University of Medicine and Pharmacy

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Habilitation Thesis

Modern approach in the diagnosis and treatment of emerging and re-emerging infectious diseases Summary

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The scientific and academic professional activity presented in this paper has been accomplished in the field of pediatric infectious diseases from when the doctoral thesis was completed (2000) until present (2023). The habilitation thesis "*Modern approach in diagnosis and treatment of emerging and re-emerging infectious diseases*" is based on original studies published in the last 23 years in ISI indexed journals and other databases and medical publications. The research activity is the result of numerous clinical studies, grants, research projects developed on a national and international level in which I have participated both as a member in the research team and as a principal investigator.

Infectious diseases are a constant challenge both for the clinician and for the personnel involved in research activity because these present with a large array of new conditions (emerging diseases) as well as "classical" conditions which become relevant through new cases (re-emerging diseases).

Part one of the habilitation thesis is structured in two sections:

- *A.* "*Scientific accomplishments*" represents the main section of this paper and describes the most important scientific contributions organized in specific sub-chapters.
- **B.** The individual capacity to coordinate research teams, to organize and manage academic activities. This quality is evident through the participation in numerous research projects/ grants/clinical studies as lead investigator, project director as well as member of the research teams.

The first chapter of part one of the habilitation thesis looks at the *emerging infectious diseases* with which we have been confronted lately.

An important sub-chapter is dedicated to HIV infection/AIDS, present since the early 80s in Europe and later in our country. Romania is one of the few countries where HIV infection/AIDS had an epidemic evolution in the 90s, registering over 15,000 pediatric cases of nosocomial nature at that time. In research papers, this theme is vastly represented by its clinical, immunological, virological, and therapeutical aspects. This research theme was the basis of the doctoral thesis presented in 2008. HIV infection/AIDS remains an important research topic as it is a yet to be fully understood condition, particularly regarding therapy and pathogenesis.

The second sub-chapter of emerging diseases is represented by hepatitis B and C virus infection. Although not emerging diseases, I have included these due to recent developments in treatment and physiopathology. Both acute and chronic clinical forms of illness are therefore studied based on pathogenesis, clinical picture, diagnosis, treatment, and prophylaxis. Studies carried out on this theme are presented as well as the clinical

experience in treatment of patients with various types of hepatitis (B, C). An important future study theme would be the less researched types of hepatitis (D, E, F, and G).

The most recent studies regarding emerging diseases are presented through research carried out on the novel coronavirus strains, SARS CoV-2 in particular, which was responsible for the pandemic between 2019 and 2022. Romania registered many COVID-19 cases resulting in many deaths especially in adults with comorbidities. In the habilitation thesis, several research papers on this topic are presented but infection with SARS CoV-2 remains an important source of research, as COVID-19 is a condition that is not yet fully understood in all aspects (diagnosis, treatment, prophylaxis). Emerging coronaviruses present before SARS COV-2 are insufficiently studied as the epidemics that these caused, SARS in 2002 and MERS in 2012, have extinguished spontaneously. These constitute study and research material for the future, to better understand the evolution of these new microorganisms in the context of new epidemics/ pandemics which we might have to deal with.

Another sub-chapter tackles a different category of emerging diseases, infection with viruses responsible for severe hemorrhagic diseases with a high mortality (Ebola and Zika viruses). Infection with these viruses has caused small epidemics in Africa, Asia, Central and South America. Import cases have been registered in Europe. These viruses represent a future research theme given that these can cause infections in our country.

The section "*Scientific accomplishments*" continues with *the second chapter* where obtained results regarding *reemerging diseases* are presented. Here, more studies and scientific papers are presented, organized in different categories by conditions: eruptive, respiratory, digestive, central nervous system, renal, and systemic illnesses.

Eruptive illnesses represent an important chapter in my personal research as shown by numerous presentations in national and international scientific gatherings as well as specialty publications. Measles and chickenpox are well represented pediatric infectious diseases in our studies and research themes.

Among *respiratory conditions*, one of the better studied conditions is influenza, as this is an illness that can have a severe evolution with severe complications and death.

