



## **Mihai CRAIU**

## **EXPERIENȚA PROFESIONALĂ**

30/09/2015 - ÎN CURS Bucuresti, România

#### SEF SECTIE PEDIATRIE V - PNEUMOLOGIE PEDIATRICA IOMC ALFRED RUSESCU

Coordonarea secției clinice de Pneumologie Pediatrică: evaluare, diagnostic și tratament pentru pacienții pediatrici cu boli pulmonare acute sau cronice, cercetare științifică în aria bolilor respiratorii, învățământ medical pentru studenți și rezidenți. Din 2019 sunt coordonatorul programului de rezidentiat in specialitatea Pneumologie pediatrica din Centrul Universitar Bucuresti si in aceasta calitate am participat la formarea abilitatilor medicilor rezidenti de a documenta complex, clinic si paraclinic diversele maladii ce afecteaza tractul respirator la copil. Medicii rezidenti au fost inclusi si in diverse programe de cercetare in sectia de Pneumologie pediatrica, primind oportunitatea de a finaliza si de a prezenta lucrari stiintifice la conferinte nationale sau internationale. Performantele activitatii de cercetare desfasurata de catre medicii rezidenti in INSMC au fost remarcabile. Acestea s-au finalizat cu mai multe premii internationale in anul 2020. Sectia noastra a fost inclusa in mai multe trialuri internationale atat de studii clinice (diverselor medicamente novatoare destinate pacientilor cu astm bronsic sau fibroza chistica) cat si in survey-uri europene multicentrice cum ar fi PERMEABLE (Biologicals in childhood severe asthma: The European PERMEABLE survey on the status quo).

30/11/2012 - ÎN CURS Bucuresti, România

#### **CONFERENTIAR UNIVERSITAR UMF CAROL DAVILA**

Management al activității clinice a studenților, cursuri pentru studenții stagiului de 8 săptămâni de formare în pediatrie [în anul 5 de studii la UMF Carol Davila], module practice în urgențele pediatrice, curs opțional de PALS (Pediatric Advanced Life Support training), coordonarea rezidenților in CPU și din clinica II Pediatrie INSMC, cercetare clinică în boli respiratorii [astm, pneumonii comunitare și fibroză chistică], coordonator al programului național de astm la copil prin Unitatea de Management a Programelor Ministerului Sănătății și al Comisiei de Pneumologie Pediatrică a Ministerului Sănătății.

60% din activitatea mea zilnică este în relație cu activitatea de îngrijire a pacienților și cu cea de predare, iar 40% cu cea de cercetare științifică [elaborare cursuri, elaborare de capitole de carte, elaborare de articole medicale, cercetare clinică, participare la congrese științifice].

09/10/2011 - ÎN CURS București, România

#### SEFUL CLINICII II PEDIATRIE UNIVERSITATEA DE MEDICINA SI FARMACIE CAROL DAVILA

Activitate clinică integrată (activitate clinică zilnică în Secția V cu profil de boli respiratorii sau în Compartimentul de Primiri Urgențe [CPU], cursuri pentru studenții anului V [romani si modul de predare în limba engleza / bursieri ERASMUS], coordonare stagiu practic al studenților ce desfășoară stagiul de pediatrie [rotație, micro cursuri, prezentări de caz, examen practic si scris-grila], curs opțional de PALS (Pediatric Advanced Life Support) pentru studenții anului V, coordonarea pregătirii rezidenților ce efectuează rotația în Secția V sau în CPU si respectiv în disciplina II Pediatrie.

Adresă bulevardul Eroilor Sanitari numarul 8, 050474, Bucuresti, România

06/06/2007 - 29/09/2015 Bucuresti, România

#### SEF CPU IOMC INSTITUTUL DE OCROTIRE A MAMEI SI COPILULUI ALFRED RUSESCU

Management al activității CPU, triaj și evaluare a pacienților critici, stabilizare post-resuscitare si tratamentul cazurilor severe, evaluare și tratament pentru pacienți cu afecțiuni respiratorii, "secondopinion" la pacienți cu astm sever /wheezing recurent / alte afecțiuni bronho-obstructive cronice, supervizarea rezidenților și training specific al acestora [coordonarea procedurilor și manevrelor practice],

management al resurselor materiale și al echipamentelor medicale din CPU, elaborarea de protocoale locale de tratament.

Adresă bulevardul Lacul Tei 120, 020395, Bucuresti, România

10/02/2000 - 29/11/2012 Bucuresti, România

#### **SEF DE LUCRARI** UMF CAROL DAVILA

Activități de predare pentru studenții seriilor în limba romană și în limba engleză, cercetare științifică [cercetare clinică, redactare de capitole de carte, elaborare articole medicale].

