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# BALKAN MEDICAL UNION

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35<sup>th</sup> **BALKAN  
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challenge  
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## HISTORY OF MEDICINE

### H1. Senile emaciation in ancient Greek art [FLASH]

Laios K<sup>1</sup>, Lagiou E<sup>2</sup>, Karamanou M<sup>3</sup>, Androutsos G<sup>4</sup>

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A group of terracotta female figurines from Smyrna dated back to the Hellenistic age depict female trunks in an excessively weakened state. In only one of them is preserved the head. The image in all figurines follows identical features: the body is too thin and weak, the chest bone appears as if there is no skin, the breasts are weak and hanging, while the belly is puffy low as if it is swollen, creating a contrast with the weak body. The legs, where and to what extent they are retained, seem to follow weakness, but not to such an extent as the trunk. No definite identification has been given, but various causes based on slimming, such as starvation, amyotrophy due to bowel cancer, tuberculosis or aging. From our point of view, these figurines depict the phenomenon of senile emaciation.

### H2. Gerocomie, prolonging life by the exposure to the effluvia of fresh and blooming youth [FLASH]

Fezoulidi G, Revelou MT, Eleftheriou A, Hatzikyriakou P, Tsoucalas G

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Ancient Greek medico-philosophers introduced the concept of diet (Greek: δίατα), which meant actually a way of life. Nutrition, exercise, sexual activities, peripatetic meditation, gymnastics, passion avoidance, personal hygiene, body homeostasis and education, were all included to this pioneering concept. Body and soul ought to be exercised in the same proportion. Skin and flesh were considered as parts of the body, thus parts which should be trained as well. Since the early classical period of the ancient Greece the custom of "Gerocomie" (Greek: γεροκομεία, intense care for the elderly) was a famous method of prolonging life by inspiring new strength and vigor into a body enfeebled under a load of many years, by exposing it to the effluvia of fresh and blooming youth. It is highly probable that the great value which the ancient Greeks and the Romans set upon inspiring the pure sound of breath, the very essence of a fresh air coming out from youth lungs and aroma from the fresh skin, may have established this idea, as testified by an inscription found in the ancient city of Rome, "To Aesculapius and Health Dedicated, By L. Clodius Hermippus, Who lived cxv years v days. By the breath of young maids). A known example of this practice may be found in the history of King David as we learn from several fragments in the writings of the ancient physicians, that this method was formerly much used,



and considered of great efficacy in relieving the infirmities of age. Even in modern times this prescription has been followed vigorously. The great Dutch botanist, chemist, humanist, and physician of European fame, Herman Boerhaave (1668-1738), caused an old burgomaster of Amsterdam to sleep between two young persons, while simultaneously he assures us that the old man acquired by this means a visible increase of vigor and activity. When one, indeed, reflects what change may be produced on diseased limbs by the vital evaporation of animals newly killed, and what may be the consequence of applying living animals to parts affected with pain (narce-torpedo fish, leeches), and what effect could be produced by the organ eating of newly killed animals or humans (heart, liver) this method of "Gerocomie" will appear not to be altogether despicable.

### **H3. Herodotus (ca 484-425 BC) and the fountain of youth [FLASH]**

Tsoucalas G<sup>1</sup>, Laios K<sup>2</sup>, Gritzalis K<sup>3</sup>, Markatos K<sup>2</sup>, Karamanou M<sup>4</sup>, Androutsos G<sup>2</sup>

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The quest for eternal youth started since the beginning of human civilization. Cosmetics and magic in antiquity attempted to revive the elderly. The prospect of immortality has always had universal appeal and all, commoners, aristocracy, kings, priests desired to be relieved from the side effects of aging which get in their way of success and eternal life. In the history of medicine a series of scholars and explorers have tried to unearth what it was believed to be "The Fountain of Youth", a spring (Greek: αναζωογονητική κρήνη) which possesses the power to restore the youth of anyone who drinks from or bathes in its waters. Surprisingly the first mention of such a fountain was made by the eminent historian Herodotus who is considered as an authority and the "Father of History" concerning the events in the known world of his era. When investigating for historical facts we accept his writings as a reliable source, however a reference for a mystique fountain extrude us to have some doubt about its authenticity. The "Fountain of Youth" was a common theme in ancient Greek mythology and the stories surrounding these waters became fabulous. Herodotus wrote about a tribe of people called the "Macrobian" (Greek: Μακρόβιοι, people able to live longer than usual), who were believed to have lived in modern day Africa (south ancient Libya, Ethiopia) and were known for their longevity and youthfulness. He recorded "When the Ichthyophagi (Greek: ιχθυοφάγοι, coast-dwelling tribe who eat fishes) showed wonder at the number of the years, he led them to a fountain, wherein when they had washed, they found their flesh all glossy and sleek, as if they had bathed in oil- and a scent came from the spring like that of violets. The water was so weak, they said, that nothing would float in it, neither wood, nor any lighter substance, but all went to the bottom. If the account of this fountain be true, it would be their constant use of the water from it which makes them so long-lived". Hebe the ancient Greek goddess who represented youth was strongly connected with springs, while reviving balneotherapy was an enjoyable practice in the era. Nowadays in Africa a series of tribes in their festivals still celebrate a "Macrobian" way of life, searching for eternal

beauty and youth. Herodotus takes both myth and history to produce truthful understanding. The fact that Herodotus mentioned the "Fountain of Youth" testifies that the Ancient Greeks were concerned with issues of longevity and youthfulness. Mythical or legendary, thermal or radioactive, healing or placebo, this fountain which supposedly reversed the aging process and cured diseases can not overshadow Herodotus as a story teller.

#### **H4. Third age conceptions and senior care in ancient Greece [ORAL]**

Kotsiou A, Tesseromatis C

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Aging and the relationships between young and old are closely related to the religions and state organizations of each era. Hippocrates (4th century BC) and Aristotle (3rd century BC) developed a theory of aging, of each individual having a reserve of innate heat or vital force gradually diminishing and leading to death of old age. Galen a prominent Greek physician (200 AD) attributed the aging and end of life to the evaporation of body humors preserving this vital flame. In ancient Greek society the elderly had an important political presence like Nestor, King of Pylos, an old man who held a powerful position on the Council of Elders, due to his heroic deeds. Regarding evidence for senior care in ancient world, among others, Egyptian Pharaohs were buried with walking sticks (canes) 3100-332 BC and recently 2013 bones of an old, severely disabled patient dated back to 500.000 years BC were discovered. To live as long as he lived suggests that senior care and human empathy are old and as humans. During the golden age of Greece, the Greeks regarded the care of the elderly as a sacred duty for the offspring. There were no public facilities for the aged so in many cities as Athens, Sparta, Delphi, those who neglected their parents or grandparents were punished by law (loss of citizenship).

#### **H5. Macrobian. Ancient Greek philosophy, the art of prolonging life [FLASH]**

Fezoulidi G

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Among the ancient Greeks, we may find several instances of great age. They are expressly called "Macrobian", and the secret to their age longevity is said to have been their lifestyle, which included the delight of journeys, the satisfaction of observation, tranquility, a sober and peripatetic life, a healthy diet, as well as homogeneous and harmonious daily activities. This was the way of the ancient Greek philosophers. Their way of life was a constant rivalry between pleasures and moral abstinence, their goal being the Gods' unmerited favour. They avoided quantity and always aimed for quality and did not forget to bless for every of their days among the living. Following are some examples of Greek philosophers and other great important figures who managed to prolong their life to a very old age, the wise Solon attained the age of 80, Epimenides of Crete is said to have lived 157 years, poet Anacreon, so fond of mirth and jollity, lived to the age of 80; as did also Sophocles and Pindar, Gorgias of Leontium, a great orator, a

man who had travelled much, and who spent a great deal of his time in the company of young people and in giving them instruction, prolonged his life to the age of 108 years, Protagoras of Abdera lived 90 years, Isocrates, a man of great temperance and modesty, lived 98, Democritus, friend and researcher of nature lived 109 years, fugal but slovenly Diogenes 90, Plato, one of the most divine geniuses that ever existed lived to the age of 81, Pythagoras, who in his doctrine recommended good regimen, moderation of the passions, and the gymnastic exercises, became also very old, about 84. It seems that the Hellenic died, and philosophy gifted ancient Greeks a remarkable for the era longevity.

## **H6. Ageing is natural, the ground-breaking Galenic doctrine [FLASH]**

Revelou MT, Eleftheriou A, Tsoucalas G

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The process of aging was viewed with different ways throughout the years. Others considered it as a stage of preparation for infirmity and even death, but the majority treated elderly people with respect, considered them wise and that is way they often held high positions in the political and military field. Galen (129-210 AD) was a physician who firmly believed that old age is a natural process and not a disease like others physicians did, due to the fact that it is not contrary to nature. Generally, the physicians of the time believed that heat was essential for the life and therefore ageing is associated with the drying and cooling of the body, which leads to an imbalance of bodily functions. In his book "De sanitate tuenda" (Greek: Υγιεινών λόγος, English: On the preservation of Health) Galen mentions his belief that aging starts the moment an organism is conceived, and he lists illnesses to which aged people were prone to. He also regarded infirmity as a stage of life with a different physical constitution and distinct needs. During his studies of old age, he suggested methods that could ameliorate the physical and mental state of the elderly, he commented on properties of foods and drugs that could make a difference in the decaying parts of the body, and he wrote extensively on the pros and cons of exercise because according to him it is a means of achieving euexia. More specifically, he mentioned how beneficial the exercise with a small ball can be in his work "De parvae pilae" (Greek: Περί του διὰ της μικράς σφαίρας γυμνασίου) as it provides "harmony between the parts of the body and virtue in the soul" and he criticized the excessive exercise. The raise in the average life expectancy in the last two centuries confirms Galen's view that we cannot stop the process of ageing, we can only delay it.

## **H7. Regimen Sanitatis Salerni, reviving the ancient Greek way of life [FLASH]**

Hatzikyriakou P<sup>1</sup>, Chondrou P<sup>1</sup>, Giatsiou S<sup>2</sup>, Tsoucalas G<sup>1</sup>, Karamanou M<sup>3</sup>

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During a period of 3 centuries, between 1050 and late 13th century, the treatise "Regimen Sanitatis Salernitanum" was written as a didactic poem in hexameter verse. It was in fact a code of daily regime for longevity to be achieved. It is also referred as "Flos Medicinae", or "Lilium Medicinae" (English: The Flower of Medicine, or The Lily of Medicine) attributed to John of Milan who actually lived in the 7th century AD. The fact that the poem bears the name of the famous medieval Medical School of Salerno does not provide certainty that it originated there. A blend of the Hippocratic doctrine for body homeostasis based upon the 4 humours theory (black bile, yellow bile, phlegm and blood), the Galenic concept of the six non-naturals (air, food and drink, sleeping and waking, motion and rest, excretions and retentions, and dreams and the passions of the soul) and the Hippocratic theory of the four temperaments (Phlegmatic, choleric, Sanguine and melancholic), tried to reintroduce the ancient Greek way of living for better health and longevity. It was firstly annotated and edited by the Aragonian physician and religious reformer Arnaldus de Villa Nova (ca 1240-1311) in its original Latin version, printed in the early days of printing, during 1480. A series of editions in various languages followed for this treatise concerning diet until mid 19th century. Fruits, beverages, balanced passions, tranquility, low body fat, wines, senses, seasons, thalassotherapy, balneotherapy, milk, hygiene, bloodletting, were all hidden in verses (i.e. Long-fasting, vomiting, and sudden fear, - It hurtful to the organ of the ear & Three special moments our text does remember,- For letting-blood April, May and September) for better understanding among the common people or most probably to attract romantic aristocracy. Due to its success, the "Regimen" was expanded from the original 364 lines to 3.526 hexameter verses, concerned to be highly revered as a scholarly medical text and was seriously discussed until the 19th century.

#### **H8. Care for the elderly in Byzantium: Gerocomeia and geriatrics [FLASH]**

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Elderly members of families (meaning those too old to work) were expected to be treated well and looked after by their children. But the expectation that families would "look after their own" was conditional upon their resources. The necessity of having many children to ensure "security in old age" was also attenuated by the growth of the charitable institutions provided by Church and State, although in many of the rural areas such considerations (of alternative "institutional" support) doubtless played a minor role. The care for the elderly in Byzantium was undertaken in special infirmaries, called "gerocomeia" which operated all over the empire mostly in or near the monasteries. Following the Christian ideal of philanthropy, numerous hospitals (nosokomeia), hospices (xenodocheia) and asylums for the elderly (gerokomeia) of a remarkable organisation and professionalism were founded in many cities of the Byzantine Empire. These welfare institutions for the elderly were founded by the Byzantine emperors, the church and some individuals who showed great interest in them in Constantinople, Jerusalem, Antioch, Alexandria, Nikaia, Ephesus, Thessaloniki and Corinth. The most important nursing home was located in Constantinople and was established by Emperor John II Comnenus (1087-1143) in the 12th century in the famous monastery and hospital of the Pantocrator. The oldest infirmary in Constantinople was founded by Saint Helen, the mother of the first Emperor of Byzantium,

Constantine the Great in the area of Psamatha. It was preserved until the 14th century. The foundation of nursing homes for the aged was at its peak in the 6th century. During the reign of Nicephorus Phocas (963-969) the number of nursing homes was so great that the Emperor published a Novella forbidding the creation of a new home; this was later (987) revoked by Emperor Basil II (958-1025) with a golden seal decree. The seventh Novella of the Justinian Laws provided measures for the good functioning of such institutions. Geriatric care and treatment constituted an essential part of the duties of the emperor himself, as he was the representative of God on earth, in cooperation with the Church. According to the rules of court procedure, the Emperors were obliged every Maundy Thursday to distribute gifts to inmates in Constantinople. By the end of the Byzantium Empire in 1453 and due to the different cultural development in the West, which was sometimes marked by conflicts between church and science and by the regulations of medicine, the knowledge about the Byzantine health care was almost lost. It survived, however, only in hospitals of occidental monastic orders, which brought their experience from East-Mediterranean area. Byzantine gerocomeia became the base for modern health care for the elderly and geriatrics.

### **H9. L'œuvre du Luigi Cornaro (1467-1566) sur la longévité [FLASH]**

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Luigi Cornaro était un noble vénitien, né au milieu du XV<sup>e</sup> siècle. Il est mort en 1566, à 98 ans. Cornaro a découvert les vertus de la sobriété à l'âge de 40 ans, après une jeunesse remarquable de l'indiscipline et du désordre. Sa nouvelle vie est caractérisée surtout de restriction et de contrôle alimentaires et est décrite comme un renoncement mais aussi comme une renaissance. Cornaro a écrit quatre traités entre ses quatre-vingt-trois et quatre-vingt-quinze ans et on trouve autant de force et de clarté d'esprit à tous ses œuvres. Il est renommé pour ces «conseils pour vivre longtemps». Ils constituent un corpus de textes très riche, sur le projet de prolongation de la vie et la conception du vieillissement. Son traité a connu assez d'éditions aux XVII<sup>e</sup> et XVIII<sup>e</sup> siècles grâce à son ton personnel, à la familiarité rassurante et à son caractère particulier. En son œuvre, Cornaro s'est éloigné des repères médiévaux et l'association entre matières précieuses et l'entretien du corps s'efface. Cornaro a souligné le rôle du contrôle de soi et de la surveillance particulière des réactions et des messages internes. La description des mécanismes corporels est basée sur les théories de l'Hippocrate et de Galien. Presque toute maladie vient de l'altération des humeurs du corps. Le mal est implacable et accentué par l'ivrognerie, la négligence des propriétés alimentaires et la vieillesse. La sobriété au contraire en évitant les mélanges des liquides diminue le risque de ces altérations. Cornaro contribue à la limitation du prestige que l'astrologie avait à l'époque et à l'affaiblissement de son rôle à l'apprentissage médicale. A ses textes Luigi Cornaro montre comment la santé et la longévité sont indissociables de la promotion

de la modèle de la médecine du soi et propose une manière insoupçonnée de prévenir les maladies et de renforcer le corps.

**H10. Old age diseases: their nature, cure and prevention in the *Nosologie méthodique* by Boissier de Sauvages (1770-1771) [ORAL]**

Droixhe D<sup>1,2</sup>

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In 1770-71 was published in 3 volumes a *Nosologie méthodique* by François Boissier de Sauvages, where are considered the diseases of the old age - a period starting after the age of sixty, for 18th century physicians. We consider gradually those diseases from the disabilities or small pathologies to the more serious health problems. First of all is examined the paracusia, or defect of hearing, and myopy, in a chapter where Boissier explains the process of evaluating the degree of the latter. The detection and treatment of cataract are analyzed. More serious is the tremo-raffecting old age persons: “a depraved movement of the limbs and of the head”. Another serious disease is the “oblivion of the age”: an “abolition or decrease of memory” that can “remove the faculty of recognizing the ideas produced in the brain”. The diseases of the backbone - rachialgy and lumbalgy – are characterized by “a difficulty in raising the trunk”. They may be caused by the fact of “carrying or raising heavy burdens” so that they especially affect the porters or the porters of sedan chairs. But the shoemakers or the cutlers, who have the “habit of working with the back bent down and always seated”, are also threatened by backbone diseases – like the people too much used to the “pleasures of love”. In the treatise entitled “De la vieillesse”, Marin-Jacques-Clair Robert wrote in 1777 that the single name of apoplexy, or stroke, “afflicts and worries”, so that “many persons who take all the imaginable precautions to protect them from it”. He considers the signs of the disease and recommends ways of evacuating the “superfluous of humors”, to provoke “a sudden loosening” of the “spasmodic effort” that precedes apoplexy. We devote a part of our paper to cancer and to the attacks against tobacco. We conclude with the perception of old age in the Enlightenment, an era of deep change in culture and mentalities, when the economic dynamics requested a stronger state of health in society. Voltaire’s thinking illustrates that conception of old age, which includes some extinction of sexual “desires”.

