

TO

**The chairman of a scientific jury
determined by Order No. 19-843 / 30.11.22
of the Executive Director and
The procurator of "Ajibadem City Clinic
UMBAL Tokuda" EAD.**

On your Protocol №1

Attached I present: REVIEW for the competition for the academic position "Associate Professor" in the field of higher education 7. Health care and sports, professional direction 7.1 Medicine and scientific specialty "Pediatrics" for the needs of the Pediatrics Clinic of "Ajibadem City Clinic UMBAL Tokuda" EAD , announced in SG no. 82/14.10.2022

Reviewer: Prof. Dr. Stefan Nedev Stefanov, MD

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MEMBER OF THE SCIENTIFIC JURY, ACCORDING TO ORDER No. 19-843 /30.11.22y, on the basis of art. 4, para. 2 and art. 29a of ZRASRB art. 2, para. 2, art. 62, para. 1 and para. 2 of PPZRASRB, Article 61 of the Regulations for the Development of the Academic Staff at "Ajibadem City Clinic UMBAL Tokuda" EAD and Decision of the Scientific Council (Protocol No. 44/24-11.2022).

The competition for the academic position "Docent" in the scientific specialty "Pediatrics" has been duly announced.

The review of the materials is based on the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Rules for its Application and the Rules for the Terms and

Conditions for the Acquisition of ONS and Occupancy of AD in "Ajibadem City Clinic UMBAL Tokuda" EAD, Sofia.

One participant, admitted by the Commission on documents, appeared at the announced competition, namely Dr. Kalin Yordanov Lisicki, MD, Head of Pediatric Clinic, "Ajibadem City Clinic UMBAL Tokuda" EAD.

All tender documents are submitted according to the requirements of the regulations, with the necessary supporting material.

PRESENTATION OF THE CANDIDATE

Dr. Kalin Yordanov Lisicki, MD,

Biographical data and professional development

Dr. Kalin Lisicki was born in 1958, graduated from secondary education in 1976, and medicine in 1984 at the Faculty of Medicine, MA, Sofia with excellent results.

Career development:

From 1984 to 1987, he worked as a pediatrician in the Regional Hospital - Dupnitsa.

From 1987 to 2007, he was successively an assistant, senior assistant and chief assistant in the Pediatric Rheumatology Clinic at the University Children's Hospital (NIH, SBALDB), MU, Sofia.

From 2007 to 2014, he was a doctor at "Ajibadem City Clinic UMBAL Tokuda" EAD, Sofia, Pediatrics Clinic, and from 2014 to the present he was the Head of the Pediatrics Clinic in the same hospital.

Acquired 2 specialties - in children's diseases in 1991 and children's rheumatology - in 1997.

In 2022 obtained the ONS "Doctor" at the Ministry of Education, SU "St. Kliment Ohridski" after defending a dissertation on the topic "Macrophage activation syndrome in childhood - analysis of clinical and laboratory changes, evaluation of the diagnostic approach and therapeutic effectiveness".

Specializations:

- Pediatrics - 2 months, under the TEMPUS program (1997) in Paris, France.
- Has professional skills in joint ultrasound and joint punctures.
- Certificate in Health Management (2001)
- Certificate in Abdominal Ultrasound (2002).

Member of: Bulgarian Medical Association, Bulgarian Pediatric Association (BPA), Bulgarian Society of Rheumatology (BDR), PRINTO, European League Against Rheumatism, Organization for International Research in Pediatric Rheumatology,

He speaks French and Russian language level B2 and English language level A2.

EVALUATION OF EDUCATIONAL AND TEACHING ACTIVITY

Dr. Kalin Lisicki has many years of teaching experience.

In the period 1987-2007, he was an assistant - successively junior, senior and head in the Department of Pediatrics, MF, MU-Sofia.

Since 2007, as a pediatrician, and since 2014, as Head of the Pediatric Clinic of "Ajibadem City Clinic", he participates and organizes study visits and lectures for medical students and interns, pediatric rheumatology specialists, pediatric specialists and general practitioners .

