Dear Colleagues and Friends,

The natural history of EPA always brings fresh and interesting news for the European pediatrician. The Newsletter will keep its traditional look and cadence to which our recipients are accustomed. The Council met last month in Milano using the facilities given by the Italian Society for Pediatric Research to whom we express our gratitude. A dense session took place dealing with the growing aspects of our activities, among these were the rules for the Newsletter, but two things merit special attention. The first one is the advanced negotiations leading to the fact that EPA is now affiliated with The Journal of Pediatrics. The scientific level, the updated clinical focus and the wide distribution of this are three out of many well known characteristics, that run along with EPA growth. The second one is that the 6th Europediatrics (Glasgow, June 2013) will be a combined meeting together with the Royal College of Pediatrics and Pediatric Health, UK. This joint-venture with one of the most traditional and updated societies in Europe will give the expected results as one can see after looking at the scientific programme development. A possibility of supporting clinical or health studies is a commitment from the Council.

In this issue you will see in the Clinical Update section a special article on ‘The Management of cow’s milk allergy in infants’. Last year EPA carried out a survey on European primary care pediatricians about their management of CMA. After analyzing more than 700 valid responses a conclusion arose- the existence of some too flexible criteria lead to an over diagnosis which probably gives rise to an overtreatment. Please do not miss this very important breakthrough because of the work of the experts has flourished in this concise document which will give you updated information allowing a precise diagnosis and consequently a proper treatment. EPA and I personally, take this opportunity to express our gratitude to our colleagues, specialists in pediatric allergy for their important work. In this section of the next issue and complementing this basic document you will find an approach to CMA prevention/tolerance induction. This is a difficult task but something can be done for the at risk infant population.

Our Russian partners continue to be very active as can be seen in the News section, and we thank them for this necessary collaboration. Finally, EPA in its independent fashion, has taken on a series of new projects: Weaning/Complementary foods, you will soon find out the different trends in Europe and the divergence with the appropriate nutrition. The Strategic Pediatric Alliance for the Future Health of Children in Europe will also give us the real picture of our care. Other projects are also underway.

Our commitment with updating clinical knowledge will never end.

Manuel Moya
Editor of Newsletter

UPDATE IN PAEDIATRIC GENERAL PRACTICE
The management of food allergy in infants with special emphasis on cow’s milk allergy

Sten Dreborg, Ralf G. Heine, Arne Host, Eva-Maria Varga, Massimo Pettoello-Mantovani, Haluk Cokugras, Manuel Moya, and Andreas Konstantopoulos

In 2011, EPA conducted a pan-European survey on the current clinical practice among general paediatricians in their work with cow’s milk allergy. The results indicated possible gaps in the understanding of key symptoms and diagnostic tests, as well as on the treatment side. EPA thus assembled a global clinical expert team to define what good clinical practice could actually mean for primary care paediatricians. This article is a summary of the discussions and will be followed by an extended document with more detailed information.

Within the Western hemisphere, cow’s milk (CM) is introduced early in the diet of infants. Thus, cow’s milk allergy (CMA) appears early and earlier than other food allergies (FA). Later during infancy, many other foods such as hen’s egg, wheat, peanuts and fish may cause allergic symptoms. The pattern of food allergy in early childhood depends on the eating habits.

According to a recent survey by EPA, European primary care paediatricians (PCP) perceive that up to 47% of all infants have cow’s milk allergy (CMA), whereas paediatric allergologists (PA) find that only 1–3% of European infants have CM allergy (and only a few further percent having allergies to other common foods). Hence, most infants believed by PCPs to suffer from CMA do not react to an oral food challenge, and do not have CM allergy. Consequently, they should not be prescribed an elimination diet. In order to improve the management of this infant population, the following aspects should be considered:
**DIAGNOSIS**  
The diagnosis of a FA should consist of (Figure 1, 2):  
1. A detailed clinical history.  
2. Serum-IgE test using a well documented brand, to investigate possible IgE sensitisation, primarily to CM, hen’s egg, wheat and soy. In some areas also rice or peanut.  
3. Classification of the disease and a stepwise oral food challenge in a specialised office.  