**H11. John Hunter (1728-1793): father of scientific surgery and pioneer in testicular transplantation [FLASH]**

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John Hunter was a Scottish surgeon, one of the most distinguished scientists and surgeons of his day. John Hunter came to London in 1748 at the age of 20. He worked as an assistant in the Anatomy School of his elder brother William Hunter (1718-1783). Under William's direction, John learnt human anatomy and showed great aptitude in the dissection and preparation of specimens. Hunter was commissioned as an army surgeon in 1760 and spent three years in France and Portugal. On his return to England in 1763 he began to build up his private practice. His scientific work was rewarded in 1767 when he was elected a Fellow of the Royal Society. In 1768 he was elected Surgeon to St George's Hospital. Hunter had an extension built to his house so that he could display all his specimens. His lectures on anatomy helped develop a more professional approach to medical training. Hunter studied many aspects of anatomy, using specimens to show the human body's structure and physiology. Hunter was also an avid collector, building up a huge collection of human and animal specimens. Furthermore, he carried out various experiments as part of a study on sexually transmitted infections such as syphilis and gonorrhoea, as well as other medical conditions like arthritis and its progressive stages. He was the pioneer who first opened the path of testicular transplantation and confirmed the gonad's action on sex characteristics, as well as the dependence of these characteristics on the gonads (1786). He believed that such transplantation could revive man's body and sexual endurance and fertility. Unfortunately, his experiments did not bear fruit, as his effort was quite ahead of his time. He died in 1793.

## **H12. Geriatrics in the work of the French physician and neurologist Alfred Vulpian (1826–1887) [FLASH]**

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Alfred Vulpian (1826-1887), physician and neurologist, was born in Paris where his father, of aristocratic descent, was a successful playwright and lawyer of the Royal Court. However, after refusing small pox vaccination, his father succumbed to this prevalent infection and his mother took over the child's upbringing. Having previously studied law, to sustain his existence, Vulpian obtained a technician's job with Pierre Flourens (1794-1867), the pioneer in cerebral function based on observation after ablative techniques. The young Vulpian must have impressed Flourens who used his influence to obtain his acceptance into the Paris medical school. His doctoral thesis in 1853, on the origin of cranial nerves III to X, was highly regarded. He was appointed 'Médecin des hôpitaux' in 1857 and 'professeur agrégé' in 1860, but taught neurophysiology until 1867. He then succeeded Cruveilhier (1791-1874) to the chair of pathological anatomy. In 1862, together with Charcot (1825-1893), he took over the chaotic Salpêtrière, a hospital for the chronic diseases, with many neurological patients. In 1856

Vulpian applied a solution of ferric chloride to slices of the adrenal glands and noted that the medulla stained green whereas the cortex did not. The same reaction was given by samples of venous blood leaving the adrenal, but not by arterial blood entering the gland. He deduced that the medulla synthesized a substance (later shown to be adrenaline and noradrenaline) that was liberated into the circulation. Many papers of Vulpian are mentioned to geriatrics studies. He showed that curare caused paralysis by affecting a point between nerve and muscle and he elucidated the actions of several drugs on the nervous system, including pilocarpine, strychnine nicotine and anaesthetics. With Charcot, he made important observations on multiple sclerosis and Parkinson's disease, where he instigated Prévost's description of conjugate deviation of the eyes and head in hemiplegia (Vulpian's law). When compared with Virchow and other German pathologists, the French had neglected the use of microscope. Vulpian set to work applying microscopy with simple stains to study issues in tuberculosis, poliomyelitis, and spinal muscular atrophy in geriatric population (Vulpian-Bernhardt spinal muscular atrophy). With Heidenhain, he showed slow contraction of denervated skeletal muscle by stimulating autonomic cholinergic fibres (the Vulpian-Heidenhain-Sherrington phenomenon). Vulpian wrote 225 papers, which disclose his depth and breadth of knowledge in pathology, physiology and experimental neurology. His merit was recognized by his appointment as Secretary of the Academy of Sciences: a signal honour. He became Dean of the Faculty of Medicine at Paris in 1875. Together with Charcot he founded the journal "Archives de Physiologie Normale et Pathologique". A stone memorial, discreet and dignified, lies in a small shaded Parisian street near the École de Médecine.

### **H13. Serge Voronoff (1866-1951): explorateur de la Fontaine de Jouvence et père de l'endocrinothérapie chirurgicale [ORAL]**

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Lorsque le donneur d'un greffon est d'une espèce ou d'un genre différent du receveur, on nomme ce type de greffe «hétérogreffe» ou «xénogreffe» (greffe étrangère). La xénogreffe, comme l'homogreffe, entraîne les mêmes problèmes biologique et éthique. Ces problèmes sont d'autant plus prégnants et actuels que les biotechnologies permettent de produire, en nombre, des donneurs transgéniques (porcs, babouins) dont l'utilité est indéniable pour la biomédecine. L'arrivée sur le marché médical de ces donneurs transgéniques n'est pas sans alerter certains observateurs qui les voient comme des porteurs potentiels d'agents viraux transmissibles et adaptables chez l'homme. Ainsi, les animaux transgéniques donneurs d'organes à l'homme pourront pallier la pénurie de greffons humains. Le porc sera «fournisseur» de vaisseaux sanguins, de valves cardiaques, de foie, de cellules du pancréas productrices d'insuline; le babouin fournira du tissu cervical, du cœur, du foie, des reins et de la moelle osseuse. A terme, et à condition que soient résolus les problèmes de rejet chez les receveurs et que soient supprimés les risques d'une infection de l'animal vers l'homme par des virus, l'élevage de porcs et de babouins transgéniques pourrait permettre de créer de véritables banques d'organes utilisables pour les «xénogreffes». Si aujourd'hui la xénogreffe est encore au stade de l'expérimentation, elle était couramment réalisée dans les années 1920 par le chirurgien Serge Voronoff qui est considéré comme l'initiateur de la pratique des greffes de testicules de singes chez l'homme.



Connu pour sa dextérité chirurgicale, ce praticien réalise une première greffe osseuse chez l'homme le 25 janvier 1908 et pratique pour la première fois une greffe d'os de chimpanzé chez un soldat pendant la première guerre mondiale (le chimpanzé donneur était un des pensionnaires de la ménagerie du Muséum). Voronoff avait également, en 1913, greffé une thyroïde de chimpanzé à un enfant et à un jeune homme myxoédémateux. Ce sont les greffes de thyroïdes de chimpanzé à l'homme qui ont conforté Voronoff dans l'idée qu'une glande endocrine de singe s'adapte parfaitement à l'organisme humain et produit des effets durables au moins égaux à ceux que peut produire une glande humaine. Le 12 juin 1920, Voronoff effectue officiellement la première greffe de morceaux de testicules de chimpanzé chez l'homme. Selon sa méthode chirurgicale, décrite plusieurs fois dans des ouvrages destinés au public, le receveur (l'homme) et le donneur (le singe) étaient simultanément opérés dans la même salle d'opération. Chirurgien de réputation internationale, élève de Jules-Émile Péan (1830-1898) et émule d'Alexis Carrel (1873-1944), Serge Voronoff entreprend, dès le début des années 1920, une endocrinothérapie chirurgicale sur les hommes âgés pour leur redonner une nouvelle « jeunesse ». « Garder durant toute l'existence les énergies de la jeunesse, les ardeurs de sentiments, cœur et cerveau affamés de vie, voilà ce que Serge Voronoff veut aux hommes. Ce sera le projet de sa vie tout entière. Ses travaux lui vaudront une célébrité retentissante. Aujourd'hui personne ne se souvient de ce grand chirurgien français, d'origine russe, qui se fit une spécialité de greffer des testicules de singes à des hommes désireux de retrouver leurs facultés défaillantes. Mais qui était donc ce chirurgien méconnu? Voronoff quittant sa Russie natale en 1885 – âgé alors de 19 ans – fait ses études de médecine en France; quelques années plus tard, après recommandation de son maître, Péan, il devient premier chirurgien du Khédive (souverain) en Égypte où il reste quatorze ans et étudie minutieusement la pathologie des eunuques du harem du roi. Après son retour en France, il acquit une pratique en réalisant de nombreuses expériences chez l'animal: expérience de greffes d'ovaires chez la brebis et testiculaires chez le bélier, le bouc, le porc et le taureau. En 1913, il présente le premier agneau né d'une brebis à qui il avait remplacé les ovaires. La même année, il greffe, à Nice, une thyroïde de chimpanzé sur un enfant atteint de crétinisme qui s'en porte mieux, puis fonde à Paris un hôpital financé par le tsar Nicolas B<sup>2</sup>; il y répare des soldats blessés au cours de la Grande Guerre, grâce aux os d'un singe fourni par le Président de France, Poincaré. En 1919, il présente les premiers résultats encourageants de « revitalisation » de vieux boucs par la greffe testiculaire. Sa technique consiste à « greffer » des morceaux de testicules de singe dans la tunique vaginale du testicule du patient. Voronoff avec ses émules – surtout avec son plus fidèle élève, Louis Dartigues – effectuèrent, jusqu'à 1939, au moins deux mille opérations réussies de greffe de singe à l'homme. La démarche biologique était fondée sur l'effet hormonal que devait produire le greffon. En 1926, il publie une synthèse de ses travaux et vulgarise le succès de sa méthode dans son ouvrage – best seller de l'époque – *Étude sur la vieillesse et le rajeunissement par la greffe*. Mais Voronoff et ses adeptes plus animés dans leur pratique par une idéologie eugéniste que par un but thérapeutique, ont à l'échelle mondiale, utilisé une pratique de « xéno greffe » (hétéro greffe): l'utilisation d'un organe animal ou partie d'organe animal greffé chez l'homme dans un but thérapeutique, pour pallier une pathologie. Finalement, Voronoff et ses émules ont été mis en marge par la pratique médicale et de la pensée biologique pour trois raisons: La première correspond à la difficulté de faire admettre la greffe animale chez l'homme; la deuxième à leur conception de l'espèce biologique et la troisième au rejet de l'identité de la glande de la masculinité (la testostérone) constituée par les cellules interstitielles (de Leydig). Concernant ce dernier point on remarque que, dans sa notice autobiographique, Voronoff admet que le tissu interstitiel (cellules de Leydig) sécrète l'hormone,

alors que dans ses publications à partir de 1923, il rejette cette idée en acceptant les conclusions erronées de son histologiste Édouard Retterer (1851-1934) (selon lesquelles les cellules de Sertoli qui revêtent les canaux séminipares sécrètent la testostérone). Curieuse est aussi la prise de position de Louis-Gaston Dartigues (1869-1940) qui admet que c'est bien le tissu interstitiel qui correspond à la glande sécrétrice. Il n'en demeure pas moins que cet aspect d'endocrinologie physiologique est particulièrement confus dans les représentations histologiques qui, en réalité, ne représentent plus rien de bien identifiable. Des structures histologiques sont masquées, d'autres sont redessinées. Notons au passage que les photos représentant les hommes greffés ont été retouchées pour mieux souligner l'amélioration physique des greffés. Les conceptions de Voronoff ne sont pas pour autant sans intérêt. D'une part l'idée de redonner une activité physiologique thérapeutique mérite d'être connue. Et d'autre part, il est le premier à promouvoir le rôle joué par les hormones sur l'équilibre de l'individu et pallier les déficiences glandulaires par les greffes de glandes jeunes. Il désirait obvier les inconvénients de la vieillesse, et, se référant à l'idée du pasteurien Élie Metchnikoff (1845-1916), allonger la vie. Il faut aussi préciser que Voronoff ne s'est limité à la pratique des greffes testiculaires. Il travaillait sur ce problème dans un contexte médical général: greffes osseuses, greffes thyroïdiennes, greffes ovariennes. Une des recherches qu'il effectue dans les années 1926-1927 est la greffe du pancréas. Dans le laboratoire de chirurgie expérimentale qu'il crée et dirige au Collège de France, il expérimente sur cette greffe et affronte plusieurs difficultés de réalisation. Il expérimente sur le chien et constate que la greffe de pancréas entier est impossible; seules les greffes de pancréas spécialement préparés et ne contenant que les îlots de Langerhans qui sécrètent l'insuline sont partiellement réalisables sur quelques jours. C'est Voronoff qui fera le premier ce type d'observation et dans le futur, ce seront les porcs transgéniques qui devront fournir les cellules sécrétrices d'insuline réalisant ainsi le projet de Voronoff. En fin de compte, Voronoff et ses émules ont sacrifié sur l'autel de la chirurgie et au profit de la défense d'une pensée eugéniste, le singe, en l'élevant au rang de l'homme et en en faisant son frère de sang. Dans les projets des futures xéno greffes il n'est pas prévu que les babouins transgéniques nous fournissent la moindre parcelle de leurs testicules: Voronof est-il condamné à une éternelle fiction? Voronoff mourut à Nice, en 1951, riche et célèbre!

#### **H14. Le ginseng, racine de santé et de longévité à travers des années [FLASH]**

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Le repoussement de l'échéance fatale et la poursuite de l'immortalité étaient toujours rêves de l'humanité. Les recherches sur la longévité ont montré que certaines substances comme les racines du ginseng arrivent à juguler le vieillissement. La consommation de ginseng remonte en Asie à plus de 4000 ans. C'est durant le règne du 1er Empereur de Chine que la racine de ginseng asiatique (*Panax ginseng*) fut considérée et reconnue une panacée (remède universel)

capable à prévenir la maladie et d'accroître la vigueur et la longévité. A cette époque la valeur du ginseng fut si grande que seulement l'empereur et les grands seigneurs de Chine pouvaient accéder à ce trésor. Le ginseng était un des cadeaux les plus précieux offert par l'empereur à un de ses sujets qu'il souhaitait voir vivre le plus longtemps à ses cotes. La tradition voulait que l'on administre en dernier lieu du ginseng à une personne à l'agonie pour la maintenir en vie et lui donner d'autres remèdes. Selon les documents chinois du 1<sup>er</sup> siècle ginseng illumine l'esprit et augmente la sagesse et sa consommation à long terme augmente la longévité. Les systèmes médicaux anciens reconnaissaient les plantes bénéfiques sur la santé de l'homme par leur ressemblance aux organes humains. Cette méthode appelée la Doctrine des Signatures proposait que la racine de ginseng ressemble à un être humain et pourrait être bénéfique pour le corps humain dans son ensemble. Au XIV<sup>ème</sup> siècle la réputation du ginseng a dépassé les frontières de l'Asie. Le célèbre navigateur Marco Polo, enchanté par les propriétés thérapeutiques de cette plante, l'a introduit dans le monde occidental à ses récits dans le «livre de merveilles». Plus que 200 ans de plus sont passés, pour que les premières racines de ginseng soient importées sur Europe par des commerçants hollandais. Pour sa part, l'usage thérapeutique du ginseng américain (*Panax quinquefolius*) est connu par les premiers Nations d'Amérique du Nord depuis de milliers d'années. La première étude en France concernant le ginseng a fait son apparition à l'Académie Royale de Sciences en 1697. C'est à la deuxième partie du XX<sup>ème</sup> siècle que la renommée du ginseng s'est peu à peu développée en Europe, grâce notamment aux recherches de Dr Brekhman. Depuis des millénaires les médecines traditionnelles chinoises, japonaises et coréennes l'utilisent pour ses effets toniques et aphrodisiaques.

### **H15. Hallmarks in longevity theories [FLASH]**

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Two major periods are recognized in the development of theories on the processes of aging. The dividing line between the two periods was drawn in the early 19th century. The first period is called period of theories. In this period the treatments of old age are affected more by the philosophical and religious thinking and magic and, to a lesser extent, by the observation and experiment. The alchemists, their main representative being Theophrastus Paracelsus (1493-1541), believed that the elixir of longevity was in the mineral kingdom and more specifically in its noblest elements. Arnaud de Villeneuve introduced in 1260 in medicine the alcohol, which he called "water of immortality". Another, equally ancient method of treatment is associated with the view that old age is due to loss of "internal heat". Another way of rejuvenation was the women's milk. Chinese alchemy followed the same path with the West. Pythagoras (580-500 BC) was fed exclusively with legumes, fruits, nuts, cheese, honey and ... mathematics. Hippocrates (460-377 BC) is the first who set the principles of preventing premature aging. The gold standard was the temperance and the self-restraint to everything. Galen (129-201) advocates the preservation of the activity, warm baths, massage and body rubbing with oil and vinegar, and

finally he emphasized nutrition. The second period in the development of geriatric medicine is called anatomo-clinical period. Leonardo da Vinci (1452-1519) is the one who performed the first dissection of the body of a very old person who had died of natural causes and left us in his "On the anatomy" a very instructive comparison of elderly arteries to those of a young person. The introduction of the anatomo-clinical method into geriatrics occurred in the 19th century thanks to the work of doctors in the geriatric hospital Salpêtrière in Paris. Both the legendary source of eternal youth and the elixir of longevity have not been found yet.

