

UDK 37

ISSN 2545 - 4439
ISSN 1857 - 923X

INTERNATIONAL JOURNAL

Institute of Knowledge Management

KNOWLEDGE



Scientific Papers

Vol. 40. 5

MEDICAL SCIENCES AND HEALTH



KIJ

Vol. 40

No. 5

pp. 831 - 1008

Skopje 2020

KNOWLEDGE



INTERNATIONAL JOURNAL

**SCIENTIFIC PAPERS
VOL. 40.5**

June, 2020

**INSTITUTE OF KNOWLEDGE MANAGEMENT
SKOPJE**



KNOWLEDGE

International Journal Scientific Papers Vol. 40.5

ADVISORY BOARD

Vlado Kambovski PhD, Robert Dimitrovski PhD, Siniša Zarić PhD, Maria Kavdanska PhD, Venelin Terziev PhD, Mirjana Borota – Popovska PhD, Cezar Birzea PhD, Veselin Videv PhD, Ivo Zupanovic, PhD, Savo Ashtalkoski PhD, Zivota Radosavljević PhD, Laste Spasovski PhD, Mersad Mujevic PhD, Milka Zdravkovska PhD, Drago Cvijanovic PhD, Predrag Trajković PhD, Lazar Stosic PhD, Krasimira Staneva PhD, Nebojsa Pavlović PhD, Daniela Todorova PhD, Baki Koleci PhD, Lisen Bashkurti PhD, Zoran Srzentić PhD, Sinisa Opic PhD, Marija Kostic PhD

Print: GRAFOPROM – Bitola

Editor: IKM – Skopje

Editor in chief

Robert Dimitrovski, PhD

KNOWLEDGE - International Journal Scientific Papers Vol. 40.5

ISSN 1857-923X (for e-version)

ISSN 2545 – 4439 (for printed version)

INTERNATIONAL EDITORIAL BOARD

President: Academic, Prof. Vlado Kambovski PhD, Skopje (N. Macedonia)

Vice presidents:

Prof. Robert Dimitrovski PhD, Institute of Knowledge Management, Skopje (N. Macedonia)

Prof. Sinisa Zaric, PhD, Faculty of Economics, University of Belgrade, Belgrade (Serbia)

Prof. Venelin Terziev PhD, University of Rousse, Rousse (Bulgaria)

Prof. Mersad Mujevic PhD, Public Procurement Administration of Montenegro (Montenegro)

Prof. Tihomir Domazet PhD, President of the Croatian Institute for Finance and Accounting, Zagreb (Croatia)

Members:

- Prof. Aleksandar Korablev PhD, Faculty of economy and management, Saint Petersburg State Forest Technical University, Saint Petersburg (Russian Federation)
- Prof. Azra Adjajlic – Dedovic PhD, Faculty of criminology and security, Sarajevo (Bosnia & Herzegovina)
- Prof. Anita Trajkovska PhD, Rochester University (USA)
- Prof. Anka Trajkovska-Petkoska PhD, UKLO, Faculty of technology and technical sciences, Bitola (N. Macedonia)
- Prof. Alisabri Sabani PhD, Faculty of criminology and security, Sarajevo (Bosnia & Herzegovina)
- Prof. Aneta Mijoska PhD, Faculty of Dentistry, University –St. Cyril and Methodius”, Skopje (N. Macedonia)
- Prof. Ahmad Zakeri PhD, University of Wolverhampton, (United Kingdom)
- Prof. Ana Dzumalieva PhD, South-West University —“Neofit Rilski”, Blagoevgrad (Bulgaria)
- Prof. Aziz Pollozhani PhD, Rector, University Mother Teresa, Skopje (N.Macedonia)
- Prof. Artan Nimani PhD, Rector, University of Gjakova —“Fehmi Agani” (Kosovo)
- Prof. Branko Sotirov PhD, University of Rousse, Rousse (Bulgaria)
- Prof. Branko Boshkovic, PhD, College of Sports and Health, Belgrade (Serbia)
- Prof. Branimir Kampl PhD, Institute SANO, Zagreb (Croatia)
- Prof. Baki Koleci PhD, University Hadzi Zeka, Peja (Kosovo)
- Prof. Branislav Simonovic PhD, Faculty of Law, Kragujevac (Serbia)
- Prof. Bistra Angelovska, Faculty of Medicine, University —“Goce Delcev”, Shtip (N.Macedonia)
- Prof. Cezar Birzea, PhD, National School for Political and Administrative Studies, Bucharest (Romania)
- Prof. Cvetko Andreevski, Faculty of Tourism, UKLO, Bitola (N.Macedonia)
- Prof. Drago Cvijanovic, PhD, Faculty of Hotel Management and Tourism, University of Kragujevac, Vrnjacka Banja (Serbia)
- Prof. Dusan Ristic, PhD Emeritus, College of professional studies in Management and Business Communication, Novi Sad (Serbia)
- Prof. Darijo Jerkovic PhD, Faculty of Business Economy, University —“Méz”, (Bosnia & Herzegovina)
- Prof. Daniela Todorova PhD, —“Dor Kableshkov” University of Transport, Sofia (Bulgaria)
- Prof. Dragan Kokovic PhD, University of Novi Sad, Novi Sad (Serbia)
- Prof. Dragan Marinkovic PhD, High health – sanitary school for professional studies, Belgrade (Serbia)
- Prof. Daniela Ivanova Popova PhD, Faculty of Public Health and Sport, SWU Neofit Rilski, Blagoevgrad (Bulgaria)