According to the attached reference, there is the following study load:

For the period 2018/2022, there is a total study load with specialists totaling 1520 equivalents. o'clock. Dr. Lisicki's lectures and study visits are met with interest, as he always manages to present up-to-date and interesting information on the discussed cases and topics.

There are 4 participations as an independent author in collective monographs.

Therapeutic and diagnostic activity

Dr. Kalin Lisicki is a clinician with over 30 years of experience in the field of pediatrics and pediatric rheumatology. He is a long-established and recognized clinician with great experience, which is also evident in his scientific activity. Works thoroughly, precisely and in detail, with a very good knowledge of clinical and organizational issues. A specialist sought after by patients and colleagues for consultation in difficult clinical cases. He is the authority and support of his team, who appreciates the qualities of his clinic manager, who knows how to organize them for teamwork.

EVALUATION OF SCIENTIFIC RESEARCH ACTIVITY

Dr. Lisicki submits the following scientific works for participation in the competition:

Publications:

- A total of 48 scientific publications
- 31 in national and 2 in international journals, all referenced and indexed in world-renowned databases of scientific information
- 13 publications - in non-refereed Bulgarian journals
- 2 - in non-refereed international journals
- dissertation work for obtaining the educational and scientific degree "Doctor"

- 4 participations as an independent author in collective monographs, and in 2 textbooks he is the independent author of a total of four chapters.

First author is in 33% of all publications, second author in 19%, third and subsequent author in 35%.

Dr. Lisicki has 19 participations/reports in scientific forums - congresses and conferences, and in 18 (95%) of them he is the first or only author.

Citations:

- A total of 41 citations have been established in the reference from the CMB - 23 in Bulgarian sources and 18 in international sources - 15 in Scopus and 3 in Web of Science (Clarivate).

- h-index - 2.

Habilitation work

Dr. Lisicki has presented 12 habilitation articles, which are referenced and indexed in world-renowned databases with scientific information.

The habilitation publications included in the list are a major contribution to modern pediatric rheumatology in terms of relevance and presentation of the candidate's clinical experience.

Competition metrics reference. Reference for compliance with the minimum national criteria for occupying the academic position "Docent", according to Table 1. Minimum required points by groups of indicators for the various scientific degrees and academic positions for District 7. Health care and sports, Professional direction 7. 1. Medicine

Dr. Lisicki fulfills and exceeds the minimum requirements for scientific activity for holding the academic position of "associate professor", according to the Reference, namely:

Accordingly, by indicators:

- Indicator A – 50 points.
- Indicator C – 149 items.
- Indicator D – 339 items.
- Indicator D- 85 items.
- Indicator E – indicated as a non-applicable indicator.

Scientific and applied contributions and directions in scientific research activity:

Dr. Lisicki's scientific interests cover various areas in pediatrics and pediatric rheumatology. The personal contributions of Dr. Lisicki are described in the extended report of his scientific research activity in accordance with the requirements of "Ajibadem City Clinic UMBAL Tokuda EAD" - Sofia.

It is structured in four sections dedicated to the most current problems in pediatric rheumatology and pediatrics. In the works presented for review, scientific and applied results were achieved and problems were investigated with contributions in the following areas and

directions, namely: 1. Macrophage activation syndrome, 2. Arthritis and spondyloarthritis; 3. Systemic connective tissue diseases and vasculitis; 4. Others

I. Macrophage activation syndrome

In the dissertation "Macrophage activation syndrome in childhood - analysis of clinical and laboratory changes, evaluation of the diagnostic approach and therapeutic effectiveness", as well as in a number of articles (24, 26, 44), the author presented the clinical picture, diagnostic criteria and therapeutic behavior, and the conclusions and recommendations are based on a statistical analysis of 20 children with SMA.