### **H16. The elixirs of life through the centuries [FLASH]**

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An elixir is a clear, sweet-flavoured liquid used for medicinal purposes, to be taken orally and intended to cure one's illness. The elixir of life, also known as elixir of immortality and sometimes equated with the philosopher's stone, is a potion that supposedly grants the drinker eternal life and/or eternal youth. This elixir was also said to cure all diseases. Alchemists in various ages and cultures sought the means of formulating the elixir. Throughout history, from the legendary ambrosia of the gods of ancient Greece, to the sought-after Philosopher's Stone among European alchemists in the Middle Ages, to the modern-day believers in such mythical substances, the idea of an "elixir of life" has been a constant illustration of our human desire to defeat mortality. It has assumed many forms throughout history, but in most legends, it takes the form of food or drink that grants the consumer immortal life. Some of the most popular ingredients used in ancient recipes include mercury, sulphur, iron, copper, and honey. Among the many mythologies of the ancient Greeks, perhaps one of the most famous is that around ambrosia, the so-called nectar of the gods. It came from the horns of Amalthea, the goat (or goatherd) foster mother of Zeus and was believed that it could heal scars, cure diseases, raise people from the dead, and banish death completely. Moving to Egyptian mythology and the legends of Thoth and Hermes Trismegistus, we will see that there are references to both of them drinking 'white drops', also referred to as 'liquid gold', which provided them with immortality. In Sumerian texts, we have references to the Ninhursag's milk, one of the seven great deities of Sumer, the goddess of fertility that is associated with a cow. The gods and the kings of ancient Sumer would drink from this milk to become strong and immortal. In the Epic of Gilgamesh, we also have reference to a thorny plant at the bottom of the ocean that would make someone immortal and this was kept as a secret of the gods. The earliest known attempts to create an elixir of life rather than just refer to it in mythology, took place in ancient China during the Qin dynasty. Taoists believed that certain chemicals and minerals like mercury and cinnabar (an ore of mercury, bright red in colour) had miraculous qualities. Ancient cultures in India, practiced ayurvedic rasayana, an early version of alchemy. The phrase loosely translates to mean the science of mercury, though it was not the only substance used to promote longevity. Amla, (a fruit similar to a gooseberry) was also a common ingredient. Other tales from ancient Indian

folklore speak of soma, a fermented drink that was said to grant the drinker immortality. The recipe has been lost to time, but historians believe it may have been made with the fermented milky sap of *Asclepias acida*, a kind of milkweed. In medieval times, there are accounts of the alchemists looking for the philosopher's stone, believed to be required to create the elixir but also to convert lead to gold. Bernard Trevisan, an alchemist of the 15th century said that dropping the philosopher's stone into mercurial water would create the elixir. We have multiple cases of alchemists that allegedly found the Elixir of Life including the infamous Cagliostro or Saint Germain. The primary function of alchemy was to find the legendary substance, process, or object that could turn base metals into gold. Known by many names — the Philosopher's Stone, the Stone of the Wise, the Diamond of Perfection, the Universal Medicine, the Forbidden Fruit — the substance was also closely associated with the elixir of life. The Philosopher's Stone was variously said to be made of red powder, liquid gold, golden seeds, and many more thousands of descriptors throughout history. Alchemists performed countless unsuccessful experiments seeking to identify it. Some have taken their quest for immortality less literally. Several historians believe that the Philosopher's Stone could signify immortality of the soul, or a symbolic wellness, much like some concepts in ayurvedic alchemy. The pursuit of eternal beauty by elixirs of youth as well as the research of the supreme panacea which equally transforms the body, spirit and soul is a never-ending story.

### **H17. Pioneering personalities and concepts in Romanian gerontology [ORAL]**

Baran D

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In Greek mythology, Medea remembered man's dream of turning the elderly into young robust individuals. In a different way, Romanian fairy-tales spoke of deathless life, necessarily associated to eternal youth. Later, senescence incessantly preoccupied philosophers and physicians, including Romanian ones. Macrobiotics dominated the XIX-th century. In the XX-th, other pioneering concepts emerged, explaining senescence, suggesting efficient treatments. New medical establishments ensured elderly's medico-social assistance. Documents reveal two interfering approaches: ageing was either a normal or a pathological phenomenon. Similarly to his mentor Charcot, Professor George Marinescu, father of Romanian neurology, considered ageing an irreversible physiological process. As dr. Panaite Zosin outlined, Charcot noticed so important texture “changes” of the body, that elders' physiology resembled pathology (1868). Zosin, a neuropsychiatrist from Iasi, trained equally in Paris, discriminated between senility and senescence. Atrophy, degeneration and atheromatosis characterized old age (1912). In 1924-1932, on experimental and clinical bases, Marinescu linked senescence to neurohistobiochemical disturbances, cellular and blood physico-chemical changes, protein and colloid alteration, oxidative and hydrolytic reactions, lipofuscin accumulation, chromatolysis, cholesterolemia. These aspects expressed regenerative-degenerative phenomena of the nervous and other biosystems, depending upon heredity, nutrition, environmental circumstances. Marinescu described the first senile plaques –plaques scléreuses (1892), he further studied in 1911-1912. These lesions also correlated with ageing. Conversely, Ilya Mechinikoff viewed senescence as a disease, phagocytes were responsible for (1901) and “probiotics” would treat. Constantin Parhon, professor of neurology and mental diseases in Iasi, thought ageing was a general dystrophy,

hygieno-dietetic prescriptions, organo- and opo-therapy possibly prevented and cured (1925). In Bucharest, Parhon and dr. Ana Aslan collaborated, inaugurating the first institute for gerontology and geriatrics (1952). Professor Aslan implemented Gerovital and Aslavital therapy and set up a national geriatric network. Updated integrative therapeutic strategies are constantly required since medicine should always add life to years, not only years to life.

**H18. Associate professor Constantin Bradu Fotiade (1928-2010): the Olympic dimension [FLASH]**

Tesoiu NJ

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Constantin Bradu Fotiade, Associate Professor of Interventional Cardiology Doctor Honoris Causa, Member of The Romanian Academy of Medical Sciences (Bucharest, Romania, 1928-2010), dedicates almost his entire professional activity, surpassing the second half of the XX-th century, to the technical study of the physiology and to the patho-physiology of the human cardiovascular system, mainly to the diagnostic and therapeutic cardiovascular catheterization, beginning at Coltea Hospital and fully developing at Fundeni Hospital. Contemporaneously with: Walter Forssmann, “Catheterization of the human heart”, 1929; Thomas Fogarty, “ Method for extraction of arterial emboli and thrombi,” 1962; Charles Dotter, “Percutaneous transluminal angioplasty of a focal stenosis of the superficial femoral artery”, 1964 and Juan Parodi, “Transfemoral intraluminal graft implantation for abdominal aortic aneurysms”, 1991. He utilizes, with his collaborators, for the first time in Romania, therapeutic endovascular procedures, today included in “Interventional Cardiology”, “Interventional Radiology” and “Endovascular Surgery”. As a vascular surgeon, I am honored to be invited to realize my Doctorial Thesis during a stage in this laboratory, thus bringing my contribution to the development of the Endovascular Surgery:” The place and the role of the percutaneous transluminal dilatation in the treatment of the Pulmonary valve stenosis,” 1998. Constantin Bradu Fotiade, conscient of the role due to his ancestors origins in the Greek island of Cos, has a major contribution to the sounding performances obtained by the Romanian athletes during The Summer Olympic Games held in 1968 in Mexico-City (approximately 2000 meters above the sea level) by preparing them in order to have the necessary physical condition for such an effort. Founding the Interventional Cardiology in Romania he is: Member of The European Society of Interventional Cardiology, 1974; Cited in “Interventional Biographical Center Cambridge”, 1992 and President of The Interventional Cardiology Section of The Romanian Society of Cardiology, 1994-1998.

**H19. Rudolf Virchow (1821-1902), Heinrich Schliemann (1822-1890), and Wilhelm Dörpfeld (1853-1940): An early paradigm of fruitful interdisciplinary cooperation in Prehistoric Archaeology [ORAL]**

Spyropoulos B

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**Introduction:** The aim of this paper is to present an early paradigm of fruitful interdisciplinary cooperation in Prehistorical Archaeology, in the late 19th Century.

**Methods:** Heinrich Schliemann (1822-1890), German entrepreneur and pioneer in 19th Century Archaeology, was an advocate of the historicity of places mentioned in Homer. He became an excavator of Hissarlik, along with Mycenae and Tiryns; however, Schliemann's excavation methods have been considered destructive. Interested in mutual influences of pre-historic cultures, multifarious Rudolf Virchow (1821-1902), carried-out an exhaustive study of the ancient amber and flint-traffic routes in Central Europe. It was largely a result of his friendship with Schliemann that he extended his studies beyond Germany. In 1879 he accompanied Schliemann to the site of ancient Troy, in 1881 to Caucasus, and in 1888 to Egypt, Nubia and Peloponnese. He was the first to adduce positive evidence for a period of Neolithic culture in the Nile Valley. Virchow's influence convinced Schliemann to entrust his later excavations at Troy, to Wilhelm Dörpfeld (1853-1940), an experienced German Architect and Archaeologist, pioneer of stratigraphic excavation and precise graphical documentation of archaeological sites. He was “accused” to over-emphasize the importance of buildings in dating of sites and to often neglect less visible artifacts, such as pottery. Dörpfeld, however, brought order and integrity into Archaeology; he has “saved” many archaeological sites from reckless excavations. He has founded in 1886, the German School of Athens (Dörpfeld Gymnasium) and he was Director of the German Archaeological Institute at Athens (1887-1912). **Results:** The synergy of three 19th/20th Century important charismatic personalities, attracted by the common “Eros to Prehistory”, has leveraged the ossified knowledge out of the excavation-sites and the oblivion. **Conclusion:** Early interdisciplinary cooperation in Science, Medicine and Humanities has gradually led, about a Century later, to the present explosion of knowledge and evidence-based Information Society.

## **H20. Archives of the Balkan Medical Union journal, a conspicuous promulgator of the History of Medicine [FLASH]**

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Marcus Tullius Cicero (ca 106-43 BC) the great Roman politician and rhetor said "History is the light of truth, the witness of the times and life teacher", those who neglect history are usually doomed to oblivion. During the last decade there is a tenancy in the international medical publications for the introducing of manuscripts concerning the history of medicine. Specialized journals but a series of medical ones as well included in their columns such papers. Archives of the Balkan Medical Union (ABMU) was not an exception. During 2008 inaugurated the publication section of the History of Medicine, publishing since December 2017 a total of 36 manuscripts. Greece since then is the main contributor with 86.1% of the publications, followed by Romania 8.3%, Bulgaria 2.8% and France 2.8%. Ancient Greece, Renaissance and the 17th-

18th century's period were the most researched time intervals. Emeritus Professor of the History of Medicine Georges Androutsos (National and Kapodistrian University, Greece), participating in 88.9% of the published manuscripts, followed by Associate Professor of the History of Medicine Marianna Karamanou (Crete University, Greece) 77.8%, Lecturer of the History of Medicine Gregory Tsoucalas (Thrace University, Greece) 36.1%, Dr Konstantinos Laios (National and Kapodistrian University, Greece) 30.5% and Associate Professor of the History of Medicine Effie Poulakou Rebelakou (National and Kapodistrian University, Greece) 8.3% respectively were the key participants. ABMU as the constant guardian of the Balkan and thus the European medical tradition continues to publish manuscripts with historical interest and encourages scientists both from the peninsula and from all around the globe to persist with their contributions.

## **H21. Dr Paul Niehans (1882-1971): cell therapy, the secret of life or a life-risking trend? [FLASH]**

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Cell therapy, also known as cellular therapy, live cell therapy or glandular therapy, is a procedure that involves the administration of whole cells, or cell components into humans for the treatment of a disease. The cells can be taken from the same individual (autologous) or from another (allogeneic) and in the majority of the cases, they derived from animals, especially sheep. Cell therapy seems to have a relatively long history. In the middle of the 19th century, German biopathologist Rudolf Carl Virchow (1821-1902) showed that the organism which appeared as a single unit, consisted of a mass of cells. He called cells "life-bearer". In the 1912, French surgeon Alexis Carrel (1873-1944) showed that cells can be very capable of adaptation and he also studied the influence of healthy cells on diseased cells. He observed that sick cells were called back to life by adding fresh, healthy cells. However, the most significant figure in cell therapy, was Swiss Dr. Paul Niehans, who in 1931, treated a patient who was suffering from severe postoperative tetany by injecting her sliced, calf's parathyroid glands in a solution. Not only did she stop convulsing but she also reported a full recovery and continued to live well into her 90s. Niehans, continued treating many patients with his cell therapy, leaving behind a new field, which many practitioners used for further research and practice. Nowadays, although cells taken from freshly slaughtered animals is the established technique, some practitioners started using freeze-dried, as well as orally taken cells as therapy products. His "success" followed by the establishment of specialized medical centers, as the "La Prairie" clinic in Montreux, Switzerland. Cell therapy claimed to treat hormonal dysfunctions as well as aging or psychiatric disorders such as schizophrenia or depression. Despite the absence of clinical observations, cell therapy evolved rapidly. Although in some countries like Switzerland and Germany clinics are permitted to use such products only within their cabinets, cell therapy is banned in many others



due to the fact that there have been reported serious consequences, even deaths. Despite both the controversy and the extremely expensive pricing, European clinics for cell therapies have become popular medical destinations for politicians and people who can afford it from all over the world.

## **H22. Geras, a trembling status among man and the Snake as the internal symbol of health in medicine [FLASH]**

Tsoucalas G, Fiska A

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Old age (Greek: γήρας) which considered as the antechamber of death, has always frightened man. The physical, mental and spiritual attenuation that characterizes it, as well as the suffering that accompanies this decline, always scared the elderly. Originally, the word "geras" (Greek: γήρας) in ancient Greek language was used for the cast skin of the snake. It was thought that creatures which cast off their skins possessed a degree of immortality as they were never trapped in old age. In the works of the poet, critic and scholar Callimachus (Greek: Καλλίμαχος, ca 310/305-240 BC) of Cyrene, the philosopher Philo Judaeus of Alexandria (Greek: Φίλων ο Αλεξανδρεύς, 20AD-45BC) and of the poet and grammarian John Tzetzes (Greek: Ιωάννης Τζέτζης, 1110-1180 AD), as well as in Anacreontea (Greek: Ανακρεόντεια, a collection of 60 ancient Greek poems on the topics of wine, beauty, erotic love, Dionysus, 1st century BC-6th century AD), creatures which renew their "geras" recover their youth (snakes, tettigies). Aristophanes son of Philippus (ca 450 BC), of the deme Kydathenaion in Athens (Greek: Κυδαθηναίων), was a comic playwright of ancient Greece to whom is attributed the nomination of the cast snake skin as "geras". The snake released from his skin, was also released from old age, able to kill and heal, became a characteristic synonym of the aggressive, negative and positive forces that rule the world. Emerging from the earth, having a chthonic nature, relative to the ancient Greek dragon (Greek: δράκος, large snake guardian of temples which sees and knows everything), soon became the symbol of immortality, power, regeneration, toxicology, healing and medicine. It was depicted alongside god Asclepius as his second nature, as well as in every votive column, statue and ancient Greek artefact related to health and death. Snake is still the paramount global internal symbol of the medical society.

## **H23. Histoire de cheveux blancs [ORAL]**

Chevallier J.

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L'apparition progressive et inéluctable des cheveux blancs est considérée, depuis l'Antiquité, comme un signe distinctif bien visible du vieillissement corporel. C'est le phénomène de canitie. Et pourtant, l'apparition précoce en dehors de la sénescence, localisée (poliose) ou généralisée,

de cheveux blancs existe et a pu susciter des situations remarquables dans l'histoire. Avant d'aborder la canitie physiologique, nous passerons en revue les canities non liées au vieillissement : avec les canities congénitales, qu'elles soient généralisées (albinisme ou syndromes apparentés) ou localisées (simple mèche blanche de cheveux ou piebaldisme avec la cas du grand résistant Pierre Brossolette) et les canities acquises : généralisées (canitie précoce avec l'exemple de Christophe Colomb, canities brutales avec le syndrome de Marie-Antoinette ou le cas de Marie Lafarge) ou localisées (vitiligo, phénomène de Sutton, repousse de pelade...). La canitie physiologique, stigmate du vieillissement, a entraîné une demande de correction esthétique permanente par tous les peuples tout au long de l'histoire. Les empiriques et les médecins ont toujours tenté de trouver des solutions pour cacher cette infamie! Nombreuses sont les tentatives de faire recolorer les cheveux et poils, par les teintures surtout mais aussi par des moyens « naturels » garantis sans teinture! De l'antiquité égyptienne, grecque, chinoise, romaine ou orientale, nous passerons à la Renaissance avec les grands cosmétologues de cette période et aux tentatives du XIX<sup>e</sup> siècle, avec la connaissance des dangers des teintures.

#### **H24. Bernardino Ramazzini (1633-1714): long live the Prince [FLASH]**

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Bernardino Ramazzini was an Italian physician born in Carpi. He was among the pioneers to propose the use of cinchona bark in the treatment of Malaria. His most important contribution to medicine was his book on occupational diseases, "De Morbis Artificum Diatriba" (Diseases of Workers), published in Modena during 1700. Professor of medicine at the University of Modena (1682-1700) appointed to the chair of "Theory of Medicine" he is considered as the founder of occupational medicine. It seems though that his attraction and affection towards the worker's class, planted concerns among aristocracy. Rammazzini to avoid losing the favour of the local benefactors he published several years later his treatise "De principum valetudine tuenda commentatio" (The principals to maintain health and commentary), dedicated to Raynald the Duke of Modena, calling him as a prince to adulate him. The book begins with the aphorism "The health of a good Prince is the greatest blessing imaginable to the public". Later on he encourages Raynald to follow his advises, a way to permanently maintain his favour, "A prince who regard his health, continues he, should permit his physician to remind him of the following particulars". Ramazzini an expert in general hygiene, epidemiology and general medicine, composed a series of 8 medical commandments for the Prince to embrace in order to achieve a healthy and long life. He succeeded once more to synthesize and to summarize thousands of years later the ancient Greek diet (body homeostasis, interaction with the environment, seasons, passion and gluttony avoidance and exercise) in only 7 simple rules for the Prince to follow. "Surprisingly" the 8th commandment was Prince's obligation to blindly and faithfully follow his

physician instructions under a continuous examination of his progress during this lifetime regime.

## **H25. Brown Sequard (1817-1894): the pioneer of modern opotherapy [FLASH]**

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I am going to speak about Brown Sequard, the great French "death enemy" and his efforts to conquer the ancient dream of the endless youth. Who really was this man who tried to defeat the flow of time? And what did he exactly do to achieve his extraordinary goals? His theory about the victorious war against senescence is truly interesting. He said once, that if the sperm of a young man is injected in the veins of an old one, the old man would regain his lost youth power and energy. In 1887 his tactic was first applied on old dogs by transplanting testicular sections to them. After many trials he started using testicular extracts of dogs and guinea pigs in saline solution. However, his most amazing effort was the experimented made on himself. The results? His strange and astonishing experiments were successful! As he admitted, his spiritual and physical energy were increased and, more or less, he was able to do things that couldn't do before the experiment. His reputation was at once spread throughout the scientific world! The results of his experiments were published in great scientific journals and in 1897 it was proudly announced the beginning of the sale of the "miraculous" youth medicine. Despite the fact that Sequard was blamed as controversial, due to the mysterious conditions under which his experiments had taken place, today it is widely admitted that Brown Sequard is the father of the modern opotherapy. That is because no one can deny that this type of therapy (called organotherapy and in particular opotherapy) based on natural organ extracts has a great and constant success. The gates of a new medical road were then opened and in the following years a series of health scientists enriched it with their novel and pioneering investigations.