- Prof. Dzulijana Tomovska, PhD, Faculty of Biotechnical sciences, Bitola (N.Macedonia)
- Prof. Evgenia Penkova-Pantaleeva PhD, UNWE -Sofia (Bulgaria)
- Prof. Fadil Millaku, PhD, Rector, University —HadžZeka”, Peja (Kosovo)
- Prof. Fatos Ukaj, University —Hasan Hshtina”, Prishtina (Kosovo)
- Prof. Georgi Georgiev PhD, National Military University —Vasil Levski”, Veliko Trnovo (Bulgaria)
- Prof. Halit Shabani, PhD, University —HadžZeka”, Peja (Kosovo)
- Prof. Halima Sofradzija, PhD, University of Sarajevo, Sarajevo (Bosnia and Herzegovina)
- Prof. Haris Halilovic, Faculty of criminology and security, University of Sarajevo, Sarajevo (Bosnia and Herzegovina)
- Prof. Helmut Shramke PhD, former Head of the University of Vienna Reform Group (Austria)
- Prof. Hristina Georgieva Yancheva, PhD, Rector, Agricultural University, Plovdiv (Bulgaria)
- Prof. Hristo Beloev PhD, Bulgarian Academy of Science, Rector of the University of Rousse (Bulgaria)
- Prof. Hristina Milcheva, Medical college, Trakia University, Stara Zagora (Bulgaria)
- Prof. Izet Zeqiri, PhD, Academic, SEEU, Tetovo (N.Macedonia)
- Prof. Ivan Marchevski, PhD, D.A. Tsenov Academy of Economics, Svishtov (Bulgaria)
- Prof. Ibrahim Obhodjas PhD, Faculty of Business Economy, University —Vitez”, (Bosnia & Herzegovina)
- Doc. Igor Stubelj, PhD, Faculty of Management, Primorska University, Koper (Slovenia)
- Prof. Ivo Zupanovic, PhD, Faculty of Business and Tourism, Budva (Montenegro)
- Prof. Ivan Blazhevski, PhD, Institute for Sociological, Political and Juridical Research, Skopje (N.Macedonia)
- Prof. Ivan Petkov PhD, European Polytechnic University, Pernik (Bulgaria)
- Prof. Isa Spahiu PhD, AAB University, Prishtina (Kosovo)
- Prof. Ivana Jelik PhD, University of Podgorica, Faculty of Law, Podgorica (Montenegro)
- Prof. Islam Hasani PhD, Kingston University (Bahrein)
- Prof. Jamila Jaganjac PhD, Faculty of Business Economy, University —Vitez”, (Bosnia & Herzegovina)
- Prof. Jova Ateljevic PhD, Faculty of Economy, University of Banja Luka, (Bosnia & Herzegovina)
- Prof. Jove Kekenovski PhD, Faculty of Tourism, UKLO , Bitola (N.Macedonia)
- Prof. Jonko Kunchev PhD, University „Cernorizec Hrbar— Varna (Bulgaria)
- Prof Karl Schopf, PhD, Akademie fur wissenschaftliche forchung und studium, Wien (Austria)
- Prof. Katerina Belichovska, PhD, Faculty of Agricultural Sciences, UKIM, Skopje (N. Macedonia)
- Prof. Krasimir Petkov, PhD, National Sports Academy —Vasil Levski”, Sofia (Bulgaria)
- Prof. Kamal Al-Nakib PhD, College of Business Administration Department, Kingdom University (Bahrain)
- Prof. Kiril Lisichkov, Faculty of Technology and Metallurgy, UKIM, Skopje (N.Macedonia)
- Prof. Krasimira Staneva PhD, University of Forestry, Sofia (Bulgaria)
- Prof. Lidija Tozi PhD, Faculty of Pharmacy, Ss. Cyril and Methodius University, Skopje (N.Macedonia)
- Prof. Laste Spasovski PhD, Vocational and educational centre, Skopje (N.Macedonia)
- Prof. Larisa Velic, PhD, Faculty of Law, University of Zenica, Zenica (Bosnia and Herzegovina)