Based on the clinical history and allergen specific IgE tests, the food(s) in question should be eliminated. Do not forget differential diagnoses and continue with steps 2 and 3.  

**1. Symptoms possibly indicating food allergy**  
In fact, any symptom can be caused by FA. In infants, the most common symptoms are from the skin (e.g. eczema or urticaria), from the GI tract (e.g. diarrhoea, abdominal pain, vomiting, bloody stools) or from the respiratory tract (e.g. rhinitis, otho-salpingitis).  

Immediate reactions to accidental exposure or to challenge tests within the first hour are most often caused by IgE antibody reactions. Reactions starting 1–2 hours after ingestion or later are most often caused by non-IgE mediated mechanisms that cannot be diagnosed by any available test other than oral provocation.  

**Food allergens in infancy.** Sensitisation appears in many infants who do not show any clinical symptoms. In most infants, low IgE antibody titres are transient. As mentioned, foods that are most often sensitizing are those dominating the food intake of infants. Thus, in westernized regions with a cow’s milk based diet/formulas, CM is the first sensitizing food. At the same time or during the following months, hen’s egg white and wheat appear as sensitisers. In some Anglo-Saxon countries, peanut plays an important role and in Asia and Southern Europe, rice is of importance.  

**Clinical histories.** The clinical history is useful in case of symptoms at the introduction of a food with immediate symptoms or symptoms/worsening over a few days. In breastfed infants, there is most often no direct association between the mother’s intake and the child’s symptoms. Foods taken daily by the breastfeeding mother or by the infant must be considered as possible cause of allergic manifestations despite the lack of a direct connection between intake and increased symptoms. It is important to stress the importance of continued breast feeding according to WAO guidelines. However, in exclusively breastfed infants, the mother’s diet should be restricted according to the

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**Figure 1.** The principal algorithm for FA diagnosis in infants with severe immediate or severe continuous symptoms, who should be referred to an S-PA. However, the PCP can order an s-IgE test and put the infant on an elimination diet, i.e. in case of possible cow’s milk allergy an eHF. If the mother is breast feeding she should completely avoid the food to which the child is IgE-sensitised. In cases where the child is not sensitised to suspected foods the breastfeeding mother should first avoid CM. When the eHF/elimination diet is not efficient, an AAF may be prescribed provided the infant is referred to an S-PA. Gray filled symbols indicate care by PCP’s, blue symbols handling by S-PA and red arrows referral to S-PA’s. No diet is indicated by green colour.

**Figure 2.** This algorithm illustrates the diagnosis and treatment of infants with slight symptoms that may be of allergic origin. The majority of these infants will not benefit from an elimination diet and should not have any long-term diet. Colouring as in figure 1. It is important to note that no diet should be given for longer periods of time, for infants with eczema or GI symptoms maximum 4 weeks, for those with urticaria no more than 2 weeks. If the infant has improved, then it should be referred to an S-PA for evaluation. Children with non-IgE mediated food allergy, i.e. eosinophilic esophagitis, eosinophilic gastroenteritis, enteropathy, enterocolitis etc. may need longer elimination periods and biopsies before and after the elimination period and after challenge. In case the infant does not improve, then it should be treated symptomatically. The majority of infants with symptoms of possible allergic origin are not food allergic and should not be given elimination diets. However, infants with persisting symptoms and with symptoms from 2 or more organ systems should be considered for elimination diet and further investigations by an S-PA. See further text.
elmination advice for the infant’s diet. Breast feeding should not be stopped and replaced by hypoallergenic formulas but in case of spontaneous weaning.

**Specific histories.** CMA often presents at the introduction of a CM formula causing immediate symptoms, but may also develop slowly without any definite connection with CM intake, e.g., during breastfeeding. Thus, the clinical history may be obvious but also without any obvious association to ingestion of dairy products. Babies with the latter history have more often non-IgE mediated symptoms. Wheat and other cereals are ingested daily after the introduction of bread or porridge and the same applies to rice. The exposure to peanut that is taken as peanut butter is also continuous but peanuts/peanut butter may also be ingested at intervals. Hen’s egg is mostly not taken on a daily basis. Thus, symptoms more often appear in connection with the intake of egg or egg containing foods and the same applies to fish that is taken now and then.