## **H26. Skévos Zervos (1875-1966): le chirurgien pionnier Grec et les premiers greffes testiculaires du singe à l'homme au début du 20ème siècle [ORAL]**

Tsoucalas G

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Naquit en 1875 dans l'île de Kalymnos, dans l'archipel du Dodécanèse alors occupé par l'Empire Ottoman, Skévos Zervos, issu d'une famille de pêcheurs d'éponges, il étudie la médecine et se transforme en un clinicien capable de capturer des idées médicales pionniers pour son temps. Après des études médicales à Athènes, il effectua des stages en Allemagne, en Autriche et en France auprès d'éminents maîtres. En 1902, il fut nommé à Athènes professeur agrégé de gynécologie-obstétrique et d'histoire de la médecine. Il s'installa ensuite à Smyrne où il entreprit des greffes testiculaires. Il eut l'idée de greffer des testicules dans un but

thérapeutique et effectua ses premières transplantations chez des lapins et des chiens. Après avoir obtenu un nombre suffisant de greffes réussies, il en présenta les résultats au Congrès International de Médecine de Budapest en 1909, par une communication intitulée "Curieuses expériences sur les organes génitaux du mâle". Malheureusement, ses premiers résultats provoquèrent une réaction des autorités turques et son retour à Athènes. En 1910, il effectua à Athènes sa première greffe de testicule de singe sur l'homme. Zervos, appliquait l'endocrinothérapie chirurgicale à la sénescence, à l'impuissance, aux anomalies sexuelles, à certaines affections neurologiques ou psychopathiques, à certains cas d'inversion sexuelle et à l'adiposité. Le grand Serge Voronoff (1866-1951) a reconnu en 1934 l'avant-garde de Servos. Skévos Zervos est donc bien le premier à effectuer avec succès la transplantation des testicules, dix années entières avant le docteur Serge Voronoff, dans des conditions particulièrement difficiles et avec des moyens modestes.

## H27. Ageing is harmony and art [ORAL]

Ioannides PD

*Dr. Litt., author, poet, historian, Athens, Greece*

Healthy ageing is about "optimizing opportunities for good health, so that older people can take an active part in society and enjoy an independent and high quality of life". Using the mathematic Greek Language lexarithm, we shall note that the title of the 35th Balkan Medical Week "Healthy Aging: a perpetual challenge" in Greek version, ΥΓΙΗΣ ΓΗΡΑΝΣΗ ΜΙΑ ΑΕΝΑΗ ΠΡΟΚΛΗΣΗ =621+370+51+65+516=1623, is equal with, "first the healthy diet", «Α» Η ΥΓΙΗΣ ΔΙΑΤΡΟΦΗ=1+8+621+993=1623. The limit- ΤΕΡΜΩΝ = 300 + 5 + 100+40+800+50=1295 is equal to "senile age"- ΠΡΕΣΒΥΤΗΣ=80+100+5+200+2+400+300+8+200=1295. "Man", ΑΝΘΡΩΠΙΟΣ=1+50+9+100+800+80+70+200=1310 is equal to "the fundamental divine analogy", Η ΘΕΜΕΛΙΩΔΗΣ ΘΕΙΑ ΑΝΑΛΟΓΙΑ =8+1111+25+166=1310, equal to "aristocrat", ΑΡΙΣΤΟΚΡΑΤΗΣ=1+100+10+200+300+70+20+100+1+300+8+200=1310, equal also to "evolve", ΕΞΕΛΙΣΣΩ=5+60+5+30+10+200+200+800=1310. «The wisdom», ΣΟΦΙΑ=200+70+500+10+1=781, is equal to «is infinite», ΑΠΕΙΡΟ ΕΣΤΙ=1+80+5+10+100+5+200+300+10=781, "serenity is analogy", ΓΑΛΗΝΗ ΑΝΑΛΟΓΙΑ ΕΣΤΙ=3+1+30+8+50+8+1+50+1+30+70+3+10+1+5+200+300+10=781. Man is a fundamental divine analogy. The senile man signals the closing of the end of life's cycle. His old age is not an obstacle, but a constant challenge to deal with, «lifelong education». The science, the knowledge and the man in Ancient Greece were inseparably united and these were together an architectural ensemble, an artwork. "It's also good for the elder to learn wisdom". (Aeschylus 525-455 b.C.). Greek language suggests that "healthy diet" is clearly a primary factor in quality of life even to senile age. (Hippocrates 4th cent.b.C.) taught through that: "Let your medicine be your food and your food become your medicine." "Deal with physical activity which promotes endurance, strength, balance and mobility". "When the bodies become soft, their souls lose their strength" (Socrates 470-469-399 b.C.). "The body is the organ of the soul" (Hippocrates). "Being employed or involved in voluntary activities which is a great way of maintaining health and avoiding social exclusion". "Deal with the environment" which helps determine how active older people can be in society". "Deal with new Technologies which can enable elderly people to

remain more active citizens”. “Participate in activities which build social connections and improves well-being”. “Deal with Long-term care which can support with self-care activities and independent living”. “Learning throughout the life-course promotes social inclusion and better health”. “Seek the appropriate health and social services which should be accessible to all older people”. Conclusion: Where appropriate, every old man has gathered a certain amount of education, experience, soul value-paideia in his life. Most important is the old man knows how to get older, with soul peace, harmony, dignity and also how to love, in a way that is one of the most beautiful ones. And this is Harmony and Art. Epilogue: “The elderly peasant, loaded with wood and tired, called Death. Death came and asked him: “Old man I am present, why you invited me?” The old man replied, “to carry the woods to my house”. (Aesop-Myths, The Old Man and Death)”

## **H28. Aging: A journey in a cultural perspective through the Ages, and not a mere biological process [ORAL]**

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It is well accepted nowadays that aging is not just a biological process, but it is also more or less a cultural one. Elder care seems to have been a core human trait through the ages, although different civilizations and cultures have different attitudes and practices around aging. Ancient Greek and Roman civilization showed a lot of caring and empathy for their elders, basically expressed by their children or extended family. Medieval Islamic World is characterized by real progress in the understanding of aging and senior care. Old age was considered as a positive evil in Europe during the Dark Ages, whereas in the Renaissance and the Age of Enlightenment, Western society seems to have changed the perception of the elders, and started appreciating the benefits of aging. In the 19th century, governments in Europe and North America built “workhouses” and “poorhouses” for indigent seniors. The basic concepts of the elders care system developed in the mid-1800’s. Germany became the first nation to institute Old Age Pension in the 1880s, whereas in the 20th century governments particularly across the Western world, began instituting social welfare programs, such as Social Security in the U.S.A., which was passed as part of Roosevelt’s New Deal in 1935. In 1946 Great Britain enacted free health care for elderly citizens through National Health Service, whereas in 1965 Medicare and Medicaid were formed in the U.S.A., ensuring that seniors had access to medical care no matter what their means. As medical advances in the 21st century promise and guarantee a rapid increase of the elderly population, and unemployment and change of the working conditions throughout the world, constitute a serious problem for the socioeconomic stability and welfare of humanity, in depth knowledge of aging and caring for the elders become an issue of paramount importance worldwide.

## **H29. A Medico-historical perspective on the life of Zaro Agha (1777-1934): the alleged longest living man in the world [ORAL]**

Tekiner H

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Born in Bitlis, Turkey, in 1777, Zaro Agha was one of the most reputed super-centenarians, as he claimed to have lived for 157 years. He came to Istanbul at an early age; worked as a construction worker, porter and janitor for many years; and married 13 times. Enjoying a stunning popularity with Turkish and Western presses, he travelled across many places in Europe, the British Isles, and the US to perform at circuses and spectacles. Despite being a lifelong teetotaler, he was an inveterate smoker to the end and was reported to have subsisted mainly on vegetables, fruits, milk, yoghurt, and ayran (a cold savory yoghurt-based beverage). After his death on 29 June 1934, Dr. Behcet Sabit performed an autopsy at the Sisli Etfal Hospital in Istanbul. Several medical professionals, including Prof. Ihsan Sukru Aksel, published papers on their examinations of Zaro Agha's body, some of which were unable to verify his claimed age. Based on a number of local and international references, this study seeks to discuss Zaro Agha's life from a medico-historical perspective and to shed light on earlier international attention in the 20th century on "longevity and healthy aging."

## **H30. Eugenics: beginning and ending [FLASH]**

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Introduction. Based on the genealogical trees, he distinguished the disorders in family (remaining) and hereditary (dominant), the founder of human genetics Joseph Adams. Method. It has been reviewed the Greek and international bibliography and specific articles referring to the creation and the end of eugenics, which have been published in the databases Pub Med and Science Direct, during 2002-2017. Results. Joseph Adams, an English pathologist of the 18th century is considered the founder of human genetics after publishing his book, which referred to the principles of medical genetics. He was more concerned with the interaction of the environment and the hereditary factors, and first Johannsen, made the distinction between genotype and phenotype. Sir Francis Galton, a 20th century scientist in the United Kingdom, has expressed a clear distinction between the nature and nurture interaction. Galton promoted his idea of genetic improvement of man and animals, with techniques, with more discreet, the selective reproduction, with the term: Eugenic. At that time, it seemed reasonable, the purpose of human genetics to be the improvement of the human species with the selective reproduction. The Eugenists, a supporter movement of Europe and America's eugenics, at the beginning of the 20th century, considered the elements of human character to be inherited. With political influence, they created eugenic laws. Targeting people who were called "lifeless lives" (German: Lebensunwertes Leben), including, among other things, penal criminals, "degenerates", dissidents, mentally or physically weak, gay, inaccurate, insane, to be expelled from the chain of

heredity. The Eugenics was directly linked to the Nazi ideology of Germany. The T4 Program was the official name of the eugenics program of Nazi Germany and the Nazi occupied areas. It went on massive executions under the pretext of “euthanasia”. The aim of the program was to maintain the so-called “genetic purity” of the German race. Conclusions. With the end of World War II, Eugenics, due to its direct connection with the Nazi movement, collapsed. Serious reasons for the Eugenic’s collapse were the many scientific contradictions, and so, an unfavorable climate was created against them in the - then - scientific world. Thus, the concept of Eugenics, disappeared from the titles of institutes, magazines, books, conferences and replaced with Human Genetics.

### **H31. Pre-mendelic time of historic evolution of genetics [FLASH]**

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Introduction: As a concept, heredity has occupied people at least 6000 years ago. Excavations have shown that the Chaldeans, the people of Mesopotamia and the Persian gulf, first studied the heredity of the horses. However, the interpretation of heredity has remained unknown for centuries. Method: It has been reviewed the greek and international bibliography and specific articles referring to the pre-mendelic age of the historical evolution of genetics, which were published in Pub Med and Science Direct databases, during 2002-2017. Results: In the 3rd century B.C., Aristotle stated his idea in the world of science and philosophy that the coming of human semen was from the blood. It has the ability to give life to the fetus, which is formed by the coagulation of the period blood in the uterus. This ideology remained acceptable for 2000 years until the 17th century. In the 17th century, William Harvey, an English scientist of the time, from his studies in deer, said that there was no evidence of blood clotting, but how a small embryo was formed, which in stages increased in size and complexity. Thus, William Harvey was the first to disagree with the idealism of Aristotle and then the Catholic Church and put his idea in science. Recognition of the concept of ovum and sperm, which is a necessary condition for creating a new life, was first made by the Dutch scientist Regnier de Graaf. Also important marking for that time, he said, that sperm alone does not create new life, meaning, it not only gives these hereditary characters to descendants, but also the hereditary characters come from the mother. Pierre Louis Moreau de Maupertuis, a -also- 17th-century French scientist, was a naturalist and was studying the hereditary characteristics of man. His ideas were pioneering and resemble at many points with Mendel’s ideology. He believed that both parents contribute the same to the creation of their descendants and proved it with experiments done on animals. Maupertuis claimed that hereditary particles were present. Each particle is intended to form a specific part of the body. The body is formed by the union of two such particles, originating from one, from the father and the other from the mother. A particle may prevail over the other, and so, the descendants may look more like one than the other parent. CONCLUSION: Finally, Gregor Mendel (1822-1884) found his theory, without knowing the nature of the genes and for this reason is considered pioneering for his time. Mendelism is considered as the basis of Human Genetics.

### **H32. Vieillir: une préoccupation médico-sanitaire de longue durée [ORAL]**

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Cette communication vise à inscrire le thème contemporain du vieillissement, préoccupation tant médicale que politique et économique, dans une histoire de longue durée, afin d'en souligner quelques caractéristiques cruciales: un développement marqué par une dynamique de continuité et de ruptures, l'existence de rapports complexes et non stabilisés entre différentes forces impliquées dans la question du vieillissement dans les sociétés occidentales, telles que la science biologique, les institutions médicales, le systèmes socio-politique et économiques.

### **H33. L'œuvre du père d'immunologie Élie Metchnikoff (1845-1916) sur le vieillissement [FLASH]**

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Élie Metchnikoff (1845-1916) a été un zoologiste russe plutôt connu pour ses recherches pionnières en immunologie. On lui attribue la découverte de phagocytes (macrophages) en 1882. Cette découverte s'est révélée être le principal mécanisme de défense de l'immunité innée. Lui et Paul Ehrlich (1854-1915) ont reçu le prix Nobel en 1908 "en reconnaissance de leurs travaux sur l'immunité". Certaines sources lui attribuent également le terme de gérontologie en 1903 pour l'étude émergente du vieillissement et de la longévité. Ainsi, il peut être caractérisé comme père de la gérontologie, de la phagocytose et de l'immunologie scientifique. Il a été aussi parmi les premiers qui ont parlé du microbiome. Élie Metchnikoff a laissé un héritage scientifique important, convaincu de l'incroyable pouvoir des ferments pour prévenir la maladie et offrir plus de bien-être. Il est mort à Paris d'une insuffisance cardiaque. En ce qui concerne le vieillissement, les idées de Metchnikoff sur celui-ci sont détaillées dans l'analyse des "Études biologiques sur la vieillesse" (1901-1902), "Études sur la nature humaine" (1903) et "Essais optimistes" (1907). Sa théorie est comparée à d'autres explications qui ont eu lieu pendant son temps. L'hypothèse de Metchnikoff sur le vieillissement comprenait quatre concepts principaux: 1) l'empoisonnement chronique des personnes âgées; 2) prolifération microbienne à partir d'entérobactéries coliques; 3) importance de l'artériosclérose; 4) enfin, le rôle de la phagocytose et de l'immunité dans le processus de vieillissement.

### **H34. Ighatz Leo Nascher (1863-1944) and the foundation of modern Geriatrics [FLASH]**



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Geriatrics is coming from the Greek words "geros" that means elderly and "iatrikos" that means medical and actually is a term exactly opposite of pediatrics. Geriatrics is the specialty of 20th century. However, in ancient Egypt was found the first written advice for elderly people treatments. Greeks had also great influence in this new specialty and Hippocrates (460-377 BC) voiced his interest for the extension of lifespan and well-being. Romans were the first that established a system of "homes" for old aged people. All these ancient routes guide us to 19th century with the speculation if aging was a natural phenomenon or a kind of disease. Ignatz Leo Nascher, a New York physician was the first modern Geriatrician and actually the father of Geriatrics. In his 517-page book explains the three major sections of the causes-relation of aging. His first section that is called physiologic old age, describes the causes of normal aging and includes many theories about aging-related factors. His second and the biggest section is titled as "pathological factors" of aging, that describes some conditions and diseases that elderly face such as dementia, senile constipation etc. He suggests some solutions that may help and maintain old -aged people status. His closing chapter is called Hygiene and medical relation that is used as a guide for age-care institutions. Nascher as a pioneer of this "modern" specialty was clear for his concept and influenced all the geriatricians of next centuries. Now the field of Geriatrics receives the importance that deserves

### **H35. Old age and death concepts in epics, bible and mythology [FLASH]**

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The concept of death has always been one of the greatest questions of the human kind, having shaped our mentality and how we view this world. Humanity has always feared the unknown and in the past; this was depicted in religion, as science was at its infancy and most of the phenomena witnessed could not be explained. Most of the cultures of the Indo European language and cultural branch have similar myths that aim to alleviate the fear of death, but even in non Indo European cultures the concept remains the same, proving the universality of the mentality of the human race, towards viewing our major concerns. From the epic of Gilgamesh to "Theogonia" of Hesiodus, death is depicted as something evil, but inevitable. 400 years later the concept is being analysed from a much different perspective due to the appearance of philosophy, but even Plato in the Last Days of Socrates makes the following mention:

“No one knows with regard to death whether it is not really the greatest blessing that can happen to man’ but people dread it as though they were certain, it is the greatest evil.” Possibly we will never have an answer on the matter, at least in our generation, but understanding how the human race dealt with it in the past, points us the way on how to understand and befriend the concept of death with the modern human.