Adresă bulevardul Eroilor Sanitari numarul 8, 050474, Bucuresti, România

14/11/2010 - 01/05/2012 Bucuresti, România

#### **COORDONATOR AL CLINICII DE PEDIATRIE** SPITALUL DE COPII MEDLIFE

Evaluarea pacienților din ambulatoriul de specialitate, vizita clinică la pacienții internați în secția de pediatrie, alte activități clinice (diagnostic și tratament pentru cazurile dificile, "second-opinion" la pacienții internați în secția de ORL și chirurgie pediatrică), coordonarea secției de pediatrie, elaborarea de protocoale de activitate, instruirea asistentelor, evaluarea nevoilor de echipamente și consumabile, etc

Adresă strada Zagazului nr7-8, 014261, Bucuresti, România

31/12/1998 - ÎN CURS Bucuresti, România

#### MEDIC PRIMAR PEDIATRU IOMC ALFRED RUSESCU

Evaluarea, diagnosticul și tratamentul pacienților din saloanele alocate în secția de Terapie Intensivă, cercetare medicală, activitate practică si de predare [studenti și rezidenti].

Adresă Bulevardul Lacul Tei 120, 020395, Bucuresti, România

## EDUCAŢIE ŞI FORMARE PROFESIONALĂ

30/04/1999 - 20/02/2005 Bucuresti, România

#### **TEZA DE DOCTORAT** UMF Carol Davila

"Rolul abordului intraosos în resuscitare la copil" / Teza de Doctorat în Pediatrie [aria de interes Medicina de Urgență Pediatrică] descrie o cale de acces vascular specială în cursul resuscitării cardio-pulmonare la copil.

Domeniu de studiu Pediatrie - Medicina de Urgenta | Clasificare națională ISCED 8 - 844

30/11/1989 - 31/05/1994 Bucuresti, România

#### MEDIC SPECIALIST IN PEDIATRIE UMF Carol Davila

rezidentiat in Pediatrie

Adresă bulevardul Eroilor Sanitari numarul 8, 050474, Bucuresti, România | Domeniu de studiu medicina |

Clasificare natională ISCED 7 - 758

14/09/1983 - 14/09/1989 Bucuresti, România

**MEDIC MD** UMF Carol Davila

medicina - pediatrie

Adresă bulevardul Eroilor Sanitari numarul 8, 050474, Bucuresti, România | **Domeniu de studiu** medicina |

Clasificare națională ISCED 7 - 746

29/07/2023 - ÎN CURS Bucuresti, România

TEZA DE ABILITARE Universitatea de Medicina si Farmacie Carol Davila

Site de internet <a href="https://umfcd.ro/wp-content/uploads/2023/SCOALA\_DOCTORALA/ATESATATE\_ABILITARE/ATESTAT\_DE ABILITARE Conf.univ.dr. Craiu Mihai.pdf">https://umfcd.ro/wp-content/uploads/2023/SCOALA\_DOCTORALA/ATESATATE\_ABILITARE/ATESTAT\_DE ABILITARE Conf.univ.dr. Craiu Mihai.pdf</a>

#### COMPETENTE LINGVISTICE

Limbă(i) maternă(e): ROMÂNĂ

Altă limbă (Alte limbi):

	COMPREHENSIUNE		VORBIT		SCRIS
	Comprehensiune orală	Citit	Exprimare scrisă	Conversație	
ENGLEZĂ	C2	C1	C1	C1	C1
FRANCEZĂ	B2	B1	B1	B1	B1

Niveluri: A1 si A2 Utilizator de bază B1 si B2 Utilizator independent C1 si C2 Utilizator experimentat

### COMPETENTE DIGITALE

Social Media | Navigare Internet | Utilizare buna a programelor de comunicare(mail messenger skype)