The contributions of an original nature are the following: for the first time in Bulgaria, the data of patients diagnosed with macrophage activation syndrome in childhood are described and summarized; data on the age and gender distribution of the disease are presented and the provoking factors, clinical manifestations, laboratory changes and their significance in SMA are established; the changes in ferritin values in SMA and non-SMA patients are analyzed; the therapeutic regimens used to treat childhood macrophage activation syndrome and their effectiveness are compared.

Contributions of an applied nature. The use of the ferritin/ESR ratio is proposed as a rapid and effective method for differentiating SMA from non-SMA patients. The effect of the application of biological therapy with anti-IL-1-receptor antagonists is described and analyzed.

Contributions of a confirmatory nature. Changes are found in all laboratory indicators currently accepted by PRINTO/EULAR as diagnostic criteria for SMA. Changes in the values of LDH, D-dimers, total protein and albumin are demonstrated, which are not diagnostic criteria, but also have a high diagnostic value in the context of SMA. It is established that the therapeutic regimen including high-dose corticosteroid (methylprednisolone 30 mg/kg/day or another corticosteroid medication in an equivalent dose) in combination or not with cyclosporine has no significant alternative at this stage.

Two cases of SMA that developed an allergy to corticosteroids (CS) during the course of treatment have also been described, and in the second case we have consecutive allergic manifestations to different groups of CS (25). The side effects of CS are well known, but allergic reactions are little known and are not accepted as a serious adverse effect. Information about these conditions in the scientific literature is scarce, the relationship between the concepts of CS and allergy is counterintuitive, even at first glance - paradoxical, which is why doctors rarely think about them. The author describes the most common clinical manifestations, the allergenic potential of different CS depending on their molecular structure and the method of administration, as well as an algorithm for diagnosis and behavior in CS allergy.

II. Arthritis and spondyloarthritis

The author participated in the first large study of antigens from the HLA system in children with juvenile chronic arthritis (according to the classification when the study was conducted). Antigens from loci A, B and DR were studied in 148 Bulgarian children. The control group included 1085 individuals for loci A and B and 170 for the DR locus. After statistical

analysis, it was established that predisposing factors for the development of juvenile chronic arthritis are the carrier of HLA antigens DR4, B27, and (CREG – B7, B22, B40) and B18 (42).

Another scientific paper included a study of 39 children with Reiter's syndrome (37) and 24 with isolated enthesopathy (17). Analyzes the frequency of indicators such as gender (ratio of boys and girls 2:1), joint syndrome (monooligoarthritis - 72%, poriarthritis - 28%, sacroiliitis - 23%), enthesitis (30%), eye involvement (87%), urethritis (64 %). 74% of patients have an enteric infection, and 10% have a urogenital infection. The carrier of HLA B27 is 65%. IgM rheumatoid factor, antinuclear antibodies, or high antistreptolysin titer were not detected in any child. Recommendations are given for monitoring for evolution to a disease from the group of spondyloarthropathies (37).

Several publications are aimed at the description of rare forms of arthritis, for which there is little information in the periodical press, due to which diagnostic and therapeutic difficulties arise. The first is a clinical variant of coxsackievirus infection, occurring with prolonged fever, skin rash, arthritis and pericarditis, evolving to acute heart failure. The child has a pronounced clinical-laboratory syndrome of inflammation, with positive antinuclear antibodies. The virological examination proved Coxsackievirus B 3. The treatment with CS and non-steroidal anti-inflammatory drugs had a good effect (12). Another article described 17 children with rubella-associated arthritis. The characteristics of the joint syndrome and its duration are given, and the gender differences determining the immune response in men and women to the rubella virus are discussed, which explains the higher incidence in the female sex (35). With the decrease in the incidence of rheumatic disease, poststreptococcal reactive arthritis (PSRA) is becoming increasingly relevant. It is estimated to affect 1-2 in 100,000 individuals. We review its clinical features, present its diagnostic criteria, as well as the differences from classical rheumatic disease. Therapeutic behavior and the need for long-term antibiotic prophylaxis are also discussed, in view of the lower incidence of cardiac involvement (15). It is known that children with immune deficiencies more often suffer from rheumatic diseases. We present a case of a child with common variable immunodeficiency and arthritis. The diagnostic algorithm in children with immune deficiency and the specifics of therapy when it is combined with joint syndrome are discussed (10).