- Prof. Łukasz Tomczyk PhD, Pedagogical University of Cracow (Poland)
- Prof. Lujza Grueva, PhD, Faculty of Medical Sciences, UKIM, Skopje (N.Macedonia)
- Prof. Lazar Stosic, PhD, Association for development of science, engineering and education, Vranje (Serbia)
- Prof. Lulzim Zeneli PhD, University of Gjakova –Fehmi Agani” (Kosovo)
- Prof. Lisen Bashkurti PhD, Global Vice President of Sun Moon University (Albania)
- Prof. Lence Mircevska PhD, High Medicine School, Bitola, (N.Macedonia)
- Prof. Ljupce Kocovski PhD, Faculty of Biotechnical sciences, Bitola (N.Macedonia)
- Prof. Marusya Lyubcheva PhD, University —Prof. Asen Zlatarov”, Member of the European Parliament, Burgas (Bulgaria)
- Prof. Marija Magdinceva – Shopova PhD, Faculty of tourism and business logistics, University —Goce Delchev”, Shtip (N. Macedonia)
- Prof. Maria Kavdanska PhD, Faculty of Pedagogy, South-West University Neofit Rilski, Blagoevgrad (Bulgaria)
- Prof. Maja Lubenova Cholakova PhD, Faculty of Public Health and Sport, SWU Neofit Rilski, Blagoevgrad (Bulgaria)
- Prof. Mirjana Borota-Popovska, PhD, Centre for Management and Human Resource Development, Institute for Sociological, Political and Juridical Research, Skopje (N.Macedonia)
- Prof. Mihail Garevski, PhD, Institute of Earthquake Engineering and Engineering Seismology, Skopje (N.Macedonia)
- Prof. Misho Hristovski PhD, Faculty of Veterinary Medicine, Ss. Cyril and Methodius University, Skopje (N.Macedonia)
- Prof. Mitko Kotovchevski, PhD, Faculty of Philosophy, UKIM, Skopje (N.Macedonia)
- Prof. Milan Radosavljevic PhD, Dean, Faculty of strategic and operational management, Union University, Belgrade (Serbia)
- Prof. Marija Topuzovska-Latkovikj, PhD, Centre for Management and Human Resource Development, Institute for Sociological, Political and Juridical Research, Skopje (N.Macedonia)
- Prof. Marija Knezevic PhD, Academic, Banja Luka, (Bosnia and Herzegovina)
- Prof. Margarita Bogdanova PhD, D.A.Tsenov Academy of Economics, Svishtov (Bulgaria)
- Prof. Mahmut Chelik PhD, Faculty of Philology, University —Goce Delchev”, Shtip (N.Macedonia)
- Prof. Marija Mandaric PhD, Faculty of Hotel Management and Tourism, University of Kragujevac, Vrnjacka Banja (Serbia)
- Prof. Marina Simin PhD, College of professional studies in Management and Business Communication, Sremski Karlovci (Serbia)
- Prof. Miladin Kalinic, College of professional studies in Management and Business Communication, Sremski Karlovci (Serbia)
- Prof. Marijan Tanushevski PhD, Macedonian Scientific Society, Bitola (N. Macedonia)
- Prof. Mitre Stojanovski PhD, Faculty of Biotechnical sciences, Bitola (N.Macedonia)
- Prof. Miodrag Smelcerovic PhD, High Technological and Artistic Vocational School, Leskovac (Serbia)
- Prof. Nadka Kostadinova, Faculty of Economics, Trakia University, Stara Zagora (Bulgaria)
- Prof. Natalija Kirejenko PhD, Faculty For economic and Business, Institute of Entrepreneurial Activity, Minsk (Belarus)
- Prof. Nenad Taneski PhD, Military Academy —Mhailo Apostolski”, Skopje (N.Macedonia)
- Prof. Nevenka Tatkovic PhD, Juraj Dobrila University of Pula, Pula (Croatia)
- Prof. Nedžad Korajlic PhD, Dean, Faculty of criminal justice and security, University of Sarajevo (Bosnia and Herzegovina)
- Prof. Nonka Mateva PhD, Medical University, Plovdiv (Bulgaria)