### INFORMAŢII SUPLIMENTARE

#### **PERMIS DE CONDUCERE**

Permis de conducere: B

#### **COMPETENTE ORGANIZATORICE**

Competente organizatorice Am fost numit în 2007 coordonator al nou înfiintatului Compartiment de Primiri Urgențe al IOMC Alfred Rusescu (actualmente INSMC Alessandrescu-Rusescu). In această calitate am construit o echipă a CPU, printr-un proces de selecție și formare/instruire a unui grup de medici și asistente. Această echipă a fost organizată de asa manieră încât să poată răspunde la cele mai dificile scenarii de resuscitare pediatrică, în vederea triajului și stabilizării posibilelor urgente majore adresate IOMC. In acești 13 ani am fost capabili să rulăm un număr de peste 400 000 de prezentări în CPU. Aceasta strategie a fost una dintre cele mai importante modalități de a crește calitatea actului medical și costeficienta acestuia în IOMC prin rezolvarea, fără internare, a unui număr impresionant de prezentări. Ca o recunoaștere a calităților mele manageriale și profesionale a venit oferta de a conduce secția de pediatrie a primului spital privat din Romania [Life Memorial Hospital] în 2010. În aceasta poziție a trebuit să elaborez o abordare strategică și să definesc targetul populațional al potentialilor pacienti, să formez asistențele și medicii tineri în spiritul acestei noi exigente pe piata serviciilor medicale din Romania. După îndeplinirea parametrilor de performantă, asumați prin contractul de colaborare cu acest spital privat, am revenit cu un program full-time în IOMC Alfred Rusescu, în poziția de Șef al Disciplinei II Pediatrie, după pensionarea domnului Prof dr Gherghina Ion. Am păstrat colaborarea cu acest spital privat [acum relocat în Spitalul de Copii Medlife, unitate medicală exclusiv pediatrică] oferind consultații de pneumologie pediatrică în ambulatoriul integrat spitalului, în afara programului meu de la IOMC, o zi pe săptămână pana în 2014. Din 2015 pană la începutul anului 2018 am condus nou înfiintata Sectie V cu profil de boli respiratorii, elaborând un plan de actiune și monitorizare care a fost validat de rulaiul mare de bolnavi și care a fost evaluat laudativ de către comisia de Acreditare a Spitalelor în iunie 2016. De la sfârsitul anului 2019 am revenit la conducerea acestei sectii pana in 2022. Din decembrie 2022 sunt membru al echipei din Compartimentul de Primiri Urgente al INSMC.

Competentele de organizare si abilitatea de a construi o cooperare eficienta intre diversele clinici de pediatrie din Romania au stat la baza acceptarii mele in calitate de Consultant Senior pentru Biroul OMS Romania. In aceasta calitate am participat la un program de evaluare al impactului Pandemiei COVID-19 asupra ingrijirilor furnizate mamei si copiilor in tara noastra, ca proiect pilot pentru Regiunea OMS Europa.

#### **COMPETENTE DE COMUNICARE SI INTERPERSONALE**

**Competențe de comunicare și interpersonale** De 30 ani am lucrat eficient în cadrul diverselor echipe medicale în care am fost delegat de către conducerea INSMC [în Compartimentul de Primiri Urgente, în Secția de Terapie Intensiva, în secția de Preșcolari, în Secția de Boli Respiratorii, etc]. Am participat la stagii de perfecționare în clinici din străinătate, pentru scurte perioada de timp: prima data 2 săptămâni la Wroxton College UK apoi 3 luni la Wilhelmina Kinderziekenhuis Utrecht, in Olanda și a treia oara 2 luni la Kosair Children's Hospital in Louisville, Kentucky, SUA. In clinicile unde mi-am desfășurat activitatea am avut rezultate foarte bune după cum reiese și din scrisorile de recomandare primite la absolvirea acestor stagii.

In Romania abilitățile mele profesionale și de comunicare au fost validate de către două societăți naționale în care am fost ales, prin vot, membru în conducerea acestora: Societatea de Pediatrie din Romania în 2013 (membru al Consiliului Național al SRPed) și Societatea Romana de Pneumologie din 2010 (membru al Consiliului din 2010, reales în 2014 si președinte al secțiunii de Pneumologie pediatrica din 2020). Proiectul meu educațional "Spitalul Virtual pentru Copii" - SVC® înființat acum 3 ani a strâns peste 200.000 urmăritori și a fost recunoscut cu Premiul special la Gala COPAC 2018, cu premiul 1 la Competiția Europeana de Comunicare "Vaccine Champion", cu Titlul "Vaccine Hero 2019" de la Organizația Mondială a Sănătății, biroul Europa și cu titlul de "Medicul anului" la RoHealth Awards 2020.

Din decembrie 2020 am fost numit ca expert pediatru in cadrul CNCAV (Comitetului național de coordonare a activitătilor privind vaccinarea împotriva COVID-19).

### COMPETENȚE DOBÂNDITE LA LOCUL DE MUNCĂ

#### Competențe dobândite la locul de muncă

Datorită formării mele chirurgicale din timpul studiilor universitare și din stagiatură am fost selectat pentru a deveni instructor PALS [Pediatric Advanced Life Support] in 1999 de către echipa coordonată de către Prof George Rodgers de la Kosair Children's Hospital și University of Louisville, Kentucky, absolvind cursul destinat instructorilor. Ulterior am fost recertificat la Erasmus University din Bruxelles, Belgia sub îndrumarea prof Florence Otte in 2007 [diploma EPLS 32-07-02866-04-08 a Comitetului European de Resuscitare].

In cursul acestor 15 ani de predare a cursului PALS [peste 60 de serii, peste 1500 de cursanți] am ajuns la un nivel de performantă ce a fost recunoscut de către comitetul de organizare al CIMU 2014 [Primul Congres Interdisciplinar de Medicină de Urgență] prin invitarea mea ca moderator al secțiunii "pacientul critic pediatric, secțiunea II" și CIMU 2015 [Al doilea Congres Interdisciplinar de Medicină de Urgență, Cluj]. In teza mea de doctorat am studiat o cale nouă de acces vascular la copilul critic, dezvoltând o strategie alternativă de obținerea unei căi de acces pe calea abordului intraosos.