## BIOLOGY - GENETICS

### **B1. Apoptosis and micronuclei frequency in relation to age of healthy subjects [FLASH]**

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**Introduction:** Both apoptosis and micronuclei formation reflect cytogenetic damage and could contribute to cell homeostasis. The aim of this study was to evaluate apoptosis and micronuclei (MN) frequency in peripheral blood lymphocytes (PBLs) of healthy subjects and to correlate it with the age of subjects. **Methods:** The study population included 43 persons divided in three groups: 3-25 (15.89 ± 5.44) years (young), 26-50 (35.69 ± 7.02) years (adult) and 51-78 (57.4 ± 8.44) years (old). Apoptotic cells were detected using the Annexin V-FITC/7-AAD kit. Micronuclei were prepared using the Fenech and Morley method. **Results:** There were no significant differences in early apoptosis of PBLs in three groups of subjects (One-way ANOVA test,  $p = 0.243$ ). But, the differences in late apoptosis between young and adult study group ( $0.89 \pm 1.03$  vs  $0.21 \pm 0.23$ ,  $p = 0.001$ ) and young and old study group ( $0.89 \pm 1.03$  vs  $0.36 \pm 0.25$ ,  $p = 0.006$ ) were statistically significant. Also, the difference in MN frequency between young and old subject group ( $2.11 \pm 1.99$  vs  $5.64 \pm 2.29$ ,  $p < 0.001$ ) was significant, as well as between adult and old subject group ( $3.07 \pm 1.65$  vs  $5.64 \pm 2.29$ ,  $p = 0.019$ ). There is a negative correlation between the level of late apoptosis and age of subjects included in this study (Bivariate correlation test, Spearman  $r = -0.489$ ,  $p = 0.002$ ), while the correlation between age and MN frequency is positive (Bivariate correlation test, Spearman  $r = 0.571$ ,  $p < 0.001$ ). **Conclusions:** Aging was associated with a reduced level of late apoptosis and an increase of MN frequency in PBLs. The both, apoptosis and MN frequency correlated with the age of subjects.

### **B2. Frequency of MDR1 and CYP3A5 genetic polymorphisms in two Balkan endemic nephropathy regions in Serbia [ORAL]**

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**Introduction:** Balkan endemic nephropathy (BEN) is a slow progressive, non-inflammatory, chronic nephropathy with frequent occurrence of uroepithelial tumors in the upper urinary tract. The development of BEN is considered to be a multifactorial process, with the possible interaction of multiple genes with multiple environmental factors. The objective of this investigation is to analyze genetic polymorphisms of xenobiotic-metabolizing enzymes, MDR1 3435 C/T and CYP3A5\*3, possibly involved in pathogenesis of BEN, in persons originating from the two regions endemic for BEN in Serbia. **Patients and Methods:** This investigation included healthy subjects coming from BEN families from Brestovac (group B), South-East

Serbia, and Lazarevac (grup L), Central Serbia, and 80 healthy subjects coming from non-endemic area of Serbia (control group, K). After the thorough clinical examination, by which the current kidney disease was excluded, blood samples were taken and DNA isolated. All subjects were genotyped for MDR1 and CYP3A5, and frequencies of alleles and genotypes were calculated. Results: The genotype frequencies of MDR1 3435 C/T and CYP3A5\*3 are given in table.

Polymorphisms	MDR1 3435 C/T			CYP3A5*3		
	C	C	T	1A/1A	1A/3	3/3
B (n=80)	0.1	0.48	0.41	0.02	0.1	0.0
L (n=80)	0.37	0.59	0.04	0.0	0.0	1.0
K (n=80)	0.17	0.64	0.19	0.02	0.0	0.0

Conclusion: The differences in MDR1 and CYP3A5 genotype frequencies found between the two BEN endemic regions could influence the effect of environmental factors involved in pathogenesis of this disease. However, further, more extensive investigations are necessary to elucidate these findings.

### **B3. Examination of the toxicological effect of copper by measuring the activity of DNA-ase in in vitro conditions [ORAL]**

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Introduction. Copper particles are released into the atmosphere in the form of dust through volcanic eruptions, anthropogenic sources (pesticides, herbicides and fungicides) or from copper smelters and ore processing facilities. Due to increased human activity, the amount of copper in air, soil and water has increased. The  $\alpha$ -Lipoic acid ( $\alpha$ -LA) was first isolated in 1951. by Reed and associates, as a catalytic agent known by different names and associated with pyruvate dehydrogenase. One of the aims of this study is the study of the in vitro effect of copper, as well as the effect of the thiol substance, -S donor ligand ( $\alpha$ -LA) as a supplements, on the activity of commercial enzymes of DNase. Methods: Purified enzymes are used in in vitro studies, in this study, these are DNase I and II, i.e. alkaline and acidic DNase as commercial pure enzymes manufactured by Sigma-Aldrich. Measurements were performed on the Beckman DU 530 spectrophotometer. Results: The genotoxic and cytotoxic effect of metals (copper) in cases where the toxic substance disrupts the homeostasis of biochemical processes in the cell is not recommended and is justifiably applicable in vivo. These tests can be repeated and justifiably used as preliminary research, ie, the basis for further preclinical and clinical research. In an in vitro study, copper increases the activity of alkaline and acidic DNase. Conclusion. In vitro conditions, copper salts lead to an increase in alkaline and acid DNase activity by leading to the

formation of free radicals and oxidative stress. The results of these studies show that this can be prevented by adding proteins ( $\alpha$ -lipoic acid). According to the results of these studies, a positive effect of the thiol substance, -S donor ligand ( $\alpha$ -LA), on the activity of DNase (I and II) during copper intoxication was recorded.

#### **B4. Genetic and epigenetic factors render our biological age [ORAL]**

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**Introduction.** Human life-span is considered to be the result of the interplay between inherited cellular or molecular mechanisms and that person's lifestyle or environment. During the last decades, research has proven how interwoven these two areas are in normal individuals as well as in case of people with chronic illnesses. Epigenetics showed the influence of environmental factors even over generations, proving the tight connection that exists between living organisms and their environment. In the last years advances in technology spurred new ways of looking at and understanding that for a given person often times the chronological and the biological age are not one and the same. The aim of the present study is to bring evidence of recently published papers that validate the causal relationship between human longevity and genetic and/or epigenetic factors. **Methods.** Online available data published in the last three years are summarized. The selected data originated in longitudinal studies and had to show significant correlation between the biological age and genetic (telomere length, mitochondrial DNA mutations) and/or epigenetic (DNA methylation pattern, histone modifications, the presence of certain miRNA) markers. **Results.** Most currently published studies investigate age related variable biomarkers correlated with a pathological state of the organism, making it difficult to extrapolate the findings to normal individuals. Another limitation was that in their papers researchers had a different approach to confounding factors, like socioeconomic status, levels of present inflammation, gender, body mass index, physical activity, multivitamin intake, dietary antioxidants, tobacco smoking, alcohol consumption, hormone replacement therapy, that are known to influence the analyzed genetic markers. **Conclusion.** Inherited or acquired cellular and molecular structures and mechanisms build up a network-like system that controls and generates the biological age and the human life-span. The need for more studies to prove a clear-cut relationship emerges from this brief but up-to-date review.

#### **B5. Effects of nitrites on mitochondrial viability and proliferation rate of cultured renal epithelial cells [ORAL]**

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**Introduction.** High water nitrites intake and dietary sources of nitrites form in vivo potential carcinogens, being considered as factors with multiple health risks. Yet their effect on renal

tissues is far from being understood. In this research were employed two methods to assess the impact of cultured renal epithelial cells exposure to nitrites, in terms of survival and proliferation rate. **Methods and Materials.** Opossum kidney (OK) proximal tubule epithelial cells were cultured in Dulbecco's standard medium supplemented with 10% fetal bovine serum and 1% L-glutamine, without antibiotics. OK cells were exposed 24 h, in triplicates, to various concentrations of sodium nitrite (1 mM to 80 mM). Cellular metabolic viability was evaluated by determining the mitochondrial enzymatic activity using the MTS Assay (CellTiter 96® AQueous One Solution Reagent). A coloured compound (formazan) is produced if cells are viable in amounts corresponding to living cells number. Then the medium was replaced with a mix of MTS reagent and culture medium without phenol red (1:6 v/v). Cells were further incubated at 37°C for 4 h in a humidified environment, 5% CO<sub>2</sub> atmosphere. The optical absorbance at 490 nm was recorded for each well, using Awareness 96-wells plate reader. Cellular proliferation rate was evaluated by impedance-based tests (Real Time Cell Proliferation Assay RTCA), by recording Cell Index, that quantify the changes in the measured impedance of the cell monolayer during cells' adherence, growth and proliferation. **Results.** The sodium nitrites showed a cytotoxic effect on OK epithelial cells. The differences for various concentrations of sodium nitrites were analyzed for statistically significance with one-way ANOVA non-parametric test. **Conclusions.** The viability and proliferation rate of kidney epithelial cells are significantly affected by nitrites in various concentrations. Further study is in process for a larger range of concentrations, addressing also a possible tumorigenic effect on renal cells.

#### **B6. CITED4 suppression inhibits hepatocellular carcinoma [ORAL]**

Meiyi Song, Lu Xia, Fei Wang, Changqing Yang

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**Introduction.** Hepatocellular carcinoma (HCC) is an aggressive tumor associated with significant morbidity and mortality. Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 4(CITED4) is reported to be involved in the process of cell proliferation. In this study, we aim to evaluate whether CITED4 is essential for the growth of HCC. **Methods.** The expression of CITED4 in liver tumor and normal liver tissue was detected by immunohistochemistry staining. CITED4 was stably knockdown in HepG2 cell and SMC-7721 by using stable shRNA gene suppression. We performed EdU staining assay, flow cytometry, and transwell assay to evaluate the effect of CITED4 knock down on proliferation, cell cycle transition and invasion of the cell. Xenograft tumors model was built by CITED4 knockdownHepG2 cells to determine the effect of CITED4 on tumor growth. Western blotting was used to detect the related pathway. **Results.** CITED4 was significantly reduced in the liver tumor than in the normal liver tissue. Suppression of CITED4 induced proliferation inhibition and G1phase arrest in both HepG2 and SMC-7721 cell lines. CITED4 knockdown HepG2 also show weakened invasion ability than the control group. Tumors derived from CITED4 knockdown cells grew slower than control xenografts. We further observed that CITED4 inhibition reduced the activation of mTORC1 signaling pathway which leads to the suppression of tumor growth. **Conclusion.** The present study revealed that suppression of CITED4 can inhibit

tumor growth by regulating mTORC1 signaling pathway. CITED4 inhibition represents a potential therapeutic strategy for HCC.

### **B7. HOXA13 promotes liver regeneration by increasing BMP7 [ORAL]**

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**Introduction.** Liver regeneration is a common process during liver damage. With aging and invasion of injury factors, regeneration capacity will reduce gradually. As an existed endogenous hormone, we previously have reported that bone morphogenic protein-7 (BMP-7) could promote liver regeneration in vivo and in vitro. Our study aims to identify the upstream of BMP7 in regulating liver regeneration. **Methods.** We performed bioinformatics calculation to predict the potential regulator of BMP7 in liver. The expression level of HOXA13 in liver of 0h, 48h, 72h and 96h post partial hepatectomy (PH) was measured by western blotting. Homeobox A13 (HOXA13) knockdown hepatocytes were built by using stable shRNA infection to NCTC1469 and L02. Cell proliferations were detected by EdU staining assay and cell cycle analysis. Western blotting and rescue experiment was used to affirm the effect of HOXA13 on BMP7 expression. **Results.** Three potential regulators were identified by the software. HOXA13 has a binding site on the promoter region of BMP7. Compared to the liver at 0h, the expression of HOXA13 was upregulated at 48h, 72h and 96h post PH. HOXA13 knockdown hepatocytes were confirmed with a reduced HOXA13 expression level. Inhibition of HOXA13 induced proliferation suppression and G1 phase arrest. Lower expression BMP7 was detected in the HOXA13 knockdown hepatocytes compared to the wild type cell. The rescue experiment showed that BMP7 mediated the effect of HOXA13 on cell proliferation. **Conclusions.** HOXA13 was an essential factor of hepatocyte proliferation as an upstream regulator of BMP7.

### **B8. FNDC5 as a tumor suppressor gene in HCC by targeting mTORC1 signaling pathways [ORAL]**

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**Introduction.** As a current research hotspot, liver lipid metabolism and body energy imbalance are important factors leading to the occurrence and development of hepatocellular carcinoma (HCC). Over expression of FNDC5 in hepatocellular can improve obesity and insulin resistance by releasing irisin. The aim of this study was to determine whether differential expression of FNDC5 exerted influence on hepatocellular carcinoma and the molecular mechanisms to enrich the relevant systems of tumor energy metabolism. **Methods.** Small interfere RNA was transfected to HepG2 to interfere with the expression of FNDC5. FNDC5 over expression plasmid was used to increase the content of FNDC5. Western blot was used to detect protein expression level. EdU staining and flow cytometry were applied to identify changes in proliferation. Migration and

invasion ability were detected by wound-healing assay and transwell assay. Results: The expression of FNDC5 was significantly reduced in HepG2 cells and human liver tumor tissue by western blot and immunohistochemical staining. Knockdown of FNDC5 promoted the proliferation, cell cycle progression and invasion of HepG2 cells in vitro. While overexpression of FNDC5 had the opposite effects. Further, the inhibitory effects of FNDC5 on HepG2 cells were emerged by activating the mTORC1 pathway. The role of si-FNDC5 in the promotion of HepG2 cells could be alleviated by rapamycin. Conclusion. FNDC5 exhibits low expression in hepatocellular carcinoma and plays a critical inhibitory role in HepG2 cell lines by activating mTORC1 pathway. FNDC5 overexpression will be a potential therapeutic target for HCC.

### **B9. The effect of supplements on telomere length [ORAL]**

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Introduction. Telomeres are specific DNA regions positioned at the ends of chromosomes that protect them from attrition and damage. Recent evidence highlights the pivotal role of critically short telomeres and aging related diseases. Environmental dietary and lifestyle factors have been related with telomere maintenance. The aim of the present study was to examine whether dietary vitamin supplements can influence telomere shortening. Methods. Telomere lengths of a total of 47 healthy volunteers, aged from 40-55 years old, measured. Metaphase spread leukocytes were isolated from peripheral blood. The telomere length measured by quantitative fluorescence in situ hybridization procedures (Q-FISH) with (C3TA2)<sub>3</sub> peptide nucleic acid (PNA) probe, photos from 10 metaphases from each individual were taken by Confocal microscopy and analyzed by image-J. Results. Our approach revealed that the whole telomere length and short telomeres were positively influenced by the nutritional supplementation. This is a very interesting result due to the fact that recent evidence highlights the pivotal role of critically short telomeres. There were no significant differences in telomere length between participants' sex. Conclusion. The results of our preliminary study suggest that nutritional supplements may affect the length of whole and short telomeres. Not to extrapolate, this study provides evidence that the antioxidant effect of nutritional supplements is implicated in telomere length maintenance. Short telomeres are critical to cell homeostasis and the only reliable method for the reliable evaluation of short telomere distribution is QFISH. Future research directions should focus on the mechanisms through which restoration of nutritional deficiencies has an impact on telomere shortening.

### **B10. Correlation between cardiac muscle aging and micro-RNA sequences [FLASH]**

Altis D

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The purpose of this review is to highlight what is aging, how aging affects cardiac muscle, what diseases are caused by aging and what molecular markers, like micro-RNAs help us (or not) in the reduction of aging process. First of all, aging is a manifestation of progressive, time-dependent failure of molecular mechanisms that create disorder within a system of DNA and its environment (nuclear, cytosolic, tissue, organ, organism, other organisms, society, terra firma, atmosphere, and universe). Continuous signaling, transmitted with different kinetics across each of these environments, confers a "mutual enslavement" that creates ordered functions among the components within the system. Accrual of this molecular disorder over time, i.e. during aging, causes progressive changes in the structure and function of the heart and arteries that are quite similar in humans, non-human primates, rabbits and rats that compromise cardiovascular reserve function, and confer a marked risk for incident cardiovascular disease. Furthermore, nearly all aspects of signaling within the DNA environment system within the heart and arteries become disordered with advancing age: Signals change, as does sensing of the signals, transmission of signals and responses to signals, impaired cell renewal, changes in the proteome due to alterations in genomic transcription, mRNA translation, and proteostasis. Moreover a very interesting finding is the fact that autophagic activity declines with age and may explain many features of age-related cardiac dysfunction. Impaired autophagic clearance of protein aggregates or deteriorating mitochondria will have multiple consequences including increased arrhythmia risk, decreased contractile function, reduced tolerance to ischemic stress, and increased inflammation; thus autophagy represents a potentially important therapeutic target to mitigate the cardiac consequences of aging. Last, but not least the correlation between miRNAs and aging is highlighted. MicroRNAs (miRNAs) have emerged as crucial regulators of cardiovascular function and some miRNAs have key roles in aging. Altered expression of miRNAs in the heart during aging contributes to the age-dependent decline in cardiac function. MiR-34a is induced in the ageing heart and in vivo silencing or genetic deletion of miR-34a reduces age-associated cardiomyocyte cell death. Moreover, miR-34a inhibition reduces cell death and fibrosis following acute myocardial infarction and improves recovery of myocardial function.

### **B11. Distribution of common thrombophilia mutations in healthy south-east Serbian population [ORAL]**

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Introduction. Thrombophilia represents an underlying ground for thrombotic conditions that are leading cause of mortality in European populations. Our study objective was to determine the frequency of genotypes and alleles of coagulation factor V G1691A (Leiden), factor II G20210A mutations, and methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism in general,

healthy, population of south-east region of Serbia. Methods: The study enrolled 210 healthy Caucasian subjects. The G1691A and G20210A mutations were determined using a multiplexed allele-specific PCR method, while C677T MTHFR was detected separately using allele-specific PCR method. Results. We determined 4.10% heterozygous factor V G1691A mutation carriers (A allele frequency 2.05%), G20210A mutation was present in 3.17% also in heterozygous form (A allele frequency 2.11%), while MTHFR 677TT genotype was present in 11.11% of subjects (T allele frequency 34.30%). All tested alterations were in Hardy-Weinberg equilibrium, without distribution difference between genders. Conclusion. The determined prevalence of factor V G1691A and prothrombin G20210A mutations are slightly higher than average in Europe, but consistent with the prevalence in the neighboring countries. The MTHFR C677T genotypes rates are similar to the average rate in Europe and mostly similar to those in the neighboring countries, but lower than European trend of the higher southern T allele distribution. Our results are applicable in assessing the health risk of the local population, especially if associated with acquired thrombotic risk factors.