- Prof. Nikolay Georgiev PhD, —Todor Kableshkov” University of Transport, Sofia (Bulgaria)
- Prof. Nishad M. Navaz PhD, Kingdom University (India)
- Prof. Nano Ruzhin PhD , Faculty of Law, FON University, Skopje (N.Macedonia)
- Prof. Oliver Dimitrijevic PhD, High medicine school for professional studies —Iphokrat”, Bujanovac (Serbia)
- Prof. Paul Sergius Koku, PhD, Florida State University, Florida (USA)
- Prof. Primoz Dolenc, PhD, Faculty of Management, Primorska University, Koper (Slovenia)
- Prof. Predrag Trajkovic PhD, JMPNT, Vranje (Serbia)
- Prof. Petar Kolev PhD, —Todor Kableshkov” University of Transport, Sofia (Bulgaria)
- Prof. Pere Tumbas PhD, Faculty of Economics, University of Novi Sad, Subotica (Serbia)
- Prof. Rade Ratkovic PhD, Faculty of Business and Tourism, Budva (Montenegro)
- Prof. Rositsa Chobanova PhD, University of Telecommunications and Posts, Sofia (Bulgaria)
- Prof. Rossana Piccolo PhD, Università degli studi della Campania - Luigi Vanvitelli (Italy)
- Prof. Rumen Valcovski PhD, Imunolab Sofia (Bulgaria)
- Prof. Rumen Stefanov PhD, Faculty of public health, Medical University of Plovdiv (Bulgaria)
- Prof. Rumen Tomov PhD, Rector, University of Forestry, Sofia (Bulgaria)
- Prof. Sasho Korunoski PhD, UKLO, Bitola (N.Macedonia)
- Prof. Snezhana Lazarevic, PhD, College of Sports and Health, Belgrade (Serbia)
- Prof. Stojan Ivanov Ivanov PhD, Faculty of Public Health and Sport, SWU Neofit Rilski, Blagoevgrad (Bulgaria)
- Prof. Stojna Ristevska PhD, High Medicine School, Bitola, (N. Macedonia)
- Prof. Suzana Pavlovic PhD, High health – sanitary school for professional studies, Belgrade (Serbia)
- Prof. Sandra Zivanovic, PhD, Faculty of Hotel Management and Tourism, University of Kragujevac, Vrnjacka Banja (Serbia)
- Prof. Shyqeri Kabashi, College –Biznesi”, Prishtina (Kosovo)
- Prof. Temelko Risteski PhD, Faculty of Law, FON University, Skopje (N. Macedonia)
- Prof. Todor Krystevich, D.A. Tsenov Academy of Economics, Svishtov (Bulgaria)
- Prof. Todorcka Atanasova, Faculty of Economics, Trakia University, Stara Zagora (Bulgaria)
- Doc. Tatyana Sobolieva PhD, State Higher Education Establishment Vadiym Getman Kiyev National Economic University, Kiyev (Ukraine)
- Prof. Tzako Pantaleev PhD, NBUniversity , Sofia (Bulgaria)
- Prof. Violeta Dimova PhD, Faculty of Philology, University —Goce Delchev”, Shtip (N. Macedonia)
- Prof. Vojislav Babic PhD, Institute of Sociology, University of Belgrade (Serbia)
- Prof. Volodymyr Denysyuk, PhD, Dobrov Center for Scientific and Technological Potential and History studies at the National Academy of Sciences of Ukraine (Ukraine)
- Prof. Valentina Staneva PhD, —Todor Kableshkov” University of Transport, Sofia (Bulgaria)
- Prof. Venus Del Rosario PhD, Arab Open University (Philippines)
- Prof. Vjollca Dibra PhD, University of Gjakova –Fehmi Agani” (Kosovo)
- Prof. Yuri Doroshenko PhD, Dean, Faculty of Economics and Management, Belgorod (Russian Federation)
- Prof. Zlatko Pejkovski, PhD, Faculty of Agricultural Sciences, UKIM, Skopje (N.Macedonia)
- Prof. Zivota Radosavljevik PhD, Faculty FORCUP, Union University, Belgrade (Serbia)
- Prof. Zorka Jugovic PhD, High health – sanitary school for professional studies, Belgrade (Serbia)

REVIEW PROCEDURE AND REVIEW BOARD

Each paper is reviewed by the editor and, if it is judged suitable for this publication, it is then sent to two referees for double blind peer review.

The editorial review board is consisted of 63 members, full professors in the fields 1) Natural and mathematical sciences, 2) Technical and technological sciences, 3) Medical sciences and Health, 4) Biotechnical sciences, 5) Social sciences, and 6) Humanities from all the Balkan countries and the region.