2. Tests for s-IgE

IgE sensitisation can be diagnosed by both in vitro s-IgE tests, skin prick tests or by prick-prick tests. However, only in vitro s-IgE tests should be used in primary care, since skin prick testing needs experience and continuous quality control (proficiency tests at regular intervals).

**In vitro s-IgE tests.** The sensitivity of in vitro s-IgE tests varies with brand and has been improved over time. Published data on the diagnostic value of different food allergen-specific s-IgE levels in relation to the results obtained by oral food challenges as the gold standard, are well established in a highly specialised setting, but are not valid in general paediatric practice.

**Tests for other mechanisms.** There are no reliable tests available for the routine testing for immune complex mediated or cell mediated allergy.

3. Classification and stepwise oral food challenge

**Criteria for referral.** Since food challenges in clinically sensitive children may be dangerous if not properly performed and the objective supervision of the result is crucial, infants with possible allergy to foods should be referred to a specialist in paediatric allergology (S-PA). In general, infants with anaphylaxis, moderate to severe eczema, or GI symptoms should be suspected to be food allergic.

If there are only few S-PA in the region, special agreements can be settled between the paediatric allergologist and a PCP, but the PCP should then be trained in the S-PA setting and adopt the same methods and criteria as the S-PA, and collaborate with the S-PA. If food allergy is suspected, then the patient should be prescribed an elimination diet, in infancy mostly an extensively hydrolysed cow’s milk formula, eHF, for a fortnight at least (Figure 1, 2). Patients with eczema improving on an elimination diet and those with severe GI symptoms, irrespective of the result of the IgE test, should be referred to a specialist for evaluation (5–10%). Infants with only mild symptoms can be handled by a PCP.

**Oral food challenges in infants.** In young children below 2–3 years of age, an open controlled oral food challenge should be used to diagnose FA, i.e., the infant should be observed by trained personnel, not by the family. In case symptoms are questionable, a double blind placebo controlled oral food challenge should be performed. Both during open and double blinded placebo controlled challenges, the observation and the documentation of the symptoms should be performed by a trained professional. Thus, provocation should be performed in a setting of an S-PA or a trained PCP.

Investigation of possible FA should be initiated depending on the symptoms leading to the consultation, i.e., eczema, urticaria and different GI symptoms. In general, infants with persisting symptoms and infants with symptoms from 2 or more organs systems should be referred for FA diagnostic approach. Infants with mild symptoms can be treated by the PCP, whereas infants with intermediate and severe symptoms should be given an elimination diet, primarily an eHF and then referred to a S-PA for proper diagnosis, including skin prick and challenge tests. This requires an efficient referral system and open contacts between the PCP and the S-PA.

**TREATMENT OF INFANTS WITH SYMPTOMS OF POSSIBLE FOOD ALLERGY**

After diagnosis by the S-PA, the follow up of allergic infants (maximum 6–7%) should be by an S-PA or by a trained PCP in close collaboration with an S-PA. On the other hand, the majority of infants with symptoms that may indicate food allergy do not have any proven allergy and should therefore be treated symptomatically by the PCP. The principle should be to deal with all non-severe cases of skin or GI origin within the PCP system, i.e., all infants with mild symptoms should be treated symptomatically by PCPs.

First, those with eczema should get instructions for intensive use of ointments. Then, it is important for the PCP to acquire the skills to instruct parents how to apply ointments, select the most suitable clothing for infants with eczema, wash and bathe the child, and to understand the role of non-allergenic irritants etc. Finally, in infants with mild GI problems, causes other than allergy should be thoroughly investigated.

In case the conventional treatment is not effective, the infant should be referred to a specialist, S-PA, paediatric gastroenterologist, dermatologist with special interest in eczema, specialist in paediatric respiratory medicine or an ENT specialist.