In tot acest interval am publicat peste 80 de articole si capitole de tratate medicale, având peste 400 de referințe bibliografice citate, un h-index de 8 și un i-10 index de 7, atat in Web of Science cat si in Google Scholar.

### **ALTE COMPETENȚE**

#### Alte competente

Hobby-urile mele sunt fotografia, muzica clasică (simfonică și opera) și drumețiile. In cursul pregătirii mele școlare am absolvit, în cursul ciclului gimnazial, cursurile Scolii de Arte Plastice nr 2 din București. Prin aceasta am dobândit calitățile necesare pentru a realiza prezentări ilustrate sugestiv, abilitate care m-a ajutat foarte mult în activitatea didactică.

#### **PUBLICAȚII**

### Safety of Adding Salmeterol to Fluticasone Propionate in Children with Asthma. - 2016

Long-acting beta-agonists (LABAs) have been shown to increase the risk of asthma-related death among adults and the risk of asthma-related hospitalization among children. It is unknown whether the concomitant use of inhaled glucocorticoids with LABAs mitigates those risks. This trial prospectively evaluated the safety of the LABA salmeterol, added to fluticasone propionate, in a fixed-dose combination in children.

N Engl J Med 375 (9), 840-9

# <u>Epidemiological, diagnostic, clinical, and therapeutic aspects of Brucella bacteremia in children in southern Israel: A 7-year retrospective study (2005–2011)</u>

- 2015

Our aim was to study the epidemiological, microbiological, diagnostic, clinical, therapeutic and outcome features of brucellosis in children <19 years of age in southern Israel during 2005–2011.

Vector-Borne and Zoonotic Diseases, 2015;15(3):195-201

# Rett-like onset in late-infantile neuronal ceroid lipofuscinosis (CLN7) caused by compound heterozygous mutation in the MFSD8 gene and review of the literature data on clinical onset signs

- 2015

NCL should be suspected and MFSD8 genetic testing should also be considered in patients with Rett like phenotype at onset and negative MECP2 mutation. Such cases should be carefully and frequently reevaluated in order to avoid delayed diagnosis and offer proper genetic advice to the family. In our knowledge, this might be the first case of CLN7 disease with Rett like onset described in the literature,

which developed typical vLINCL clinical phenotype after age 5.5 years. A short review of the literature showing NCL onset modalities is presented.

European Journal of Paediatric Neurology, 2015;19(1):78-86

# <u>Epidemiologic and microbiologic characteristics of occult bacteremia among febrile children in southern Israel, before and after initiation of the routine antipneumococcal immunization (2005-2012)</u>

- 2016

Little is known about the incidence and dynamics of occult <u>bacteremia</u> (OB) among infants/young children following the introduction of <u>pneumococcal conjugate vaccines</u> (PCVs) into the national immunization program in Israel in 2009–2010. The aim of this study was to characterize the epidemiologic and microbiologic picture of OB among febrile infants/children aged 3–36 months in southern Israel, before and after PCVs introduction.

Pediatrics & Neonatology 2016;57(5):378-384

# The adenoviral infections in children admitted to hospital with pneumonia, acute bronchiolitis or respiratory viral infections

- 2012

The objective of this study was to investigate the percent of infections with adenovirus (ADV) in children who had pneumonia, acute bronchiolitis or viral respiratory infections and were admitted to two pediatrics hospitals in Bucharest (Grigore Alexandrescu Hospital and Alfred Rusescu Hospital).

ROMANIAN ARCHIVES 2012;1:24-28

#### Role of optic microscopy for early diagnosis of Menkes disease - 2014

We report the case of a male patient with a normal development in the first three months of life, presenting for global regression, central axial hypotonic syndrome, pyramidal syndrome, focal epileptic seizures, and a particular aspect of the hair - almost absent, short, sparse, lightly colored, at age of five months, becoming coarse, twisted (kinky hair) by the age of 21 months. Different diseases associate similar neurological and macroscopic aspect of the hair (biotinidase deficiency, argininosuccinic aciduria, aminoaciduria, giant axonal neuropathy, trichothiodistrophy and Menkes syndrome). The microscopic aspect of the patient's hair showing normal hair, silver colored hair, hair shafts twisting 180°, trichoclasis, and trichoptilosis, was highly characteristic for Menkes disease. Diagnosis was further supported by the low concentration of serum copper and ceruloplasmin and exclusion of other metabolic disorders with similar macroscopic aspect of the hair. Molecular genetic testing by multiplex PCR indicated deletion of exon 22 in the ATP7A gene situated in Xq21.1 region, consistent with the clinical and biochemical phenotype. Physicians should use microscopic evaluation of the hair more often when suspicion of Menkes disease is raised, aiming a narrow further diagnostic workup and early positive diagnosis and genetic advice for the affected families.