CONTENTS

3D - PRINTED DRUGS - A BRAVE NEW WORLD IN PHARMACEUTICAL MANUFACTURING	847
Daniel Argilashki.....	847
Anna Mihaylova.....	847
Nina Koleva.....	847
Bozhidarka Hadzhieva.....	847
TELEPHARMACY - NEW OPPORTUNITIES FOR PHARMACISTS AND PATIENTS (OVERVIEW)	855
Kristina Kilova.....	855
MORPHOLOGICAL, ANATOMICAL AND PHYTOCHEMICAL STUDY OF PUNICA GRANATUM LINN	863
Stefan Harkov.....	863
MULTIDISCIPLINARY APPROACH TO PREVENTION OF CHILDREN'S EYE HEALTH IN OPHTHALMOLOGICAL PRACTICE.....	867
Krassimira Dimitrova.....	867
Christina Grupcheva.....	867
Elica Hristova.....	867
Silvia Borisova.....	867
ORTHODONTIC-PROSTHETIC APPROACH IN THE TREATMENT OF HYPODONTIA.....	875
Sandra Atanasova.....	875
Ljubica Prosheva.....	875
HEREDITY AND THE INFLUENCE OF STYLE OF LIFE AND BAD HABITS ON DEVELOPMENT OF CHRONICAL VENOUS DISEASE.....	881
Mihaela Mireva.....	881
HEREDITARY ANGIOEDEMA (HAE): A CASE REPORT AND LITERATURE OVERVIEW.....	885
Martina Gjorgjievska Kamceva.....	885
Julijana Maksimovikj Mileva.....	885
Lidija Petrovska.....	885
Gordana Kamcheva Mihailova.....	885
PERSON-CENTERED CARE IN CHRONIC DISEASE - A REVIEW OF CONCEPTS.....	889
Boryana Levterova.....	889
NURSES'APPROACH TO MOTHERS' INTENSIVE CARE UNITS TO REDUCE ANXIETY AND DEPRESSION.....	893
Svetla Ivanova.....	893
HEALTH CARE, EDUCATION AND TREATMENT OF PATIENTS WITH TUBERCULOSIS.....	897
Natasha Artinova.....	897
Gordana Panova.....	897
VALIDATION THERAPY FOR WORKING WITH DEMENTATIC PATIENTS - FIRST STEPS IN BULGARIA.....	901
Mariya Dimova.....	901
CARE, TREATMENT AND EDUCATION OF RESPIRATORY DISEASES IN THE MUNICIPALITY OF KOCANI IN THE PERIOD FROM 2014 TO 2019.....	907
Goce Markov.....	907
Gordana Panova.....	907

MODERN NUTRITION - THE RIGHT PATH TO A HEALTHY AND LONG LIFE.....	913
Snežana Fatić.....	913
Milenka Vraneš – Grujičić	913
Jelena Jevtović.....	913
Stefan Grujičić.....	913
THE ROLE OF PATRONAGE SERVICE IN EARLY SCREENING, EDUCATION AND TREATMENT OF PATIENTS WITH DIABETES MELLITUS	919
Ivan Nikovski	919
Gordana Panova.....	919
CONTEMPORARY ASPECTS OF EVALUATION OF HEALTH TECHNOLOGIES IN MEDICAL DEVICES.....	925
Nikola Sabev.....	925
CONFLICT COMPETENCE OF MEDICAL SPECIALISTS	931
Ekaterina Raykova.....	931
Maria Semerdjieva.....	931
Vasil Kotetarov.....	931
MEDICS IN EMERGENCY DEPARTMENT - SOME PSYCHOLOGICAL ASPECTS	937
Rostislav Kostadinov	937
Kiril Atliev.....	937
THE ROLE OF THE NURSE IN APPLYING INTEGRATIVE MEDICINE IN TREATMENT OF PATIENTS WITH NEPHROLITHIASIS	941
Lidija Janjik	941
Gordana Panova.....	941
EFFICACY OF ACUPUNCTURE ON PAIN RELIEF IN PATIENTS WITH RHEUMATOID ARTHRITIS.....	949
Lence Nikolovska	949
Silvana Mitkovska	949
STUDY OF THE EFFECT OF STRESS ON THE HEALTH OF REHABILITATORS AND MASSAGERS.....	955
Mariana Albert.....	955
HYPOPRESSIVE AND KEGEL EXERCISES IN WOMEN WITH ABDOMINAL AND PELVIC FLOOR DISFUNCTION.....	963
Margarita Avramova.....	963
KINESITHERAPY IN PATIENTS WITH ISCHEMIC STROKE.....	969
Krasimira Zlatkova	969
COMPARISON OF TWO HIP FRACTURE REHABILITATION PROGRAMS.....	973
Sara Nikova	973
Toshe Krstev.....	973
NECESSITY OF PLANNED MOTOR PROGRAMS WITH ELDERLY PEOPLE, RESIDING IN RESIDENCIES FOR ELDERLY PEOPLE, IN ORDER TO DECREASE THE RISK OF FALLING ..	979
Daniela Manova.....	979
Mihaela Mireva.....	979
TREATMENT OF PATELLAR TENDINOPATHY	987
Lence Nikolovska	987
Bozidar Simic	987
ALGORITHM FOR DETERMINATION OF KINESY THERAPEUTIC POTENTIAL IN PATIENTS WITH SUBARACHNOID HEMORRHAGE	993
Mariela Filipova	993
Daniela Popova.....	993