**About the clinical support team behind this article:** Professor Sten Dreborg, Uppsala University, Sweden, is a leading international expert in cow’s milk allergy. Doctor Ralf G. Heine, University of Melbourne, Australia, is a leading international expert in cow’s milk allergy. Professor Arne Host, is a leading international expert in cow’s milk allergy. Professor Eva-Maria Varga, is a leading expert in general paediatric allergy. Professor Massimo Pettoello-Mantovani, University of Foggia and the Secretary General of EPA. Professor Haluk Cokugras, is a general paediatrician highly trained in cow’s milk allergy and active member of the Turkish paediatric Association. Professor Manuel Moya, Vice President of EPA and Editor of the EPA Newsletter, University M. Hernandez, Alicante, Spain. Professor Andreas Konstantopoulos is the President of EPA.

**Acknowledgement.** Pfizer Nutrition sponsored the EPA Cow’s Milk Allergy Initiative which was independently developed and controlled by the European Paediatric Association.

**REFERENCES**


NEWS FROM EUROPE

Child Health at the Russian Academy of Medical Sciences: 248 years of history, development and prosperity

PART 1. HISTORY

Along the lines of the interesting article about the history of paediatrics in Europe, raised by Professor Rosa Ballester in one of the previous issues of the EPA Newsletter, Russian pediatricians are pleased to offer you an essay about the history of pediatrics in Russia.

In the XVI–XVII centuries pediatrics hadn’t emerged as a distinct discipline but prominent Russian public figures and scientists were interested in the questions of the child health care. For example, the brilliant Russian scientist Mikhail Lomonosov (1711–1765) wrote in particular about the need for state control over the maternity and postpartum women care in order to decrease infant mortality in his treatise «On the propagation and preservation of the Russian people». The principal aims for protecting the life of newborns and the needs for orphans houses development were outlined in this treatise. It is important to note here that the idea of the necessity of orphan’s houses became one of the main concerns since the epoch of the great Russian reformer Emperor Peter the First (1672–1725).

I.I. Betsky, the great statesman of the XVIII century, became the founder of the first Russian Imperial Orphan’s House in Moscow. The story of the creation, development and its reformation into the Scientific Center of Children’s Health — the main federal center of the Russian pediatric society, — will be presented below.

The date of September 1st 1763, which marks the birthday of the Moscow Imperial Orphan’s House can be considered as a historical day in the formation of Russian national pediatrics. Its creation marks the birth of the state system of children’s health care in our country.

The Moscow Imperial Orphan’s House (end of the XVIII century)

Ivan Betsky (1704–1795) — founder of the Imperial Moscow Orphan’s House. In September 1st 1763 the Russian Empress Catherine the Great had signed the Manifest of establishing «The Orphan’s House» with an affiliated hospital for infants and a hospital for poor women in childbirth, located in the center of city, which became known as the Moscow Imperial Orphan’s House. Its motto «feeds the birding without sparing itself» is still preserved in the form of a sculpture of a pelican feeding its nestlings in the gable of the historical building.

The gable of the Moscow Founding Hospital (XXI century)

Since the first days I. Betsky, Ch. Mertens — the first head physicians, and their colleagues introduced such fundamental but nevertheless uncommon for that period principles of medical care such as: state approach and patronage of the heads of state; the continuity of obstetrical and neonatal services — initially the Moscow Orphan’s House included a maternity hospital and a hospital for infants; the observance of sanitary and epidemiological measures during epidemics. Remarkable that during the plague epidemic in Moscow (1771–1772) a special quarantine isolation department was introduced for newly entering orphans. Children in this department stayed under the supervision of doctors for about a month and only in the absence of plague signs of the disease could be transferred to join the other healthy orphans. All other patients were examined every day and were isolated in a separate infection department if the first symptoms of plague were found. Such strict preventive steps ensured the absence of the epidemic among inmates. These coordinated efforts formed the basis of the first scientific monograph authored by Dr. Mertens «Traite de la peste contenant l’histoire de celle qui a regne a Moscou en 1771» in which he described not only the diagnostics and treatment of plague, but also, for the first time, proved the necessity of disease prevention.

During the same period of time the vaccination became one of the main preventive activities of the Hospital. Only 4 years after it had been discovered by Professor E. Jenner (England) the method of vaccination against smallpox was successfully introduced in the Moscow Orphan’s House.