Romanian journal of morphology and embryology 2014;55(3):953-956

### Pneumocystis pneumonia in infants - 2005

The goal of this study is to present the clinical and evolutive features of Pneumocystis infection (PCP) in infants admitted in our clinic. We summarise these aspects from 17 cases (10 male and 7 female infants), admitted between 1st January 2004 and 31st May 2005. PCP infection is rare. It represents 1,5/1000 children (17 cases of 11328 total patients) admitted in our hospital. The risk factors for PCP were age between 6 weeks and 6 months (average 3,38 months) low birth weight (average = 2428 grams), low weight for age, prolonged hospital admission (88,23% of the 17 infants were abandoned in nursery). Only one of them had HIV infection and none presented neoplastic disease. The most prominent clinical aspect was tachypnea (average 78 breath/minute, maximum 130). 16 (94,11%) had difficult breathing with chest indrawing and flaring of ala nasi. 14 (82,35%) had generalised cyanosis. Only two (11,72%) infants had fever. Radiologic aspects were evocative, with diffuse pulmonary involvement in almost all cases (88,23%), 6 infants (35,29%) had pneumothorax and 2 (11,76%) presented pneumomediastinum. Positive diagnosis was made by microscopic examination of secretions from endotracheal tube aspiration (Grocott methenamine silver stain and Romanowsky stain). 14 infants were ventilated with a good outcome--12 surviving infants (85,7%). All infants had a full course of intravenous Co-trimoxazole. The deceased infants had more risk factors--congenital heart disease 1 case, severe cerebral palsy with organic epilepsy 2 cases. The apparent increase of PCP cases can be related to the number of abandoned children in Romanian pediatric hospitals and nurseries.

#### Features of severe asthma in young children from Romania. - 2014

Asthma is the most frequent chronic disease of childhood. In spite of significant improvement of treatment options and diagnostic tools, asthma remains in many patients uncontrolled. The term of "severe asthma" seems to be rather a large umbrella for a heterogeneous group of diseases. This paper is presenting our experience in two respiratory disease clinics that evaluate asthmatic children. Current study was designed to test an algorithm for daily practice in a special group of patients: children with previously diagnosed asthma or recurrent-wheezing, evaluated by family physician or pediatrician as severe disease ("Asthma Decalogue in Children"). Out of 313 referrals (during a six months inclusion time) we had 202 children completing study per-protocol. 49 (22.69%) had severe disease, but only 8 had severe asthma (3.7% of total patients and 18.6% of severe patients). They were older, with less male predominance and with more frequent rhino-conjunctivitis and D vitamin deficiency than other asthmatic children with less severe disease. Asthma Decalogue in Children seems to be an efficient tool to differentiate severe asthma from the rest of children with reactive airway diseases.

Pneumologia (Bucharest, Romania) 2014;63(1);44-47

# <u>Social media education decreases unscheduled outpatient visits in paediatric asthma patients</u> – 2017

Inner-city paediatric asthma patients experience a significant increase of unscheduled and emergency department visits if they are not included in a continuous monitoring and educational program. Parental education represents a corner-stone of complex approach in these patients. The aim of our study was to document outcome of a structured parental involvement in management of asthmatic children.

Archives of Disease in Childhood 2017;102:Suppl2 A4-A4

# STUDY ON PARENTAL PERCEPTION AND APPROACH REGARDING COMMUNITY ACQUIRED PNEUMONIA IN PRESCHOOL CHILDREN FROM ROMANIA

\_ 2018

Community acquired pneumonia is a common disease that accounts for 16% of all deaths in children aged 5 years or younger. The purpose of the study was to identify potential modifiable factors in relation with parental perception of pneumonia management in children. Outlining such factors would allow development of approaches in order to reduce pneumonia-associated morbidity.

Romanian Journal of Pediatrics 2018;67(2):68-74

# Monitoring of excess body weight in children in the emergency department of a tertiary pediatric hospital in Bucharest, Romania

- 2021

Excess body weight in children has become a public health issue in most countries. The aim of our study was to determine the prevalence of overweight and obesity in children over two years of age who presented at the Emergency Department of a tertiary pediatric hospital in Bucharest, Romania. A total of 335 children aged 2 to 18 years were included in our study. A quarter of them had above normal body mass index values, 7.5% were overweight and 18.5% obese. Also, when measuring blood pressure, we observed increased values in 29.3% (n=98) of them. Among children with excess body weight, nearly a half (49.4%, n=47) had higher than normal blood pressure values.