REHABILITATION IN DUCHENNE MUSCULAR DISTROPHY - CASE STUDY	997
Doris Starcheva.....	997
Toshe Krstev.....	997
EMERGENCY DEPARTMENT CONTEMPORARY CHALLENGES RELATED TO THE GENERAL PRACTITIONERS PRACTICES	1003
Kiril Atliev.....	1003
Rostislav Kostadinov	1003

HEREDITARY ANGIOEDEMA (HAE): A CASE REPORT AND LITERATURE OVERVIEW

Martina Gjorgjievska Kamceva

“Clinical Hospital” – Stip, N. Macedonia, martinakamceva@hotmail.com

Julijana Maksimovikj Mileva

“Clinical Hospital”- Stip, N. Macedonia, julijanamaksimovikj@gmail.com

Lidija Petrovska

“Clinical Hospital”- Stip, N. Macedonia, lidija81miteva@gmail.com

Gordana Kamcheva Mihailova

“Clinical Hospital”-Stip, N. Macedonia, gordana.kamceva@ugd.edu.mk

Abstract: Recognition of the unique clinical and immunological characteristics of the rare causes of Hereditary angioedema (HAE) is important in order to obtain proper and timely diagnosis and treatment of the patient. Hereditary angioedema is a rare disease with great heterogeneity of symptoms like edema of the skin, gastro-intestinal mucosa and larynx or pharynx. The changes are spontaneously withdrawn in 12 to 72 hours. Hereditary angioedema is autosomal-dominant but can occur spontaneously in a healthy family without clinical manifestations or immune defects. Based on the mechanism of occurrence, it is conventionally classified as angioedema mediated by mastocytic degranulation, bradykinin or idiopathic, while in terms of clinical and pathophysiological manifestation it is divided into acquired and congenital or congenital angioedema with or without urticaria. Three types of HAE are described. The most frequent is type I, which is a result from a mutations in the SERPING 1 gene, they cause hereditary angioedema type I and type II. The SERPING 1 gene provides instructions for creating C1 inhibitor protein, which is important for controlling inflammation. C1 inhibitor protein leads to blockage of the activity of certain proteins that lead to inflammation. Mutations that cause hereditary angioedema type I lead to decreased levels of C1 in the blood, deficiency of the complement C1 inhibitor. Without an adequate level of functional C1 inhibitor, excessive amounts of a protein fragment called bradykinin are generated. Bradykinin causes inflammation due to the increased elimination of fluid through the walls of blood vessels in the body's tissues. Excessive accumulation of fluid in body tissues causes episodes of swelling observed in individuals with inherited angioedema type I and type II.

Case presentation: A 25-year old woman who was first diagnosed with Oedema Quincke, of the face, after an insect bite, when she was 9 years old. Since then, almost every month, swelling of the arms or legs occurs before the menstrual cycle, and swelling of the hands also occurs when blood is drawn from the finger, while several times a year there is swelling in the facial region. The patient was brought for the first time as an emergency to the Department of Dermatovenereology at the Clinical Hospital Stip with pronounced circumscribed edema of the face without erythema and without a feeling of itching and pain that appeared 3-4 hours before admission. Due to the frequent occurrence of swelling in the facial region, immunochemical analyzes have been performed. The analysis showed a reduced level of C1 inhibitor esterase 0.0365g / l (0.18-0.39) and the results are in favor of HAE typ I. The patient was treated few times with isogroup plasma 2x220 ml and within 24 hours the edema receded, later she was included in the program for patients with HAE, with parenteral inhibitor of C1 esterase, ie with amp. Beriner.

Keywords: hereditary angioedema; case report; C1 inhibitor esterase.