### **B12. DNA ploidy in endometrial carcinomas [FLASH]**

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Introduction: Worldwide, endometrial carcinoma is the 5th most frequently diagnosed cancer among women and the 13th as cause of death. The number of new cases and cancer deaths for 2015 was 455.000 and 90.000 respectively. The important prognostic factors for patients with endometrial carcinoma include age, surgical FIGO stage, myometrial invasion, histological subtype and grade and lymphovascular invasion. In addition to these factors, assessment of DNA ploidy has repeatedly been reported to be of prognostic importance with aneuploidy as a marker for aggressive disease. Methods: Endometrial samples freshly resected from 126 women who underwent total abdominal hysterectomy were studied. The mean age of the patients was 68.3 years with a range from 37 to 82 years. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues and stained with Feulgen stain. Results: According to our results, in terms of quantitative estimation of cellular DNA, all case-control samples from proliferative, secretory and atrophic endometrium (total number 30) were exclusively diploid (DNAindex 0.9-1.1), while at least 75% of Grade 3 (total 27/126) tumors present an euploidy of DNA (DNA index <0,9 or >1,1) as opposed to about of 36% of Grade 1 (total 42/126) and Grade 2 (total 57/126) endometrial carcinomas. In our study, the percentage of aneuploid neoplasms mainly concerned stage III and VI tumors and less those of Stages I and II. Conclusion: We believe that the use of the quantitative assessment of cellular DNA may help identify tumors with high malignant potential and possible aggressive behavior or ability relapse offering valuable information, both in prognosis and in the treatment of patients with endometrial carcinoma. According to international literature, aneuploidy is an independent prognostic marker of relapses, a sign of malignant transformation and can therefore predict a poor prognosis.

## **CITOLOGY - PATHOLOGY**

### **CP1. A retrospective review of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) cytology [FLASH]**

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**Introduction.** EBUS-TBNA is a minimal invasive sampling technique which has been applied for investigation of pulmonary and mediastinal lesions of both benign and malignant diseases. Multiple studies have shown that EBUS-TBNA has similar diagnostic yield to other available techniques such as conventional TBNA and mediastinoscopy. **Method.** This is a retrospective review of 625 patients that underwent EBUS-TBNA between the years 2015-2017. The smears were processed by the conventional method and stained with Papanicolaou stain. In cases positive for malignancy the type of tumors was classified according to their morphological and immunocytochemical criteria. **Results.** Of all 625 cases 313 were negative for malignancy while the left 313 cases were positive and more specifically: 122 (47,2%) cases of adenocarcinoma, 57 (22%) squamous cell carcinoma, 10 (3,8%) small cell carcinoma, 48 (18,6%) non-small cell carcinoma and 21 (8,1%) were metastatic carcinomas. In 54 cases the diagnosis concerned cells atypical or suspected for malignancy. **Conclusion.** From our results it seems that adenocarcinoma is the most common type of lung cancer followed by squamous and small cell carcinoma. Moreover EBUS-TBNA provides a reasonable degree of sensitivity and specificity in the diagnosis of lung, mediastinal and hilar lesions. Cytology combined with immunocytology has important clinical value in diagnosis, subtyping and guiding the treatment strategy.

### **CP2. Cytological evaluation of effusions: a retrospective study (FLASH)**

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**Introduction.** The abnormal accumulation of fluid in pleura, pericardial and peritoneal cavities is a relatively common complication of both benign and malignant conditions. Cytological examination of effusions plays an important role in the diagnosis of the underline condition. In the cases of malignancy immunocytochemistry can also be used in malignant cells of both primary and metastatic lesions. **Method.** A retrospective analysis of 9.305 pleura, 242 pericardial and 207 peritoneal fluid samples between the years 2015-2017. All specimens were processed by the conventional method and stained with Papanicolaou stain. The diagnosis was based on cytomorphologic and immunocytochemical features. **Results.** Of total 9.754 samples received and evaluated, 7.332 were negative, 1.596 were positive and 826 cases concerned cells atypical or suspected for malignancy. Among positive effusions the principal malignant tumors were lung

carcinomas and more specifically: 938 adenocarcinomas, 143 small-cell carcinomas and 28 squamous cell carcinomas. 143 positive cases concerned breast cancer, 41 ovarian cancer, 12 gastric cancer, 22 urinary bladder carcinoma, 5 renal carcinoma, 7 liver cancer, 4 cholangiocarcinoma, 6 prostatic cancer, 14 malignant melanoma, 3 multiple myeloma and 13 mesotheliomas. Conclusion. Cytology of body cavities effusions is the most informative and definitive initial diagnostic step in benign and malignant conditions. It is also a rapid, cost effective and highly sensitive method of diagnosis especially regarding malignant effusions which in combination with immunocytochemistry can detect the subtype of primary or metastatic tumor and provide important aid in treatment choice.

### **CP3. The role of EBUS-TBNA in the diagnosis of metastatic renal cell carcinoma: report of an interesting case [FLASH]**

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Introduction: Endobronchial ultrasound-guided needle aspiration (EBUS-TBNA) is a well-established procedure with high diagnostic accuracy for the evaluation of mediastinal and hilar lymphadenopathy. Renal cell carcinoma is the seventh most common type of cancer in the western world and clear cell renal cell carcinoma (CCRCC) is the most common histological subtype and one of its most frequent sites of distant metastasis is the lung. Method: A 41-year-old ex-smoking Caucasian male presented with cough and fatigue in the emergency department. Chest X-Ray and computed tomography (CT), revealed a right hilar mass. The patient had a history of CCRCC treated six years ago with nephrectomy. At the time of diagnosis, the patient was found with right pulmonary metastasis and a lobectomy was performed followed by chemotherapy. During his last submission a high clinical suspicion for metastatic CCRCC was present. EBUS-TBNA was the diagnostic method of choice where cytologic and histologic samples were collected. Results: The cytological examination revealed loosely cohesive groups and single malignant-appearing cells with round nuclei, eosinophilic granular cytoplasm with ill-defined borders and dense blood infiltrate in the background. The tumor cells exhibited immunoreactivity for Vimentin in cytologic samples while in histologic samples immunostains for CD10, CK8-18 and RCC markers were positive. Conclusion: In the presented case we were able to obtain a definitive diagnosis of mediastinal lymph node metastasis from CCRCC by EBUS-TBNA. Clinical evidence indicates that patients with mediastinal and/or hilar lymph node metastasis have a poorer prognosis. Therefore accurate diagnosis and staging is critical for the patient.

### **CP4. Conventional tranbronchial needle aspiration (c-TBNA) cytology: a retrospective study (FLASH)**

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**Introduction:** TBNA was developed in 1980s by Wang and Terry. It is a method of sampling performed via flexible bronchoscope under conscious sedation with a low risk of complications. It is cost-effective, safe and efficacious bronchoscopic modality that can be used in diagnosis of both benign and malignant conditions. Although multiple studies have established the utility of c-TBNA in diagnosis and staging of lung, mediastinal and hilar lesions, in Greece remains an underused technique with only 21% of pulmonologists reporting its use. **Method:** A three years retrospective study (2015-2017) of c-TBNA cytological samples. The smears were processed by the conventional method and stained with Papanicolaou stain. In malignant cases the type of tumor cells was classified according to their morphological and immunocytochemical criteria. **Results:** Out of 716 cases 327 were negative for malignancy. In 331 cases the diagnosis confirmed malignancy and more specifically: adenocarcinoma in 172(52%), squamous cell carcinoma in 85(25,6%), small-cell carcinoma in 12(3,6%), non-small cell carcinoma in 52(15,7%), while 10 (3%) cases were metastatic carcinomas. In 58 cases the diagnosis concerned cells atypical or suspected of malignancy. **Conclusion:** From our results it seems that the adenocarcinoma is the most common type of lung cancer followed by squamous and small-cell carcinoma. C-TBNA can be used as a standard first-line minimal invasive technique for the diagnosis of lung, mediastinal and hilar lesions. Furthermore c-TBNA cytology in combination with immunocytochemistry improves the diagnostic accuracy and clinical staging in cases of malignant neoplasms.

#### **CP5. The value of ki-67 expression in endometrial carcinomas [FLASH]**

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**Introduction:** Endometrial carcinoma is the most common malignant tumor of the female genital tract and the fourth most common female cancer in the developed countries followed by breast, colon and lung cancer. It is clear today that, cytomorphology alone is not often sufficient to provide an accurate diagnosis, but additional techniques such as immunocytochemistry are required to solve differential diagnostic problems. Our aim was the value of Ki-67 expression in endometrial carcinomas since the human nuclear antigen Ki-67 is a protein whose existence is associated with a high rate of proliferation of cancer cells and hence a faster progression of the disease and therefore smaller survival. **Methods:** Endometrial samples freshly resected from 126 women who underwent total abdominal hysterectomy were studied. The mean age of the patients was 68.3 years with a range from 37 to 82 years. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues. The specimens stained with Papanicolaou stain and Ki-67 antibody (clone MIB-1, dilution 1:150, DAKO). **Results:** Out of 126(100.0%) cases, 102 were endometrioid (81.0%) and

24nonendometrioidcarcinomas (19.0%). High expression of Ki-67 was more frequent in type II (87.5%) comparatively to type I (52.9%) adenocarcinomas (p=0.00). In addition, high expression of Ki-67 was found to be related to more aggressive features such as advanced stage of disease (stage I: positivity 43.0%, stage II: 77.0%, stage III: 84.2% and stage IV: 100.0%) (p=0.00) and poor grade of differentiation (grade1: 47.6%, grade 2: 59.7% and grade 3: 77.8%) (p=0.00). Conclusion: Immunocytochemical findings from Ki-67 stain, in addition to cytomorphologic features, appeared to be useful for the diagnosis of endometrial carcinoma in endometrial cytology with imprint smears and may help to organize the appropriate therapeutic strategy for the survival of these patients.

#### **CP6. Study of the p53protein expression in endometrial carcinomas [FLASH]**

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Introduction: Endometrial cancer is the most common malignancy of the female genital tract in developed countries at a rate of 12.9 and a mortality rate of 2.4 per 100.000 women. It is clear today that cytomorphology alone is not often sufficient to provide an accurate diagnosis, but additional techniques such as immunocytochemistry are required to solve differential diagnostic problems. Our aim was the value of p53 expression in endometrial carcinomas since the p53 gene has a tumor-suppressive effect that plays a particular role in inhibiting the cell cycle by limiting uncontrolled cell proliferation and its loss leads to inhibition of apoptosis. Methods: Endometrial samples freshly resected from 126 women who underwent total abdominal hysterectomy were studied. The mean age of the patients was 68.3 years with a range from 37 to 82 years. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues and stained with Papanicolaou stain and p53 antibody (clone DO-7, dilution 1:50, DAKO) Results: Out of 126 (100.0%) cases, 102 were endometrioid (81.0%) and 24 nonendometrioid carcinomas (19.0%). High expression of p53 was more frequent in type II (87.5%) comparatively to type I (28.5%) adenocarcinomas (p=0.00). In addition, high expression of p53 was found to be related to more aggressive features such as advanced stage of disease (stage I: positivity 22.8%, stage II: 46.2%, stage III: 57.9% and stage IV: 100.0%) (p=0.00) and poor grade of differentiation (grade1: 14.3%, grade 2: 40.4% and grade 3: 77.8%) (p=0.00). Conclusion: Immunocytochemical findings from p53 stain, in addition to cytomorphologic features, appeared to be useful for the diagnosis of endometrial carcinoma in endometrial cytology with imprint smears and may help to organize the appropriate therapeutic strategy for the survival of these patients.

#### **CP7. The contribution of cyclooxygenase-2 in endometrial carcinomas [FLASH]**

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**Introduction:** Endometrial cancer is the most common malignancy of the female genital tract in developed countries at a rate of 12.9 and a mortality rate of 2.4 per 100.000 women. It is clear today that cytomorphology alone is not often sufficient to provide an accurate diagnosis, but additional techniques such as immunocytochemistry are required to solve differential diagnostic problems. Our aim was the value of COX-2(cyclooxygenase-2) expression in endometrial carcinomas since the prostaglandins play an important role in initiating and promoting the carcinogenic process and have been positively correlated with growth, metastasis, advanced stage, relapse, and survival. **Methods:** Endometrial samples freshly resected from 126 women who underwent total abdominal hysterectomy were studied. The mean age of the patients was 68.3 years with a range from 37 to 82 years. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues and stained with Papanicolaou stain and COX-2 antibody (clone 33, dilution 1:50, DAKO). **Results:** Out of 126 cases, 102 were endometrioid (81.0%) and 24 nonendometrioid carcinomas (19.0%). High expression of COX-2 was more frequent in type II (79.2%) comparatively to type I (6.9%) adenocarcinomas ( $p=0.00$ ). In addition, high expression of COX-2 was found to be related to more aggressive features such as advanced stage of disease (stage I: positivity 0.0%, stage II: 30.8%, stage III: 57.9% and stage IV: 73.3%) ( $p=0.00$ ) and poor grade of differentiation (grade 1: 0.0%, grade 2: 17.5% and grade 3: 59.2%) ( $p=0.00$ ). **Conclusion:** Our study showed that in cytological specimens the expression of COX-2 in quantitative level alone cannot contribute substantially to the diagnosis and differential diagnosis of endometrial carcinomas. However, it was observed that expression of COX-2 is related to more aggressive and advanced stage of disease and therefore with a less favorable survival prognosis.

#### **CP8. Contribution of immunocytochemistry in effusion cytology. A 1-year retrospective study [FLASH]**

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**Introduction:** The cytological examination of the fluids is considered an important diagnostic tool in detecting the cause of the fluid collection in the body cavities. The main utility is to identify a malignancy and our purpose was the evaluation of the results of the cytological examination of pleural, peritoneal and pericardial effusions with the contribution of immunocytochemistry. **Methods:** Retrospective study of the results of the cytological examination of 1432 pleural, 48 ascites and 46 of pericardial fluids of the year 2016. Most of our patients had more than one sample. The smears were processed by the conventional method and stained with Papanicolaou

stain. Several combinations of immunocytochemical markers were applied in correlation to cell morphology and patient's history (Calretinin, TTF-1, Ber-EP4, CD56, WT-1, CEA, S-100, HMB-45, EMA, Vimentin, LCA, CK7, CK20, etc.) Results: A total of 1526 cases were identified as: a) Negative for malignancy 1171 b) Suspicious for malignancy 104 c) Positive for malignancy 251 cases, out of which the origin of malignant cells was detected either morphologically alone or in combination with the use of immunocytochemical markers. More precisely 42 breast, 14 ovarian, 9 stomach, 3 liver, 1 cholangiocarcinoma, 1 kidney, 3 bladder, 1 prostate, 3 mesotheliomas, 2 melanomas, 1 multiple myeloma, 3 lymphomas, 131 lung adenocarcinomas, 17 small cell carcinomas, 2 squamous carcinomas and 18 tumors of unknown primary origin. Conclusion: Although in several body cavities malignant neoplastic cells are relatively easy to recognize, there are some cases where the site of primary origin is not easy to identify and a question arises as to whether it is a primary neoplasm or a metastatic one. As we have seen from our study, the use of immunocytochemistry technique contributes to a safe conclusion and can help to organize an appropriate therapeutic strategy for the survival of these patients.

### **CP9. Results of EBUS-TBNA in cytological specimens: Retrospective study of one year [FLASH]**

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Introduction: EBUS-TBNA is a technique that combines the characteristics of ultrasound and endoscopy. It gives information about the bronchial wall and its surrounding areas and allows tissue samples to be taken under direct guidance, thus improving diagnostic effort and eventually therapeutic intervention, thereby preventing invasive techniques. It can replace more invasive methods in the staging of lung cancer and in the diagnosis of lymphadenopathy of the mesothorax. The accuracy in the diagnosis of central tumor invasion is 94%, the sensitivity 89% and the specificity 100%. Our aim was the evaluation of 320 cytological results of EBUS-TBNA samples in order to highlight the incidence of lung cancer types. Methods: Retrospective study of the year 2016, the cytological results of EBUS-TBNA specimens from 320 patients. The average age was 60.2 years (44-73 years). The smears were processed by the conventional method and stained with Papanicolaou stain. The type of tumors was classified according to their morphological and immunocytochemical criteria. Results: Out of 320 cases, 184 were negative for malignancy. In 119 (72.1% men) cases the diagnosis was malignancy and more specifically: adenocarcinoma in 57 (48%), squamous carcinoma in 31 (26%), small cell carcinoma in 2 (1.7%), non-small cell carcinoma in 20 (16.8%), while 9 (7.5%) cases were metastatic carcinomas. In 17 cases, the diagnosis concerned cells atypical or suspected of malignancy. Conclusion: From our results, it seems that adenocarcinoma is the most common type of lung cancer followed by squamous and small cell carcinoma. Additionally, we would like to add that EBUS-TBNA remains an important technique in the diagnosis and staging of lung cancer and



that the expertise of a cytopathologist is obligatory for reaching high levels of accuracy, sensitivity and specificity.

## INTERNAL MEDICINE

### IM1. Liver biopsy: useful for the diagnosis of ovarian adenocarcinoma? [FLASH]

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Introduction: Most frequently, ovarian adenocarcinoma metastasizes in the liver, peritoneum, lung and lymph nodes. Case presentation: A 74-year-old hypertensive and dyslipidemic woman presented for bilateral leg edema, increased abdominal volume and dyspnea at moderate efforts. The patient was known with a history of ovarian adenocarcinoma, with hysterectomy and bilateral anexectomy 8 years ago. Physical exam: balanced cardio-pulmonary, with bilateral leg edema, abdomen sensitive to palpation in the right upper quadrant, with the inferior edge of the liver at 3-4 cm below the rib cage, of medium consistency and irregular surface. Abdominal ultrasound revealed a non-homogeneous mass in the right liver lobe, of 8 cm in diameter and 2 hypoecogenic masses, with a diameter of 2 cm and 1.8 cm, pelvic ascites. The CT exam revealed a small amount of bilateral pleural fluid, calcified pulmonary micronodules; paraortic adenopathies with tendency to confluency, of max 18/16 mm, nodules in the right thyroid lobe with cystic appearance and calcifications; a iodophilic tumor mass, encompassing ileo-cecal valves; carcinomatosis and large ascites fluid. Liver with multiple hypodense lesions, with areas of necrosis, suggestive of secondary determinations. Spleen with numerous nodal lesions, suggestive of secondary determinations. Hepatic biopsy was performed, with histopathological examination and immunohistochemical tests, that supported the diagnosis of a poorly differentiated hepatic metastasis of a genital or mammary adenocarcinoma. Considering the patient's history, the origin of the tumor is most likely ovarian. Conclusions: In spite of performing imaging investigations, sometimes the determination of the primary tumor site can be confirmed only by histopathological and immunohistochemical examination of secondary tumors.