Juvenile ankylosing spondylitis (JAS) is a rare disease of childhood. The authors present a literature review (13) and the first study in Bulgaria of 17 children (16 boys and 1 girl) with JAS (14). The emphasis is that in children, as a rule, there is no involvement of the spine, which is why the diagnosis is difficult and is built on the basis of other clinical symptoms. For the purposes of statistical processing, there is a control group of 50 children with JHA. A significant statistical difference was found in relation to male sex, age over 9 years, peripheral oligoarthritis, enthesopathy, sacroiliitis, involvement of TZBS, carrier of HLA B27. It is emphasized that due to the fact that approximately half of the population is male, and HLA B27 carrier is found in 9.2% of the population, these indicators are highly sensitive, but poorly specific. In another work, the carrier of HLA B27 and HLA B7 CREG antigens in children with JAS was investigated. It was found that the association between HLA B27 and SAU was 83.3%, and when HLA B7 CREG was also examined, it increased to 91.7%. The recommendation for practice is that the carrier of CREG antigens can be used as an additional diagnostic criterion for JAS (18).

III. Systemic connective tissue diseases and vasculitis

Protein-losing enteropathy (PGE) is a rare and uncommon complication of systemic lupus erythematosus (SLE). A girl with generalized edema, hypoproteinemia, and hypoalbuminemia who does not have proteinuria is presented. Examination of faecal alpha 1-antitrypsin proves the presence of PGE in SLE. Aggressive CS and cytostatic therapy improve the condition and lead to remission (11).

Thyrostatics have been used since the 1940s and their side effects are well known. They are observed in 3-5% of those taking them. The most common are skin rashes, arthralgias, and gastrointestinal disorders. Drug-induced lupus (MIL) is extremely rare. We report two girls, 16 years and 12 years of age, with MIL who received propicyl and methysol. In all nine children, the clinical picture includes fever, photosensitivity rash, joint syndrome, positive antihistone antibodies, and the second one has immunological abnormalities characteristic of antiphospholipid syndrome. Thyrostatic therapy was stopped and treatment with prednisone was started. In the first girl, the resumption of treatment resulted in a relapse of MIL. Due to exhaustion of options with both available thyrostatics, surgical treatment is performed, preserving only the thyroid isthmus and switching to replacement therapy. After 6 months, the child is in clinical and immunological remission. In the second case, thyrostatic and CS therapy was carried out in parallel, after 1 year and 3 months. no data on MIL (9).

Kawasaki disease (CD) is an acute febrile disease that is characterized by medium-caliber arteritis, most often affecting the coronary arteries, which determines its social significance. Usually seen between 6 mo. and 5 years of age. 10% of the children are under 3 months of age, and 1.67% are 1 month old. We describe 2 cases of children under 3 months. age with BC (29). At this age, incomplete forms prevail. The emphasis in the article is precisely on them, noting the clinical manifestations that are not diagnostic criteria, but can help to make the correct diagnosis in a timely manner, namely: aseptic meningitis, irritability, respiratory symptoms, sterile pyuria, diarrhea, increased aminotransferases, ECG changes. Another study described a case of chronic arthritis in CD (11). Coronary involvement determines the prognosis of BC. Another article analyzes coronary risk in BC. 52 children with BC were followed. Coronary dilatation or aneurysms were found in 42.3% of children. Most children are referred with diagnoses such as: scarlet fever (19.2%), angina and an allergic rash that occurred during treatment (19.2%), sepsis (19.2%), JHA (17.3%), other infectious diseases (13.5%), urinary tract infection (11.6%). This leads to late diagnosis, as of the cases with coronary involvement only 2 children (9.1%) were treated in the acute phase, and 90.9% - in the subacute (38).