doi: 10.26574/maedica.2021.16.3.389

Link www.ncbi.nlm.nih.gov/pmc/articles/PMC8643556/pdf/maedica-16-389.pdf

#### Streptococcal pharyngitis in children: A tertiary pediatric hospital in Bucharest, Romania - 2021

We conducted a retrospective study among patients who presented to the ED, of the National Institute for Mother and Child Health "Alessandrescu-Rusescu", Bucharest, Romania, and were diagnosed by RADT with streptococcal pharyngitis or streptococcal tonsillitis, between September 1, 2018, and August 31, 2019. Of 4627 patients diagnosed with acute pharyngitis/acute tonsillitis, 29.9% (n = 1383) had positive RADT for streptococcus. The majority were schoolchildren (5–13 years; 49.3%, n = 682) and preschoolers (3–4 years; 27.0%, n = 374) [Table 1]. Thus, the median age of the studied group was 5.3 years (interquartile range [IQR]: 3.4, (8.2)). There was a slight predominance of positive cases for *Streptococcus* among males (748 cases, 54.1%), and we did not identify significant differences (P = 0.663) in age between males (5.3 years [IQR: 3.4, (8.3)]) and females (5.3 years [IQR: 3.4, (8.3)]).

In conclusion, we identified an increased incidence of acute streptococcal pharyngitis. RADT is a useful and effective tool in the positive diagnosis of GAS pharyngitis, which leads to a rational use of antibiotics among children with sore throat and/or fever.

J Glob Infect Dis. 2021 Jul-Sep; 13(3): 154-155. doi: 10.4103/jgid.jgid\_59\_21

Link www.ncbi.nlm.nih.gov/pmc/articles/PMC8491814/pdf/JGID-13-154.pdf

#### Biologicals in childhood severe asthma: the European PERMEABLE survey on the status quo - 2021

Severe asthma is a rare disease in children, for which three biologicals, anti-immunoglobulin E, anti-interleukin-5 and anti-IL4RA antibodies, are available in European countries. While global guidelines exist on who should receive biologicals, knowledge is lacking on how those guidelines are implemented in real life and which unmet needs exist in the field. In this survey, we aimed to investigate the *status quo* and identify open questions in biological therapy of childhood asthma across Europe.

We interviewed 37 experts from 25 European countries and Turkey and found a considerable range in the number of children treated with biologicals per centre. All participating countries provide public access to at least one biological. Most countries allow different medical disciplines to prescribe biologicals to children with asthma, and only a few restrict therapy to specialised centres. We observed significant variation in the time point at which treatment success is assessed, in therapy duration and in the success rate of discontinuation. Most participating centres intend to apply a personalised medicine approach in the future to match patients *a priori* to available biologicals.

Substantial differences exist in the management of childhood severe asthma across Europe, and the need for further studies on biomarkers supporting selection of biologicals, on criteria to assess therapy response and on how/when to end therapy in stable patients is evident.

ERI Open Research 2021 7: 00143-2021; DOI: 10.1183/23120541.00143-2021

# <u>Urinary tract infections in children: clinical and antimicrobial resistance data from Bucharest area, Romania</u>

- 2021

Urinary tract infections (UTIs) are among the most common bacterial diseases of childhood with an increased frequency in infants and young children. A total of 264 children were included in the analysis. Females (71.6%, n=186) and infants (52.7%, n=139) were more commonly affected. The recurrence rate was 27.7% and was positively associated with the presence of renal malformations. Age under 1-year, increased leukocyte and neutrophil counts, and elevated C-reactive protein were associated with hospitalization. *E. coli* (80.3%, n=212) was the main etiological agent isolated, followed by *Proteus mirabilis* (9.8%, n=26) and *Klebsiella* spp. (6.4%, n=17). We identified increased resistance for all germs to common antibiotics used in pediatrics: ampicillin, amoxicillin/clavulanate, cefuroxime, ceftriaxone, and trimethoprim/ sulfamethoxazole.

We identified an increased resistance of uropathogens to antimicrobials commonly used in children. Reporting antimicrobial resistance from real-world clinical practice is necessary for accurate mapping and continuous updating of initial treatment recommendations until antibiogram results are received. In Romania and other countries, extensive studies are needed to follow up uropathogen resistance in both children and adults.

Germs. 2021 Dec; 11(4): 583-591.

#### "Red throat" or acute pharyngitis - challenges in real life clinical practice - 2021

Our clinical experience in Romania has shown that "red throat" is one of the most common diagnoses provided to febrile children (with or without sore throat) and one of the main drivers of antibiotic prescription. Is "red throat" a disease? Romanian doctors often explain the diagnosis of acute pharyngitis to parents with the expression "red throat". However, we believe that this label is too often used and does not always reflect the real diagnosis. The clinical examination of a febrile child can often reveal hyperemia of the tonsils and pharyngeal mucosa as result of general vascular changes during an inflammatory process. This is not necessarily equivalent to acute pharyngitis. The final diagnosis is a complex puzzle built on the patient's other clinical signs and symptoms.