### IM2. Oral conditions with systemic reflection in older people (ORAL)

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Oral cavity comes directly in contact with external world and is exposed to infectious agents, traumatic and environmental factors older people being particularly vulnerable. Mouth could

represent a monitor of the health both locally and systemically. It reflects healthy and unhealthy behaviors, physiological activities, and its integrity is sustained or damaged by nutrition and hygiene. Dental disorders and poor oral hygiene influence physical and cognitive homeostasis and also frailty in older people. Moreover, many of the symptoms and signs of systemic conditions appear in or around oral cavity including by inducing alterations in mucosa and its underlying structures. Several such disorders that occur most often in people beyond the age of 65 years will be reviewed. Missing or defective teeth influence selection of food and predispose to a diet containing mainly carbohydrates and refined sugars, predisposing to many deficits including vitamins (especially vitamin C and B12, with their impact on immunity and cognitive function) and micro- and macronutrients. In older people this unvaried diet can lead to a drop in gastric pH and this increases the risk of caries and various oral infections. In addition, older people that do not have their dental problems corrected or who have defective dentures are predisposed to avoid fibrous fruits and vegetables, which leaves them prone to gastrointestinal disorders and signs of collagen damage in the mucous membranes and periodontium. A good oral condition significantly influences general health and the quality of life in older people and should not be overlooked.

### **IM3. Comparison of general and clinical characteristics among children of different ethnic background suffering from scarlet fever in the region of central Kosovo [ORAL]**

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**Introduction:** Scarlet fever is a contagious disease characterized by sore throat and tiny bumpy skin rash. The causative agent is a group A hemolytic streptococci, which causes inflammation of nasopharynx and toxemia. Scarlet fever is related to different ethnicities, their culture and health-care education in the region of Kosovo. The aim of our study was to analyze general and clinical features in children suffering from scarlet fever in the Kosovo region. **Methods:** This study enrolled 82 children treated at the Department of Pediatrics, Clinical Hospital Center Priština. It was conducted from November 2017 to February 2018. Data were obtained from medical histories of patients with scarlet fever. Diagnosis was established according to epidemiological and clinical data, blood count, and determination of serum ASOT. **Results:** Average age of patients was  $7.97 \pm 2.03$  years, (MIN- 4, MAX- 17 years). The majority of children were between 7 and 16 years of age (55.7%) Roma children, (27.6 %) Albanian children and children of other nationalities, between 4 and 11 years of age – Serbian children (21.1%). There were 46.5 % undernourished and 28.6 % obese Roma children. Clinical manifestations in Roma children (58.2%) included: temperature  $>38.5$  C, pharyngitis (19.7%), angina (34.7%), ‘raspberry’ tongue (27.5%), peeling of the palms and soles (77.6%); Serbian children (33.7%): temperature ( about 38.5 C), angina (24,7%), sore throat ( 29.7%), small red bumpy skin rash (49.8 %), sporadic outbreaks (33.7%), rash resembling rubella (13.1)%; ‘raspberry’ tongue (39.5 %), flaking of the skin (21.7%), and peeling of the skin (14.5%); nephritis in 11.1% and glomerulonephritis in 3.4% of Roma children. **Conclusion.** Most cases of scarlet fever in Kosovo

enclaves occurred in Roma children. Special efforts should be made regarding education about scarlet fever and identification of the carriers and affected individuals.

#### **IM4. Aging and kidney transplantation [ORAL]**

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Kidney transplantation remains the treatment of choice for ESRD in elderly patients, providing a survival advantage and better quality of life when compared with dialysis. Elderly patients (>65 years old) represent the fastest growing population among the ESRD patients and those awaiting kidney transplantation. However, conflicting results have been reported regarding the effects of donor age, recipient age and donor-recipient age difference on short- and long-term outcomes after kidney transplantation. Advanced age is often considered a relative contraindication for transplantation, but there is much variability in the actual age limit for transplantation among transplant centers. Moreover, chronological age alone seems to be a less important predictor of poor outcomes after transplantation when compared with factors like comorbidity burden, disability, and frailty. Cardiovascular disease, risk of infection, and malignancy are associated with poor outcomes in elderly transplantation patients and should be carefully evaluated during the pretransplantation screening process. Due to the well known circumstances in the Balkan region during the last 25 years, some transplant centers started to use elderly donors as a suitable source of kidneys. The authors widely elaborated the issue of elderly, even in advanced age, living donors presenting the own very good 20 years clinical experience. Despite the slightly worse long term graft survival compared with the younger donors, the authors fully recommended use of elderly living kidney donors which could ameliorate the severe organ shortage, especially in the Balkan region. Aging and kidney transplantation still remains a challenging issue for the further clinical use of this complicated procedure among the elderly patients and kidney donors.

#### **IM5. Epidemiological and clinical characteristics of adult patients suffering from morbilli in Serbian enclaves in Kosovo [ORAL]**

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Introduction: Morbilli is a contagious condition manifested by catarrhal changes of the conjunctiva and mucous membrane of the upper respiratory tract, as well as by maculopapular

rash. Morbilli poses a significant health problem in the regions of Kosovo that have not reached adequate levels of vaccination. The aim of the study was to investigate epidemiological and clinical characteristics, as well as vaccination status of persons affected by morbilli in Serbian enclaves in Kosovo. **Methods:** This was a prospective study including 97 adult patients (69 males and 28 females) in the period from October 2017 to March 2018. The patients were treated at the Infectious Diseases Clinic, Clinical Hospital Center Priština. The diagnosis was established according to epidemiological and clinical characteristics, blood count, and findings of specific IgM antibodies in serum. **Results:** Average age of patients was  $33.25 \pm 12.83$  years, (MIN 20, MAX 47 years). They were divided into 3 age groups: 20 – 29 years (32.7%), 30 - 39 years (48.7%), and > 40 god (21.6 %). As for nationality, there were 43.7% of the Roma population, 42.2% Serbian population, and 21.7% Albanian and other nationalities. There were unvaccinated (58.7%) and incompletely vaccinated (22.3%) patients, Clinical signs and symptoms included: temperature: > 39°C (57.8 %); about 38.5 °C – 44.5 %, about 37.5 °C - 9.4 %; facies morbillosa – 53.5%, dry cough – 63.7 %; Koplik’s spots – 13.4 %; nausea and vomiting –34.7 %, diarrhea – 61.2 %, fatigue 81%. Rash: on face – 65.2 %, on the trunk - 78.2 %. Complications: pneumonia – 61.2 %. **Conclusion:** Appropriate strategies for measles eradication should include mandatory vaccination, epidemiological surveillance and therapeutic measures.

#### **IM6. The beneficial effect of calcitriol on the status of anaemia in chronic kidney disease patients [ORAL]**

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**Introduction:** Metabolic Bone Disease (MBD) is one of the major complications of Chronic Kidney Disease (CKD). Lack of kidney functional tissue understands also lack of many regulatory mechanisms including hormonal homeostasis for both, Erythropoietin and PTH. The clinical results are anaemia and secondary hyperparathyroidism (HP) which are dominant clinical issues practically in every CKD patient. Fortunately, both are treatable with appropriate medications. The authors report unusual effect of Vit D3 therapy (Calcitriol) on anaemia status in CKD patients. **Material and Methods:** Thirty six CKD patients on regular three times weekly dialysis treatment were treated with Calcitriol per os 0.25 and 0.50 µg on daily policy during a period of 6 months for the purpose of preventing MBD. None of the patients was on Erythropoietin. Regular once a month laboratory follow up including HB, HTC, Ca, P04, and APH was introduced among the others clinical parameters. More than 10% of increase of HB was considered as a relevant difference during the therapy. **Results:** During the times of follow up we noticed a significant increase (more than 10%) in 30 of 36 HD patients which represents 83.3% of the treated population. Bearing in mind that only the start of Calcitriol therapy was a significant change in the time of follow up, we strongly believe that the better control of HP means also a good clinical outcome in anaemia in CKD patients. **Conclusion:** Our small study confirms that orally administered calcitriol is also effective in the treatment of uremic anemia. More detailed multicentre and control studies with larger number of patients are needed for any relevant conclusion.

### **IM7. Erectile dysfunction in patients with chronic kidney disease [FLASH]**

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**Introduction:** Erectile dysfunction is a frequent complaint of patient with chronic kidney disease and end stage kidney disease or those who undergo hemodialysis. This pathology implies the inability to obtain and maintain an erection which is sufficient for achieving a satisfactory sexual intercourse. **Objectives:** The purpose of this paper is to underline the pathophysiology of erectile dysfunction and to review its management in patients with chronic kidney disease. It is estimated that its prevalence ranges between 50% and 80% in the population of patients with chronic kidney disease. **Methods:** According to literature, several factors can be involved in the pathogenesis of erectile dysfunction: alterations of the neuro-endocrine system and of the hypothalamic-pituitary-gonadal axis, peripheral neuropathy, vascular wall damage and alterations of the cavernosal smooth muscle, drug related erectile dysfunction, stress, depression. Over the years, several therapeutical options have emerged for the management of erectile dysfunction, some of them offering great results: phosphodiesterase 5-inhibitors, intraurethral suppository or intracavernosal Alprostadil injections, vacuum erection devices, constriction rings and penile prosthesis. **Conclusions:** The presence of erectile dysfunction is a sign of vascular damage and it can predict a vascular event in future. Therefore patients diagnosed with erectile dysfunction at a younger age have higher risks of cardiovascular events, chronic kidney disease, end stage kidney disease and dialysis.

### **IM8. Xanthogranulomatous pyelonephritis: at the border between two specialties [FLASH]**

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**Introduction:** Xanthogranulomatous pyelonephritis is a rare form of chronic pyelonephritis, dubbed the "great imitator." It is associated in many cases with renal lithiasis and sometimes with renal neoplasms, especially in its focal forms. It is a pathology that, untreated, leads in most cases to renal destruction. **Methods:** This type of pyelonephritis is a serious pathology that often requires an interdisciplinary approach involving both the urologist and the nephrologist. **Assessment of presentation forms, clinical-pathological aspect and therapeutic approaches** are the subject of this article. **Results:** The clinical spectrum varies greatly from classical pyelonephritic appearance to combinations involving other pathologies of unusual diversity: renal lithiasis, renal abscess, renal neoplasia. Neighborhood organs are not "forgiven" by this disease, there are cases involving involvement digestive tract, respiratory system, etc. **Treatment of this pathology** requires close collaboration between the urologist and the nephrologist sometimes requiring the involvement of other specialties. **Conclusions:** Xanthogranulomatous pyelonephritis is a rare pathology with a serious prognosis for the patient. For a good prognosis, aggressive treatment of the condition involving both the urologist and the nephrologist is often needed.

### **IM9. Irritable bowel syndrome [FLASH]**

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Irritable bowel syndrome (IBS) is a chronic and debilitating functional gastrointestinal disorder that affects 9%-23% of the population across the world. Patients with IBS are often referred to gastroenterology, undergo various investigations, take various medicines, take time off work and have a poor quality of life. The pathophysiology of IBS is not yet completely understood and seems to be multifactorial. Many pathogenetic factors, in various combinations, and not all necessarily present in each patient, can play an important role. Discomfort or abdominal pain relieved by defecation, associated with a change in stool form, is a typical clinical manifestation of IBS. Many factors, such as emotional stress and eating, may exacerbate the symptoms. A timely diagnosis of IBS is important so that treatment which will provide adequate symptomatic relief (diarrhea, constipation, pain and bloating) can be introduced. The diagnosis of IBS is not confirmed by a specific test or structural abnormality. It is made using criteria based on clinical symptoms such as Rome criteria, unless the symptoms are thought to be atypical. Today the Rome Criteria IV is the current gold-standard for the diagnoses of IBS. Treatment of patients with IBS requires a multidisciplinary approach. Some patients respond well to non-pharmacological treatment, while others also require pharmacological treatment. This review will provide a summary of pathophysiology, diagnostic criteria and therapies for IBS.

### **IM10. The efficacy of kinetotherapy in knee osteoarthritis [FLASH]**

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**Introduction:** Kinetotherapy is indicated as the non-pharmacological treatment method for knee osteoarthritis (OA) by the EULAR and OARSI recommendations. The importance of manual therapy as specific form of kinetotherapy has not been studied in small group. **Objective:** To evaluate the effectiveness of conventional conservative kynetotherapy combined with manual physical therapy in patients with knee OA. **Methods:** According to American College of Rheumatology (ACR) criteria, knee OA patients were included in a randomized, controlled, open-label trial and treated in University Rehabilitation Center, in the Republic of Moldova. Participants received both a conventional kinethotherapy and manual therapy, over 10 days. For functional knee evaluation, we used the evaluation of joint mobility with goniometer and muscle strength from 0 to 5 points. The pain was assessed by Visual Analogue Scale (0 to 100mm). This study was conducted according to the principles of the Declaration of Helsinki (1996) and good clinical practice. **Results:** There were 28 patients integrated in the study including 20 females and 8 males, mean age  $64.19 \pm 6.9$  years (range 42 to 72 years). Disease duration was  $8.7 \pm 6.4$  years (range 1-22). The pain level was  $78.5 \pm 4.7$ mm. The patients with knee OA have improved the knee flexion after kinetotherapy with  $18 \pm 4.0$  degree ( $p < 0.05$ ), and knee internal and external rotation with  $7 \pm 2.9$  and  $6 \pm 1.7$  degree respectively ( $p < 0.05$ ), but there were no changes in the articular extension. We also established the significant decrease of pain level ( $p < 0.05$ ). **Conclusion:** Results suggest that manual therapy treatment is beneficial in reducing knee OA pain and improvement of joint mobility. Further studies should be conducted to clarify the role of different treatment components and non-specific effects.

**IM11. Superior vena cava syndrome in a patient with lung cancer [FLASH]**

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**Introduction:** Dypnea is a common symptom that sometimes can be a challenge for the diagnosis. **Case presentation:** A 84-year-old woman, known with primary arterial hypertension, treated with metoprolol and baby aspirin, long-time smoker, without respiratory symptoms in the recent history, presented with altered general status, anorexia, rest dyspnea and orthopnea, installed progressively in the last two weeks. The patient had abolished vesicular murmur on the right side and subcrepitant rales on the left, SatO<sub>2</sub> 93% under oxygen therapy, blood pressure of 110/90 mmHg, and a heart rate of 100 bpm. Also, she had clinical signs of a superior vena cava syndrome. **Lab tests:** leukocytosis ( $20.72 \times 10^3$ ), anemia (Hb 8.9 g/dL), trombocytosis ( $612,000/\text{mm}^3$ ), creatinine 1.62 mg/dL, BUN 148.5 mg/dL, INR 1.62, LDH 319 U/L. The ECG was normal. The abdominal ultrasound showed bilateral pleural effusion. The chest X-ray confirmed the ultrasound findings: massive pleural effusion on the right lung, but no pulmonary masses. Thoracocentesis was performed, which showed few red cells, increased leukocytes, with benign cytology. After 4 days, the patient was admitted to ICU because her general status deteriorated, she was intubated and mechanically ventilated. A CT scan of the chest was ordered, which showed a massive tumor in the upper lobe of the right lung, extending into the mediastinum. The evolution was rapidly unfavourable. **Conclusions:** Smoking is a major risk



factor for lung cancer. Chest X-ray is not a sensible method for the diagnosis of lung cancer. In patients with known risk factors, a CT scan should be done in order to confirm the diagnosis.

### **IM12. A rare association between primary hyperparathyroidism and acute pancreatitis [FLASH]**

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**Introduction:** A rare presentation, acute pancreatitis secondary to hypercalcemia, is one of the symptoms caused by hyperparathyroidism, and usually occurs at an advanced stage of parathyroid disease. **Case presentation:** A 43-year-old smoker, denying alcohol consumption, without a pathological personal history, was admitted for upper abdominal pain with posterior irradiation, nausea and vomiting. **Clinical examination:** altered general condition, without fever, a mass fixed to the deep planes, palpable about ½ cm at the level of the anterior cervical region, upper abdomen pain. **Biological:** leukocytosis with neutrophilia, mild elevated aminotransferases (AST>ALT), elevated lipase (4xN). Pulmonary X-ray revealed two bilateral opacities in the upper lobes, suggestive for metastasis. Abdominal imaging revealed a non-homogeneous, volume-increased pancreas with microcalcifications. Parenteral hydration and symptomatic treatment were initiated with favorable evolution. IgG4 and triglycerides were within normal limits. Serum calcium levels and intact parathyroid hormone (iPTH) were elevated (Ca 13.8 mg/dL, iPTH 398 pg/mL). The preliminary diagnosis was acute pancreatitis secondary to hypercalcemia induced by primary hyperparathyroidism. A CT scan was performed, that showed edematous, unstructured pancreas with a few microcalcifications, as well as a right parathyroid tumor. Later, the biopsy of the cervical tumor confirmed the diagnosis of parathyroid carcinoma. A multidisciplinary team decided on the surgical resection of both the tumor and pulmonary metastases. Thymectomy was also performed due to tumoral infiltration. **Conclusions:** Unknown hyperparathyroidism with hypercalcemia is a rare cause of acute pancreatitis. Even a mild increase in serum calcium can be the main trigger.

