patients had a better physical condition (step test: + 295m [187;402]) , 29/37 patients showed an increase in muscle mass (+3,05 kg [1,83; 4,28]) (mean [p25; p75]) and in 22/37 patients BMI improved from under (15/37) or above (7/37) normal range towards normal range.

Regular surveys by telephone between 3 and 42 months after discharge show that 13/32 reached children remain fully and 12/32 are partly reintegrated in school and hobbies. All of these were socially isolated at home before treatment.

Conclusion
children with severe chronic functional complaints can be helped by an intensive multidisciplinary inpatient rehabilitation program.

PW 30.

Diffuse large B-cell lymphoma as lead point for an ileocecal intussusception in a 4 year old boy: a case report and literature review.

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Introduction

Intussusception also known as “invagination” is a telescoping movement of the intestine into itself, which is a frequent abdominal emergency in children. Pathological lead points causing intussusception exist in up to 25% of cases. Lymphomas as a lead point are rare and certainly diffuse large B-cell lymphomas (DLCBL) (they represent 10-20% of all Non-Hodgkin lymphomas in children). To our knowledge, this is the first case of a child with an ileocolic intussusception caused by a DLBCL.

Methods

A literature study was performed including case studies, reviews and systematic reviews using PubMed and Up-to-date.

Results

A 4-year old boy presented himself with 3 weeks of abdominal pain, presenting as intermittent episodes of pain with increasing intensity and vomiting after oral intake. He had no stool for two days. He had no significant medical history. He consulted his paediatrician earlier that week, a work-diagnosis of constipation was made. Laxatives were prescribed and an ambulant echography of the abdomen was scheduled. The echography showed an ileocolic invagination with a hypo-echogenic zone 3 x 1,8cm without sings of bowel ischemia. Hydrostatic reduction under fluoroscopic monitoring showed smooth opacification of the colonic frame up to the hepatic angle, with here a sparing appearance corresponding to the visualized invagination. Contrast passage beyond this invaginate with opacification of the caecum floor was visualized, however no complete reduction of invagination obtained. A circumbilical laparotomy was performed, with complete manual reduction of the invagination. A small bowel lesion was visualized at 20 cm from the ileocecal junction, with an enlarged mesenterial gland. The lesion in the ileum was resected with an end-to-end anastomosis. The patient had an uncomplicated recovery. On histopathological and molecular analysis, the rare diagnosis of a DLBCL was made. A PET-CT scan showed multiple non-to-light FDG capitating adenopathy's retroperitoneal, mesenterial and axillar. Our patient was referred to an oncological center for further treatment and follow-up.

Conclusion

We reported a case of a young boy with ileocolic intussusception, caused by a high-grade B-cell lymphoma. Lymphomas are rare causes of intussusception, and specifically a DLBCL as a lead point is even rarer. When in suspicion of a lead point, further investigations are required and being aware of a malignant origin is of great importance.

PW 31.

An Update on Somatic Inpatient Treatment of Anorexia Nervosa: A Comparison of International Clinical Guidelines.

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Introduction

Anorexia nervosa (AN) affects up to 0.5% of adolescents. It is now considered the third most common chronic disease in adolescence and also the psychiatric illness with the highest mortality rate , ranging from 2-8%.

A part of the high morbidity and mortality is explained by the multi-organ stress and failure caused by prolonged fasting, especially on the cardio-vascular system.

Aim & Results

A Pubmed search was conducted started in 2017 and updated recently in march 2022, using the keywords anorexia nervosa and management guidelines and adolescent (children & young adults). Finally we searched and analyzed the national and international clinical (somatic) guidelines about the “red flags” for hospital treatment in AN and the intervention who are necessary and effective during hospitalization.

Conclusion

Despite the lack of proper standardized criteria for hospitalization and the absence of clear guidelines addressing all somatic aspects of this crucial period , is the hospitalization of the AN patient with multi-organ failure a real challenge for the general pediatrician especially for those working outside of a specialized eating disorder unit.

This review of the current literature can be used as a simple aid in inpatient admission for adolescents with severe AN for the all care providers who are not so familiar with the somatic multimorbidity of eating disorders.