In the next few decades the institution experienced a lot of dramatic historical moments. For example, during the war with Napoleon, when the French army occupied Moscow, the Imperial Orphan’s House was saved by the heroic efforts of the staff, doctors and nurses, because during that time not only the inmates were treated in the House but also wounded Russian and French soldiers, as well as the children of French officers. The basic commandment for doctors to work exclusively in the interests of a patient regardless of gender, race, nationality, language, origin, property and official status, religion or faith was again confirmed.

Newborn’s Department Vaccination Center. With time The Moscow Imperial Orphan’s House has collected valuable material about the course of child diseases and methods of their treatment, the physicians investigated new directions of clinical and social pediatrics actively. Since the second half of the 19th century the House began to maintain a record of child morbility and mortality, their dynamics and half of the 19th century the House began to maintain a record of child morbility and mortality, their dynamics and main causes, and became the main vaccination center in Russia. Since 1805 it was asked to produce and dispatch the smallpox vaccine all over the country, to provide immunization to all who required it and to train all who were interested for vaccination.

It also became the first medical center where obstetrics were one of the main activities and were studied as a discipline. Thus, the Moscow Imperial Orphan’s House deserves by right the honorary title of the «cradle» of the national pediatrics and obstetrics.

After the Russian October Revolution of 1917 the emerging Soviet health care system focused on maternal and child health. The basic principles of the Soviet and in the future modern Russian pediatric health care system was founded by the great pediatrician academician professor G. Speransky. The Imperial Moscow Orphan’s House was gradually reorganized into the Institute of Pediatrics:
**Professor G. N. Speransky.** The Institute of Pediatrics was headed by the most famous Russian pediatricians: academician G. Speransky (1947–1951), professor M. Kazantseva (1951–1954), academician O. Sokolova-Ponomareva (1954–1960), academician M. Studenikin (1960–1998), and since 1998 till the present day — academician A. A. Baranov.

The Institute continued to develop as a diversified research clinical pediatric institution. In the 1960-s the Departments of Nephrology, Hematology, Allergology, Surgery, Gastroenterology, labs of Functional Diagnostics, of Clinical Virology, Department of Therapeutic Physical Training and Sports Medicine and many others were created for the first time. The infection department worked actively and made a considerable contribution to the significant decrease of morbidity and mortality due to vaccination. Consequently, the Institute of Pediatrics started its development as a hospital with multiple specializations.

**PART 2. PRESENT OF SCIENTIFIC CENTER OF CHILDREN’S HEALTH**

So, in 1998 in accordance with the decision of the Presidium of Russian Academy of Medical Science Scientific research institute of pediatrics (with 370 beds for in-clinic patients) merged with Scientific research institute of hygiene and health of children and adolescents to form Scientific Center of children’s health. From 2006 the structure of SCCH included a newly created establishment — Scientific research institute of preventive pediatrics and rehabilitation treatment with the consultative-diagnostic and rehabilitation out-patient department for 120 beds.

Understanding the importance of child health care in modern society, the desire to develop and implement new approaches as well as committal to the traditions of Russian pediatric school lead to creation the unique multidisciplinary pediatric center that now has all the capabilities to support the entire cycle of pediatric care to children from birth under 18th years: out clinic, hospital and rehabilitation stages (Figure 1).

**Baranov Alexander Alexandrovich** — director of Scientific Center of children’s health, vice-president of Russian Academy of Medical Science, academician of Russian Academy of Medical Science, professor.

Professor A. Baranov — the famous Russian scientist, pediatrician, prominent organizer of public health care, he is one of the founders of scientific research for pediatric gastroenterology, ecopathology, preventive pediatrics.