Digestive conditions represent a particular category because of multiple reasons. Firstly, infection with Clostridium difficile has been very well represented by multiple and ample studies regarding its treatment and management. I have described and carried out for the first time in Romania fecal matter transplant in children with recurrent Clostridium difficile infection, procedure which was successfully carried out in 5 cases. Another well studied digestive condition is infection with rotavirus. Clinical forms and complications of this infection have been presented, therefore defining the new concept of rotaviral illness. Furthermore, studies on antibiotic sensitivity of *Salmonella spp* and *Shigella spp* strains in children with diarrheal disease have been presented, the results being important and useful in the initial treatment of these illnesses.

Central nervous system infections constitute an important segment of emerging diseases, and studies and scientific papers are presented regarding conditions from this category: meningitis, myelitis, acute encephalitis, acute cerebellitis, ADEM, and cerebral abscesses. Also, cases of rabies in children as well as patenting a diagnostic method for this condition (RT-PCR from CSF for rabies virus) are presented and published in specialty publications (ISI).

Another category of conditions that have been analyzed and scientifically researched are *diseases of the urinary tract*, renal infectious complications in particular (hemolytic uremic syndrome of infectious origin).

Systemic infections are a well-represented subject in the habilitation thesis through numerous studies published in specialty literature or presented in various national and international gatherings (sepsis, Lyme disease, botulism, infections with enteroviruses).

In chapter 3 of part one, studies and scientific papers are presented which are based on infectious diseases diagnosis emphasizing modern diagnostic methods (Multiplex PCR technique, molecular and genetic techniques of identifying infectious pathogens) as well as classical diagnostic methods (epidemiological, clinical, and laboratory).

Chapter 4 contains *modern principles of treatment of infectious diseases* based on international protocols and guides as well as local adapted versions of these. Multiple studies regarding anti-retroviral treatment of HIV infection/AIDS, research regarding antibiotic treatment and sensitivity of pathogens, as well as antifungal treatment are presented, results being compared to specialty literature. Also, diagnostic and treatment protocols for emerging infections (HIV/AIDS, COVID-19) are presented, as well as fecal matter transplant for recurring Clostridium difficile infection in children. Numerous national and international clinical and research studies are presented regarding efficacy and tolerance of various drugs utilized in infectious diseases treatment.

Another important chapter is dedicated to studies and research regarding *prophylaxis of emerging and re-emerging infectious diseases* (classical methods of prophylaxis, immunoglobulins, and vaccines. Also, clinical studies and research projects

regarding safety, tolerance, and efficacy of certain vaccines and immunoglobulins utilized in infectious diseases prophylaxis are presented.

The last chapter contains work on the *complications and prognosis of infectious diseases*. Here, studies and published papers regarding severe complications of infectious diseases (polyradiculoneuritis, Kawasaki disease, ADEM) and presented.

Part two of the habilitation thesis consists of the *evolution of the academic career* where promotion stages are presented (assistant lecturer to associate professor) as well as professional and academic accomplishments during this period.

Part three includes the *professional achievements*, starting with the medical training, going through all the stages of professional promotion (resident doctor, doctor, specialist, primary doctor). Also, in this chapter are presented the most important medical achievements both as a doctor in the departments where I worked and as a primary care physician Head of Department since 2013. In this chapter I presented my involvement in the specific medical activities of the National Institute of Diseases Infectious "Prof. Dr. Matei Baş" through my presence in numerous medical commissions but also through the management of the Clinical Section IX Infectious Diseases - Pediatrics starting from 2013. Also presented are the professional medical achievements as well as the training activity of doctors through EMC courses but also resident doctors. The professional prestige is emphasized by the awards/diplomas obtained for dedication and involvement in the provision of medical care in the children's infectious disease wards where I worked and where I continue my work to this day.

Part fourth of the habilitation thesis continues with *plans in university career development as well as opportunities in academic, professional, and research development.* In this section, development trajectories of academic activity are laid out through academic materials for students, medical residents, and doctoral students but also for the continuous medical education of doctors of other specialties. The premises of research regarding modern diagnostic methods and latest generation treatments of emerging and re-emerging infectious diseases are put forward. Professionally, medical activity and caring for patients will have an important growth by applying newer methods of diagnosis and treatment obtained through research activities. Therefore, there will be an increase in patient satisfaction and quality of life.

The last part contains the conclusions of this work and the bibliographic references used to prepare this habilitation thesis.