Two articles reviewed the localized (12 children) and linear forms of scleroderma (10 children) (34, 36). Complications of linear scleroderma have been studied. Muscle hypotrophy was found in 100% of the children, joint contractures and reduced range of motion - in 60%, shortening of the lower limb by 1.5-2.5 cm - 40% and EEG changes in 20%. The main recommendation for practice is that scleroderma is not just a dermatological problem and children should be promptly referred to a rheumatologist.

IV. Others

Coronaviruses are long-known pathogens of both humans and animals. The COVID-19 pandemic has presented many challenges to doctors and health systems. In view of the lack of information and the massive and unnecessary prescription of antibiotics, we proposed a therapeutic algorithm for the treatment of childhood COVID-19 depending on the severity of the disease and the results of laboratory tests (8).

Vaccines are one of the great achievements of modern medicine. Due to the autoimmune pathogenesis and the ongoing immunosuppressive therapy, children with rheumatic diseases (RH) have an increased risk of infections, higher morbidity and mortality. Effective yet safe vaccination is key. We have published guidelines for immunizations in children with RH (28). We examine the effectiveness and safety of vaccines, as well as their immunogenicity, depending on the ongoing treatment with CS and immunosuppressant, intake of disease-modifying agents, biological medications, intravenous immunoglobulins. Separately developed section on safety of vaccines in children with RH, as well as the possibility of activation of RH after immunization.

Acute muscle pains and difficulty walking are symptoms associated with both benign and severe degenerative diseases. This necessitates frequent unnecessary invasive examinations, which can be spared to children if the clinical picture of benign acute infantile myositis (BAIM) is known. The most common cause is infection with the influenza virus. We present for the first time in our country in two articles cases of DODM, in the first with enterovirus etiology and extreme rhabdomyolysis (creatin kinase 183,000 U/l) (23), and in the second SARS COV 2 was proven (30). In both children, the movement regime without heavy physical exertion and the intake of fluids intravenously and orally lead to a favorable outcome.

Other publications:

Dr. Lisicki has publications and lectures on "Febrile conditions in childhood" in which he presents the complex diagnostic problem of fever without a focus of infection. Practically important behavior algorithms are derived.

Long-term clinical practice has put him before the provocation of differentiating rare diseases representing casuistics. A scientific contribution is their description and familiarization of the pediatric community with its accumulated experience. Such publications are Vogt-Koyanagi-Harada Disease (6), Mucha-Habermann Disease with contribution of two cases(19). Primary septic myositis - with contribution of one case, Amyopathic dermatomyositis-diagnostic and therapeutic problems (20).

CONCLUSION:

It is clear from the presented presentation that Dr. Kalin Yordanov Lisicchi, PhD, is an established teacher and specialist in pediatrics and pediatric rheumatology. He has sufficient clinical and teaching experience, and has acquired the necessary organizational experience that allows him to cope with daily practical tasks and case studies.

The output of his work is sufficient in terms of volume and quality for the requirements for "Associate Professor" in "Pediatrics", reflected in the Regulations for the terms and conditions

for acquiring scientific degrees and holding academic positions at "Ajibadem City Clinic UMBAL Tokuda" EAD, Sofia. It has the required volume of scientific activity, publications and diagnostic-therapeutic activity.

Dr. Kalin Lisicki is a built doctor, teacher and researcher.

Based on the above, I consider that Dr. Kalin Yordanov Lisichki, MD meets the quantitative and qualitative indicators for occupying the academic position "Associate Professor" in the scientific specialty "Pediatrics" in the competition for the needs of the Pediatric Clinic of "Ajibadem City Clinic UMBAL Tokuda" EAD.

I vote "yes" and recommend to the members of the Scientific Jury to vote for the appointment of the academic position of "docent" by Dr. Kalin Yordanov Lisichki, PhD.

15. 01. 2023
City. Sofia


Prof. Dr. Stefan Nedev Stefanov, MD