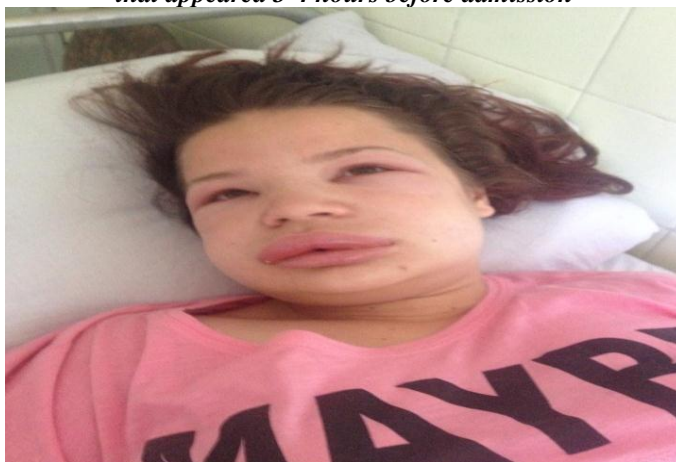
1. INTRODUCTION

Hereditary angioedema is a more or less pronounced circulatory-localized edema localized to the skin or mucous membranes, most commonly affecting the face, eyelids, lips, genitals, tongue, pharynx, and larynx. The skin colour over the edema is unchanged or pale pink, there is a feeling of tightness, and sometimes there may be itching of varying intensity. Based on the mechanism of occurrence, it is conventionally classified as angioedema mediated by mastocytic degranulation, bradykinin or idiopathic, while in terms of clinical and pathophysiological manifestation it is divided into acquired and congenital or congenital angioedema with or without urticaria. (Wolff, Johnson, 2009. Wolff, Goldsmith, Katz, Gilchrest, Paller, Leffel, 2008). Hereditary angioedema is a rare but serious disease that is autosomal-dominant but can occur spontaneously in a healthy family without clinical manifestations or immune defects. It is characterized by recurrent circus-edema without itching and erythema (Papamantios, Matiakis, Tsirevelou, Kolokotronis, & Skoulakis, 2010). The changes are spontaneously withdrawn in 12 to 72 hours.

2. CASE REPORT

A 25-year-old, mother of one child, with a positive family history of HAE (mother and mother's mother). The patient was diagnosed with the disease 5 years ago. In 2014, the patient was brought for the first time as an emergency to the Department of Dermatovenereology at the Clinical Hospital Shtip with pronounced circumscribed edema of the face without erythema and without a feeling of itching and pain that appeared 3-4 hours before admission. From EMC has been prescribed antihistamine and corticosteroid therapy (amp. Methylprednisolone a 120 mg).

Figure 1. Pronounced circumscribed edema of the face without erythema and without a feeling of itching and pain that appeared 3-4 hours before admission



From the anamnesis we received data that at the age of 9 the patient was hospitalized in the children's ward as Oedema Quincke of the face, after an insect bite. Since then, almost every month, swelling of the arms or legs occurs before the menstrual cycle. Swelling of the hands also occurs when blood is taken from the finger, while several times a year there is swelling in the facial region. In our ward, the patient was treated with isogroup plasma 2x220 ml and within 24 hours the edema receded.

Figure 2. Patient after treatment with isogroup plasma 2x220 ml. Left pictures after 24 hours and right pictures after 72 hours.



Due to the frequent occurrence of swelling in the facial region, immunochemical analyzes have been performed. The analysis showed a reduced level of C1 inhibitor esterase 0.0365g / l (0.18-0.39) and the results are in favor of HAE typ I. On several occasions during the same year the patient was hospitalized in our ward, most often due to swelling of the face, and after conducting isogrup therapy (1-2x220 ml) the changes are withdrawn. In the next few years, in addition to edema in the facial region, the cause of frequent hospitalizations is edema in the neck region, intense

abdominal pain followed by nausea and vomiting, as well as laryngeal edema. After treatment with isogrup plasma or amp. Ruconest stable remission in a few hours is achieved. In 2015, the patient was included in the program for patients with HAE with parenteral inhibitor of C1 esterase, i.e. with amp. Beriner.