A diagnosis that may seem easy to provide can be a major challenge for the clinician, especially in the current pandemic when parental attitudes toward the child with acute signs of illness have changed. The history and full clinical examination play an important role in guiding the therapeutic measures we take. The use of clinical scores can increase parental compliance (especially if calculated face-to-face) when deciding that a RADT is needed or when prescribing treatment.

Germs. 2021 Sep; 11(3): 351-353.

### <u>First Case of COVID-19 Treated with Monoclonal Anti-Spike Antibodies in a Patient with Cystic</u> Fibrosis in Romania

- 2022

Patients with chronic lung conditions, including cystic fibrosis, may be prone to severe COVID-19. Therefore, therapeutic intervention should be prompt and tailored to all associated comorbidities. We report the case of a 17-year-old male adolescent with cystic fibrosis and multiple chronic conditions

(bronchiectasis, exocrine pancreatic insufficiency, chronic multidrug resistant *Pseudomonas aeruginosa* colonization, nasal polyposis, chronic sinusitis, ventricular extrasystoles and multiple drug allergies), who presented with an acute episode of productive cough, and was confirmed with moderate COVID-19 based on positive RT-PCR for SARS-CoV-2 and lung imaging showing isolated foci of interstitial pneumonia. Intravenous treatment with the monoclonal antibody cocktail casirivimab and imdevimab was administered. The evolution was favorable, with rapid remission of the inflammatory syndrome and gradual decrease of cough, without progression to severe or critical COVID-19, but with complications such as repeated hemoptysis, which was due to the patient's underlying conditions, and which required close monitoring for timely adjustment of the patient's chronic treatment.

Diagnostics 2022, 12(1), 137; https://doi.org/10.3390/diagnostics12010137

### <u>Liver Transaminases in Pediatric Adenovirus Infection—A Five-Year Study in Two Major Reference</u> Centers from Romania.

-2023

Human adenovirus causes infections with a very heterogeneous clinical picture, and children are often the most frequently affected group. Interest in adenovirus has increased with the 2022 outbreak of severe acute hepatitis of unknown aetiology as human adenovirus was considered as one of the possible etiological agents. We conducted a retrospective study over a 5-year period in two major tertiary hospitals in the Romanian capital with the aim to characterize the clinical picture and the dynamics of liver function tests in children with confirmed adenovirus infection. The study included 1416 children with a median age of 1.1 years (IQR: 0.3, 2.3 years). Digestive symptoms were predominant in 95.2% of children, mainly diarrhoea (90.5%) and vomiting (50.5%), and 38.0% had respiratory symptoms. Increased transaminases were identified in 21.5% of patients. Age over 1 year, lethargy, vomiting and dehydration significantly increased the odds of liver cytolysis independent of other risk factors such as chronic conditions or coinfections. Aspartate aminotransferase (AST) was more commonly increased compared to alanine aminotransferase (ALT). Only six children had transaminase increases above 500 U/L, three of which had co-infections with rotavirus, Epstein-Barr virus (EBV), or respiratory syncytial virus (RSV). Liver function tests should be part of routine monitoring for paediatric patients with adenovirus infection. The current study fills a gap in current knowledge related to the frequency and the extent of liver involvement in human adenovirus infection among paediatric patients.

Săndulescu O, et al. 2023, Microorganisms 11(2):3 02.

#### Laboratory Findings in Children with Excess Body Weight in Romania. - 2023

Background and Objectives: Childhood obesity has been increasing at a worrisome pace and emerging as a non-infectious pandemic in the paediatric population in recent years. Raising awareness on this problem is of utmost importance, in order to take action to control body weight from an early age. *Materials and* Methods: We performed a retrospective study among overweight or obese children evaluated on an outpatient basis in the Department of Paediatric Endocrinology of a tertiary care hospital in Bucharest Romania in 2021 in order to identify laboratory changes occurring according to age and sex. Results: A total of 268 children were included in the analysis, with a median age of 10.9 years (IQR: 8.3, 13.3 years); 61.8% were obese and 38.2% overweight. We identified a subclinical pro-inflammatory status characterized by increased neutrophil count (12.7%) and increased C-reactive protein (16.4%). Biochemically, we identified the highest increases for uric acid (35.4%). More than half of the children included in the study had dyslipidaemia-specific changes: high low-density lipoprotein cholesterol (LDL) (50.0%), low high-density lipoprotein cholesterol (HDL) (58.9%) and increased triglyceride levels (12.7%), especially children with a body mass-index (BMI) percentile above 95%. Increased thyroid stimulating hormone (TSH) was identified in 20.3% and low thyroxine (T4) level in 13.4%, especially in females. Conclusions: Early measures to control excess body weight are needed since preventing obesity is easier than treating it. However, this is often difficult to do in our country because parents frequently do not recognize the problem until it is advanced. Furthermore, doctors are not always adequately prepared and sometimes they do not have the support of the health systems to provide children in need with the adequate care. Educational strategies and awareness of issue should be revisited in current post-pandemic context that facilitates increase of obesity prevalence in children. Increase of efficient communication could be achieved by pointing to these objective findings.