Under the leadership of professor Baranov the Concept of pediatric care in Russian Federation was developed and approved by the Russian Government. Professor Baranov has also earned the respect of worldwide pediatric leaders. The Scientific center under his leadership has fruitful cooperation with International pediatric association, European Pediatric Association, American Academy of pediatrics, leading children’s hospitals in China, Germany, France, Turkey and many other countries. Since 2007 professor Baranov —
NEWS FROM EUROPE
EPA Vice-President’s visit to the first children’s hospital built in Sudan

Professor Gaafar Suleiman founder of the first Children Hospital which carries his name in Sudan, located in Khartoum and Professor Manuel Moya at the entrance before visiting and meeting the staff. The nutritional aspect of the children staying in the hospital was deeply discussed apart from the format lecture on cow’s milk allergy given by Professor Moya.

In December last year, the annual clinical practice conference Excellence in Paediatrics (EiP 2011) took place in Istanbul. The conference was highly supported by the Host Country Committee in Turkey, and by the National Turkish Paediatric Association.

Lectures in this area attracted numerous delegates both individually and together, and we were proud to learn about their high comparative rating also in the post-conference surveys.

In addition to the lectures, there was also a small clinical expert group meeting, a so called KOL session, in dermatology. The focus of that meeting was on emollient use on infant skin. leading international experts discussed whether to use emollients at all on infants, what the benefits may be, and what could characterise a good emollient for infants.

All in all, last year’s event was a real success. While there are still some months to go until December this year, we already look forward to the upcoming conference in Madrid in 2012.
ANNOUNCEMENT
European Paediatric Association (EPA/UNEPSA)

Join the most extensive paediatric network in Europe!
Since the launch of the individual membership scheme, the European Paediatric Association (EPA/UNEPSA) embraces a constantly increasing number of individual members from all over Europe.
EPA/UNEPSA welcomes all doctors who are certified as paediatricians in Europe and are members of their respective National Paediatric Society/Association participating in EPA/UNEPSA.

By joining EPA/UNEPSA, you gain access to a network of 41 national European associations and open yourself to a new world of opportunities.

Benefits
The individual membership is offered at a privileged 50 Euro annual fee and encompasses a set of benefits that aim to provide value to the wide community of European paediatricians.
• On line access to the The Journal of Pediatrics is a core benefit of individual membership to our association and we are excited by the prospect of making such a valuable resource widely available to paediatricians across Europe.
• Our members will enjoy reduced registration fees to Europaediatrics as well as to other events organised by our Association.
• The quarterly e-newsletter aims to be a source of current information relevant to the interests of European paediatricians.
• Finally, our members will find in our new website a valuable tool and resource (access to the members-only section, members’ forum and working groups, access to educational programmes, complimentary or privileged prices for additional on-line services, etc.)

Individual membership is offered on an annual basis starting on the 1st January of each year and ending on the 31st of December.
You may apply on line for an individual membership. Please visit our website www.epa-unepsa.org for more details and to fill out a registration form.
We look forward to welcoming all of you in EPA/UNEPSA!

CALENDAR OF EVENTS
List of upcoming conferences in 2012

EPA-UNEPSA MEETINGS

6th Europaediatrics Congress jointly held with the Royal College of Paediatrics and Child Health
5–8 June 2013, Glasgow, United Kingdom

MEMBER SOCIETIES' MEETINGS

Summer School of the Romanian Society of Paediatrics
3–7 September 2012, Moeciu-Brasov, Romania

Annual Congress of the Hungarian Paediatric Society
6–8 September 2012, Tapolca, Hungary

108th Annual Conference of the German Society of Paediatrics (DGKJ)
12–16 September 2012, Hamburg, Germany

13th Annual Congress of the Portuguese Society of Paediatrics (SPP)
11–13 October 2012, Troia, Portugal

X Congress of the Croatian Paediatric Society
18–21 October 2012, Pula, Croatia

Paediatric Days in Helsinki
25–26 October 2012, Helsinki, Finland

NVK-Congress 2012-Dutch Association of Paediatrics
31 October — 2 November 2012, The Netherlands

OTHER PAEDIATRIC MEETINGS IN EUROPE

First Balkan Congress of Pediatrics
31 May — 3 June 2012, Plovdiv, Bulgaria

3rd congress of European Confederation of Primary Care Paediatricians (ECPCP)
22–24 June 2012, Strasbourg, France

Excellence in Paediatrics 2012
28 November — 1 December 2012, Madrid, Spain
### INFORMATION

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