3. DISSCUSION

The prevalence of HAE is relatively low, 1 in every 10,000 or 1 in every 500,000 citizens (Frank,2010). Most people with HAE get a mutation in a C1 inhibitory protein from one of the parents. Mutations in the SERPING 1 gene cause hereditary angioedema type I and type II. The SERPING 1 gene provides instructions for creating a C1 inhibitory protein, which is important for controlling inflammation (Wolff, Johnson, 2009. Wolff, Goldsmith, Katz, Gilchrest, Paller, Leffel, 2008). C1 inhibitory protein leads to blockage of the activity of certain proteins that lead to inflammation. Mutations that cause inherited type I angioedema lead to decreased levels of C1 inhibitor in the blood, while mutations that cause type II result in the production of C1 inhibitor but its functioning is abnormal. Without a corresponding level of functional C1 inhibitor, excessive amounts are generated on a protein fragment called bradykinin (Wolff, Johnson, 2009. Wolff, Goldsmith, Katz, Gilchrest, Paller, Leffel, 2008). Bradykinin leads to inflammation due to the increased elimination of fluids through the walls of blood vessels in the body tissues. Excessive accumulation of fluid in body tissues causes episodes of edema observed in individuals with inherited type I and type II angioedema (Wolff, Johnson, 2009. Wolff, Goldsmith, Katz, Gilchrest, Paller, Leffel, 2008, Papamantios, Matiakis, Tsirevelou, Kolokotronis, & Skoulakis, 2010). The symptoms of HAE can occur at any time in childhood. Attacks of swelling generally begin in school or adolescence. In 50% of the cases, the first changes appear when children are between 5 and 11 years old. The attacks are unpredictable, sometimes they appear without prior warning, but they can also develop in hours. The onset of edema may be preceded by prodromal symptoms such as: tingling in the area where the edema will develop, erythema rash, sudden mood swings, anxiety, fatigue, cramps or intense abdominal pain. Possible trigger factors are: stress, frequent infections in childhood, pregnancy, trauma, some drugs (ACE inhibitors, contraceptives), dental interventions, oral contraceptives, stings, certain foods, etc. In most cases the exact trigger is not known (Wolff, Johnson, 2009. Wolff, Goldsmith, Katz, Gilchrest, Paller, Leffel, 2008). The most common and earliest symptoms that occur: edema - can affect any part of the body, is most often localized in the facial region, swelling of the face and genitals can lead to severe impairment of normal patient function, edema of the respiratory tract - tongue, larynx accompanied by difficult breathing, difficult speaking and swallowing as well as the appearance of stridor (Sacha, Mmarcel, 2016. Bork, Frank, Grundt, Schlattmann, Nussberger & Kreuz, 2007). Such attacks can be fatal due to asphyxia, erythema marginatum - occurs in 42-58% of children, often can be interpreted as urticaria, abdominal symptoms - intense pain, cramps, nausea, vomiting, diarrhea, dehydration which many times it is misdiagnosed. The frequency of seizures without prior preventive treatment also varies and it is estimated that one third of patients have more than 12 seizures during the year, 40% of patients about 6 to 11 seizures per year, while one third occur much less number of seizures or have no symptomatology (Soni, Kumar, Alliu, & Shetty,2016). Concentrated C1 inhibitor (derived from plasma or recombinant) and icatibant (antagonist of B receptor for bradykinin) have been registered for the treatment of acute attacks of HAE in Europe, while ecalantide (an inhibitor of calicrain) has been registered only in the United States. The action of these drugs begins 30-60 minutes after their application and it takes several hours for the changes to completely subside. It is most effective if the drug is taken immediately after the first symptoms appear (Papamantios, Matiakis, Tsirevelou, Kolokotronis, & Skoulakis, 2010, Sacha, Mmarcel,2016)

4. CONCLUSION

From the above we can conclude that the disease is very rare and it is not uncommon for patients to remain undiagnosed for many years or to be diagnosed as Oedema Quincke. Many patients reported that their frequent and severe abdominal pain was misdiagnosed as psychosomatic with referral to a psychiatric evaluation. We should always think that it is possible for a patient to have HAE if anamnesis gives us information that there is often abdominal pain attack, headache attack, family history of hereditary angioedema, occurrence of angioedema as a side effect of ACE inhibitor therapy.

REFERENCES

- Bork, K., Frank, J., Grundt, B., Schlattmann, P., Nussberger, J., & Kreuz, W. (2007). Treatment of acute edema attacks in hereditary angioedema with a bradykinin receptor-2 antagonist (Icatibant). *The Journal of allergy and clinical immunology*, 119(6), 1497–1503. <https://doi.org/10.1016/j.jaci.2007.02.012>
- Frank, M. M. (2010). Recombinant and plasma - purified human c1 inhibitor for the treatment of hereditary angioedema. *The World Allergy Organization journal*, 3 (9 Suppl), S29–S33. <https://doi.org/10.1097/WOX.0b013e3181f1428d>

Genetics and rare disease. Hereditary angioedema

Genetics Home Reference, Hereditary angioedema

Marcus, M., Marcus, M., Timothy, C., (2018). The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Clin Dermatol*

Papamantinos, M., Matiakis, A., Tsirevelou, P., Kolokotronis, A., & Skoulakis, H. (2010). Hereditary angioedema: three cases report, members of the same family. *Journal of oral & maxillofacial research*, 1(1), e9. <https://doi.org/10.5037/jomr.2010.1109>

Sacha, Z., Mmarcel, L. (2016). Hereditary and Acquired C1-inhibitor-dependent Angioedema: From Pathophysiology to Treatment. *Clin Dermatol* 27018196

Soni, P., Kumar, V., Alliu, S., & Shetty, V. (2016). Hereditary angioedema (HAE): a cause for recurrent abdominal pain. *BMJ case reports*, 2016, bcr2016217196. <https://doi.org/10.1136/bcr-2016-217196>

Xavier, C.M., Rozita, B.M., Amin, K., Gina, L., Georges, E., Eric, W., Susan, W., Bill, Y., Christian, D., (2018). The diagnosis of hereditary angioedema with C1 inhibitor deficiency: a survey of Canadian physicians and laboratories. *Allergy Astma and Clinical immunology* 6269

Wolff, K., Johnson, R., & Fitzpatrick, A. (2009). *Color atlas and synopsis of clinical dermatology*, sixth edition, The McGraw hill companies. *Urticaria and angioedema*

Wolff, K., Goldsmith, L., Katz, S., Gilchrist, B., Paller, A., & Leffel, Df. (2008). *Fitzpatrick's Dermatology in general medicine*, seventh edition, The McGraw hill companies