Pascu BM, Miron VD, Matei ER, Craiu M. Medicina. 2023; 59(2):319.

# <u>Current and Future Therapeutic Approaches of Exocrine Pancreatic Insufficiency in Children with Cystic Fibrosis in the Era of Personalized Medicine.</u>

- 2023

This review presents current updates of pancreatic enzyme replacement therapy in children with cystic fibrosis based on literature published in the last decade and some special considerations regarding pancreatic enzyme replacement therapy in the era of new therapies, such as cystic fibrosis transmembrane conductance regulator modulator therapies. Few articles evaluate the efficacy of pancreatic enzyme

replacement therapy in the paediatric population, and most studies also included children and adults with cystic fibrosis. Approximately 85% of cystic fibrosis patients have exocrine pancreatic insufficiency and need pancreatic enzyme replacement therapy. Faecal elastase is the most commonly used diagnostic test for exocrine pancreatic insufficiency, although this value can fluctuate over time. While it is used as a diagnostic test, it cannot be used for monitoring the effectiveness of pancreatic enzyme replacement therapy and for adjusting doses. Pancreatic enzyme replacement therapy, the actual treatment for exocrine pancreatic insufficiency, is essential in children with cystic fibrosis to prevent malabsorption and malnutrition and needs to be urgently initiated. This therapy presents many considerations for physicians, patients, and their families, including types and timing of administration, dose monitoring, and therapy failures. Based on clinical trials, pancreatic enzyme replacement therapy is considered effective and welltolerated in children with cystic fibrosis. An important key point in cystic fibrosis treatment is the recent hypothesis that cystic fibrosis transmembrane conductance regulator modulators could improve pancreatic function, further studies being essential. Pancreatic enzyme replacement therapy is addressed a complication of the disease (exocrine pancreatic insufficiency), while modulators target the defective cystic fibrosis transmembrane conductance regulator protein. Exocrine pancreatic insufficiency in cystic fibrosis remains an active area of research in this era of cystic fibrosis transmembrane conductance regulator modulator therapies. This new therapy could represent an example of personalized medicine in cystic fibrosis patients, with each class of modulators being addressed to patients with specific genetic mutations.

Ritivoiu M-E, Drăgoi CM, et al - Pharmaceutics. 2023; 15(1):162.

# Prevalence, Antibiotic Susceptibility Profile and Associated Factors of Group A Streptococcal Pharyngitis Among Pediatric Patients with Acute Pharyngitis in Gondar, Northwest Ethiopia [Letter]

- 2023

We have read with interest the paper by Tadesse et al that was recently published in your journal reporting data on the prevalence and susceptibility profile of group A *Streptococcus* (GAS) isolates in children with acute pharyngitis in Ethiopia. Acute pharyngitis is very common in the paediatric population, and it has a significant impact within this age group. Antibiotic over-prescription is a major driver of antimicrobial resistance, and while susceptibility to penicillin is generally conserved in GAS, there are increasing reports indicating a reduction in antibiotic susceptibility to other antimicrobial classes.

A noteworthy example of related streptococcal species prone to acquiring resistance is that of *Streptococcus pneumoniae*, which have a high recombinogenic potential and are very competent in acquiring virulence and antibiotic resistance determinants through lateral gene transfer from other streptococci, particularly from commensal strains seen in asymptomatic carriage. Commensal GAS isolates also exhibit enhanced in vivo biofilm forming capacity, which in turn facilitates the genetic exchange process. *S. pneumoniae* poses a major clinical burden, being the etiologic agent of otitis media, pneumonia, meningitis, and other types of invasive pneumococcal disease, and potentially associated with high rates of antimicrobial resistance or tolerance, depending on the setting and geographical area. Gene transfer through conjugation from GAS to *S. pneumoniae* has been demonstrated for the macrolide efflux gene mef(l) and the chloramphenicol inactivation gene catQ, occurring in vitro at a frequency of  $1.7 \times 10^{-4}$ . While transfer of genetically encoded vancomycin resistance determinants has not yet been shown to occur in *S. pneumoniae*, it has been demonstrated for other Gram-positive cocci, and needs to be further explored.

In conclusion, continued careful monitoring of the resistance rates of streptococcal isolates retrieved from clinical practice is warranted, including GAS. To better inform future treatment decisions, this should be coupled with molecular analysis to assess the occurrence of genetically encoded resistance determinants, as well as their potential transferability to and from other microbial species.

Miron VD, Săndulescu O, Craiu M. Infect Drug Resist. 2023 May 8;16:2783-2785.