### **IM13. Acute pyelonephritis – one year prevalence in the Clinical Emergency Ilfov County Hospital, Romania [ORAL]**

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**Introduction:** Pyelonephritis represents the inflammation of the kidney. Acute pyelonephritis is a serious and severe urinary tract syndrome, due to an infection. The symptoms are variable and consist on local and general manifestations. Most often, the patients present fever, chills, malaise, flank pain or tenderness, dysuria with urinary frequency or urgency. Studies pointed also that up to 20% of patients have lack of any bladder symptoms, and some of patients do not have even fever. Estimated annual incidence in the USA varies largely, between almost 500.000

to over 1.100.000 cases. Worldwide, the incidence is estimated between 10.5 million and 25.9 million. The incidence of hospitalized patients is lower than 20% in young adults, and higher in patients over 65 years old. Higher concern should be considered in patients with atypical or misleading clinical presentation, polymicrobial infection and multidrug-resistant organisms. Methods: We studied the frequency of the acute pyelonephritis in our hospital for one year (1 January 2017- 31 December 2017). It is a retrospective study based on clinical presentation, imaging tests and urine cultures. Results: 5143 urine cultures were performed, with 1194 antibiotic sensitivity tests. The patients' age varied between 19 and over 85 years old. We found 146 patients with acute pyelonephritis, with 94 female patients. 80% of positive urine cultures were with *Escherichia coli* strains. Most of the patients were between 25- 35 years old and over 80. Conclusions: Acute pyelonephritis was diagnosed upon clinical, imaging and urine tests. 146 patients were diagnosed with acute pyelonephritis, 94 patients being female. Most cases were either between 25-34 years old, or over 80. Most of the cases were from the obstetrics-gynecology and urology department.

#### **IM14. The involvement of gut microbiota in autoimmune disorders [FLASH]**

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Introduction. Autoimmune disorders are characterized by increased immune reactivity and by the presence of antibodies against the own structures of the body. Microbiota is defined as the presence of commensal microorganisms in the body and its interaction with the physiological processes that drive human life. Methods. A literature search was performed by independent investigators using Web of Science, PubMed-MEDLINE, Google Scholar, and other search services with the following keywords and word combinations: "microbiota", "systemic autoimmunity", "lupus erythematosus", "diet", "autoimmune arthritis", and "autoimmune encephalopathy". Inclusion criteria included relevant articles in English and French, published between 1st January 2011 and 1st May 2018 that addressed autoimmune diseases and microbiota involvement as their main theme. Exclusion criteria were case reports, unavailability of any full article, unclear presentation, non-relevant studies and reports of different languages other than English or French. Results. Recent studies have shown an important link between autoimmune disorders, such as lupus erythematosus, antiphospholipid syndrome, rheumatoid arthritis or type 1 diabetes mellitus, and gut microbiota. This link, correlated with the major changes in diet and with the antibiotic abuse of the last decades, may explain the peak in the incidence of autoimmune disorders in the last years. Moreover, commensal microbiota directly interacts with the immune system by influencing the immune-commensal axis, which differentiates commensal microorganisms of the body from pathogens from outside of the organism. Conclusions. When imbalance of the axis develops, the autoimmune process against organs with a commensal population is triggered. New therapies directed against the modified microbiota appear to be beneficial in the control of autoimmune disorders.

### **IM15. Cardiovascular risk assessment in non alcoholic fatty liver disease [FLASH]**

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The aim of the study was to evaluate the link between subclinical atherosclerosis and nonalcoholic fatty liver disease (NAFLD) in patients with diabetes mellitus type 2. Methods: We included 92 patients with diabetes mellitus type 2 who were treated with antidiabetic drugs or diet. The grade of steatosis and subclinical atherosclerosis, evaluated using intima-media thickness of the carotid artery (CIMT) were assessed by ultrasonography. Results: The average age of the patients was  $60,38 \pm 10,37$  years, of which 44 men and 48 women. Even if there were no significant differences by gender between the incidence of different grades of hepatic steatosis, it should be mentioned that the cases with normal liver were nearly two times higher in men compared to women. The frequency of intermediate and moderate steatosis was higher in women. Severe steatosis had an almost equal frequency among genders. 61% of the patients had CIMT values above the normal range. It was showed that the average value of CIMT is continuously increasing according to the level of hepatic affection. A direct statistically significant correlation between the grade of hepatic steatosis and CIMT ( $r = 0.3636$ ,  $p = 0.0004$ ) was found. A number of 9 subjects were diagnosed with atheroma of the carotid arteries, 8 of the 9 cases showing a moderate or severe steatosis level. Conclusion: The degree of hepatic fat accumulation is associated with subclinical atherosclerosis in patients with diabetes mellitus type 2.

### **IM16. The outcomes of idiopathic inflammatory myopathies in elderly patients [ORAL]**

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The aim of the study: To determine the outcomes of idiopathic inflammatory myopathies (IIM) in elderly patients. Methods: We performed a cross-sectional study from May 2016 to December 2017, as inclusion criteria were defined diagnosis by ACR/EULAR criteria for IIM and the age of patients more than 60 years old. Demographic, clinical and laboratory data were collected including Myositis Damage Index (MDI) questionnaire. The study received the permission from the Bioethical Committee of SUMPPh since 21 May 2016 and was performed according to the Declaration of Helsinki of human rights. Data was analyzed using MedCalc software version 12. Results: The group included 21 patients, female: male ratio was 3.7:1, the mean age at time of examination was  $66.14 \pm 4.81$  years versus  $58.24 \pm 6.85$  years at the time of the disease onset with a disease duration of  $98.05 \pm 65.70$  months. According MDI the most affected system were the muscles, 14 (66.7 %) patients had clinical muscle atrophy and 18 (85.7 %) muscle dysfunction characterized by decrease in aerobic exercise capacity. Regarding the skeletal damage, osteoporosis without fracture was in 17 (80.9 %) patients, less common was avascular necrosis - 2 (9.5 %) patients. Cutaneous damage was present by alopecia - 13 (61.9 %), lipodystrophy in 5

(23.8 %) and calcinosis - 4 (19.1 %) patients. Dysphagia and gastrointestinal dysmotility was found in 12 (57.1 %) patients. The most common pulmonary damage were pulmonary fibrosis and dysphonia determined in 10 (47.6 %) and 7 (33.3 %) patients, respectively. Arterial hypertension was in 14 (66.7 %) patients and one case of myocardial infarction. Vascular peripheral damage was in 2 (9.5 %) cases, diabetes and dyslipidemia in 7 (33.3 %) and 12 (57.1 %) patients, respectively. Cataract resulting in visual loss was found in 2 (9.5 %) cases and visual loss due to diabetes, arterial hypertension was more frequent-12 (57.1 %) cases. Chronic secondary infections was in 5 (23.8 %) patients. We determined weak correlation between MDI, disease duration and women ( $r=0.42$ ,  $r=0.49$ ) and a moderate correlation with GCS cumulative dose ( $r=0.53$ ). Conclusion: Elderly patients with idiopathic inflammatory myopathies have a diverse spectrum of outcomes, the most common are muscle and skeletal damage which correlates moderate with glucocorticosteroid cumulative dose.

### **IM17. Clinical patterns, epidemiology and risk factors of community-acquired urinary tract infection caused by extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* [FLASH]**

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Aim: To assess incidence rate, risk factors and susceptibility patterns associated with extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* in community-acquired urinary tract infections (CA-UTIs). Methods: A retrospective study was conducted from Jan 2016 to Dec 2017. The results of microbiology cultures were initially screened to include only patients with positive *E. coli* urine cultures. To investigate the risk factors in patients with a positive urine culture for ESBL-producing isolates. Results: Out of 112 patients included in this study, 27% ( $n = 30$ ) had positive *E. coli* ESBL producers urocultures. Most patients were women (78 patients, 69.6%) over 50 years of age, with recurrent urinary infections. In terms of antibiotic susceptibility, the following were found: a low sensitivity to Ampicillin and Gentamicin (13 to 30%), 63% to Ciprofloxacin, 60% to Ceftriaxon and Ceftazidime, and increased sensitivity to Carbapenem, Phosphomicine and Nitrofurantoin. No *E. coli* carbapenemases producers were detected. Conclusions: Our results suggest that the incidence of ESBL producers among CA-UTIs is high. Female gender, comorbidity and UTI in the previous 12 months were associated with a higher risk for infection. Continuous surveillance and prudent antibiotic use by healthcare professionals are important factors for effective control of ESBL associated infections.

### **IM18. *Pancreas divisum* [FLASH]**

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**Introduction:** Pancreas divisum is a common congenital anomaly of the pancreatic duct(s). The human embryo starts life with a pancreas that is in two parts, each with its own duct; the ventral duct and the dorsal duct. The two parts of the pancreas fuse during development. In most embryos, the dorsal and the ventral ducts also will fuse to form one main pancreatic duct. The main pancreatic duct will join the common bile duct (the duct that drains bile from the gallbladder and the liver) to form a common bile and pancreatic duct which drains into the duodenum through the major papilla. In some embryos, the dorsal and the ventral ducts fail to fuse. Failure of the ventral and the dorsal pancreatic ducts to fuse is called pancreas divisum (because the pancreas is drained by two ducts). In pancreas divisum, the ventral duct drains into the major papilla, while the dorsal duct drains into a separate minor papilla. **Case presentation:** A 40-year-old woman presented with significant abdominal pain in the epigastric area. She had no history of smoking, consumed small amounts of alcohol occasionally, and did not take any medications or herbal products. Laboratory work-up was significant for increased levels of amylase of 2774 U/L (normal range 30–110 U/L) and a lipase of 17 863 U/L (normal range 7–60 U/L). Bilirubin and liver enzymes were within normal limits. An abdominal ultrasound showed no gallstones or any other abnormalities. A CT scan, performed for further evaluation of pain, demonstrated calcification of the uncinata process and dilation of the ventral duct to 1.2 cm. Further evaluation with MRI showed not only the calcification but also pancreas divisum. The patient was treated with supportive care and was discharged after 3 days. **Conclusions:** Pancreas divisum is the most common congenital anomaly of the pancreas. Pancreas divisum is involved in the etiopathogeny of acute and/ or chronic pancreatitis, especially in children and young people. Diagnosis of pancreas divisum is supported by imaging investigations ERCP (Endoscopic Retrograde Cholangio Pancreatography). Pancreas divisum treatment is endoscopic and/ or surgical and aims at improving pancreatic drainage in the minor papilla. In the case of pancreas divisum associated with chronic pancreatitis, most authors recommend a surgical drainage procedure (pancreatic-jejunostomy).

### **IM19. Coxartrosis in an advanced stage or should we continue searching? [FLASH]**

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**Introduction:** The research over the past three decades showed that the physician’s ability to explain, listen and empathize can have a profound effect on the evolution of the patients, as well as on the patient’s satisfaction. **Case presentation.** A 75-year-old man, with multiple hospitalizations, smoker, known with arterial hypertension, chronic obstructive pulmonary disease, chronic heart failure NYHAclass III, bilateral coxarthrosis with articular prosthesis indication, is hospitalized for weight loss over the last 2 months (24kg) and pain in the right hip. **The clinical examination:** pain when mobilization of the right lower limb, otherwise normal. The laboratory investigations showed mild normocytic hypochromic anemia, inflammatory syndrome, mild leukocytosis with neutrophilia, mild diselectrolytemia. The thoracic radiography showed an enlarged heart and accentuated peribronchovascular drawing, with bronchiectasis, on fibrotic background. The lumbar and bilateral hip X-rays revealed massive arthritis calcifications, osteoporotic changes and bilateral coxarthrosis (more severe on the left),

sacroiliitis. Because the patient complained of intense pain at the level of the right hip, we have continued the investigations with an abdominal echography that detected a hepatic/renal mass with an irregular contour, hypoecogenic, about 5 cm. The abdomino-pelvic CT-scan revealed an extra-pelvic mass in the right obturator area, with acetabular osteolysis and of the right ischiopubic ram, and a pulmonary right mass extending transdiaphragmatic into the abdomen. Conclusions: The diagnosis of a right obturator muscle tumor with multiple secondary determinations in a patient with multiple hospitalizations for coxarthrosis drug cure.

### **IM20. Monoclonal gammopathy of renal significance - a growing health issue in elderly patients [ORAL]**

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Introduction: Monoclonal gammopathy (MG) of undetermined significance (MGUS) is one of the most frequent premalignant condition, with increasing prevalence in elderly patients because of aging population. Nephrological surveillance is mandatory, since an important percentage of patients may develop kidney lesions because of monoclonal (M) protein, condition called MG of renal significance (MGRS). We present the case of a patient with IgM monoclonal kidney deposition disease in whom the final diagnosis was established only by kidney biopsy and we review the management of MGRS. Case presentation: A 69 years old female patient is admitted for proteinuria discovered during routine evaluation. Seven years before hemicolectomy for colon cancer was performed. The patient was cancer-free during check-ups. At admittance patient had a mild inflammatory syndrome and serum creatinine 1.27 mg/dl. Urinalysis showed dysmorphic red cells and red cell casts. Proteinuria was 3102 mg/day with albuminuria 2634 mg/day. Screening for viral and autoimmune diseases was negative. Immunofluorescence of kidney biopsy revealed massive deposits of IgM and kappa light chains in the glomerular capillary walls and electron microscopy showed sub endothelial dense deposits together with hyaline thrombi in the glomerular capillaries. She had elevated serum total IgM (3.6 g/dl), but serum protein electrophoresis with immune fixation was negative and kappa to lambda serum free light chains ratio was normal. No plasma or B-cell clone was found. After 3pulses of cyclophosphamide SCr is 0.9 mg/dl, proteinuria decreased to 1.5 g/day and serum total IgM level is normal. Conclusions: Significant kidney damage in MGRS usually appears because of nephrotoxic properties of M-protein, with important negative impact on patients' outcome. Like in our case, rarely no serum and urine M-protein and no pathologic clone can be found, so kidney biopsy is essential for diagnosis and for choosing proper chemotherapy targeting the pathologic clone responsible for M-protein secretion.

### **IM21. Chylothorax in a patient with chronic lymphocytic leukemia: case report and literature review [FLASH]**

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**Introduction:** Chylothorax represents an accumulation of lymphatic fluid in the pleural space secondary to leakage or impaired drainage from the thoracic duct or one of its main tributaries. It may result from traumatic, non-traumatic causes, but there are also idiopathic forms. Treatment of chylothorax is controversial and depends on both its cause and symptoms. The approach may range from conservative treatment to elective surgery. **Case presentation:** We present a case of bilateral chylothorax in a female patient with chronic lymphocytic leukemia, chronic kidney disease stage 3B, atrial fibrillation, arterial hypertension and recent pacemaker implantation for third degree atrioventricular block. We will discuss the etiology, possible pathogenesis in our case, along with diagnostic options and treatment modalities. Diagnosis was confirmed based on the milky appearance and composition of the fluid, chest x-ray and CT scans results. The cause of chylothorax in the reported patient is difficult to establish, because there was no obvious mediastinal mass effect, which could have disrupted or compressed the thoracic duct. We hypothesized that the chylothorax could have been due to the presence of an extremely large number of abnormal lymphocytes in lymphatic fluid due to chronic lymphocytic leukemia, which might have caused sludging in the lymphatic system, resulting in the pseudo obstruction of the lymphatics draining the pleura and subsequent chylothorax. Because the patient showed pleural effusion on the chest x-ray previous to the pacemaker implantation, we decided to exclude the possibility of a traumatic chylothorax. **Conclusion:** In patients with chronic lymphocytic leukemia who present with a new pleural effusion, chylothorax should be suspected and pleural fluid triglycerides levels should be checked due to sludging of lymph.

### **IM22. Zollinger-Ellison syndrome associated with gastrinoma: case report and literature review [FLASH]**

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**Introduction:** Gastrinomas are functionally active pancreatic neuroendocrine tumors (NETs), characterized by the excessive secretion of gastrin leading to an increased gastric acid production. They can occur within the triangle defined as the confluence of the cystic and common bile ducts superiorly, the second and third portions of the duodenum inferiorly, and the neck and body of the pancreas medially. Sporadic tumors occurring in the pancreas tend to be solitary and have a greater malignant potential as compared to duodenal gastrinomas. The clinical manifestations of gastrinomas include gastric acid hypersecretion, abdominal pain related to peptic ulcer disease, and secretory diarrhea. In about 80% of the cases, gastrinomas lead to the Zollinger-Ellison syndrome, which is characterized by pain, diarrhea, and gastroesophageal reflux disease. The primary determinants of survival in patients with gastrinomas are the size of the primary tumor and the occurrence of tumor metastasis in the local lymph nodes or

liver. Case presentation: We present the case of a 60-year-old Caucasian man, with multiple cardiovascular risk factors (obesity, hypertension, dyslipidemia, diabetes), who presented to our hospital with abdominal bloating and pain, nausea, vomiting, diarrhea and weight loss of 6 kg over 4 months. The ECG excluded a possible myocardial infarction, but the upper digestive endoscopy shows multiple ulcerations in the stomach and duodenum, raising the suspicion of Crohn's disease, Zollinger Ellison syndrome, or a viral pathology. Several other paraclinical tests, such as CT scans, echoendoscopy with fine needle aspiration, gastrin determination were performed in order to exclude these diseases. The results came positive for Zollinger-Ellison syndrome, due to pancreatic gastrinoma. He declines initially the surgical intervention and came back a year later with worsening symptoms. The surgeon has found multiple metastases in the liver, and multiple adenopathies near the aorta and celiac trunk. Despite the maximum treatment of vital functions, the evolution was unfavorable, with exitus. Conclusions: Gastrinomas are rare neuroendocrine neoplasms. Only 1 to 3 people in every million develop gastrinomas each year; 60 to 90% of them are malignant and can metastasize to regional lymph nodes and the liver. Surgical treatment is considered a curative treatment for patients with resectable NETs and limited disease. In case of nonresectable NETs, metastatic, or with an aggressive clinical course, alternative treatment options include SSAs, biotherapy, targeted radionuclide therapy, loco-regional treatments, and chemotherapy. The choice of treatment depends on the symptoms, stage, and histological features of the tumor. Despite the fact that our patient was diagnosed in an early stage of disease, the evolution of the disease was unfavorable, because he refused surgery.

### **IM23. Infrarenal metastases from endometrial cancer: a case report [FLASH]**

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Introduction. Patients diagnosed with endometrial cancer report a high risk of developing pelvic and even para-aortic lymph node metastases, the most frequently incriminated para-aortic lymph node stations including the infra-mesenteric area. However, in certain cases para-aortic metastases above the inferior mesenteric artery might be encountered. Methods. We present the case of a 63 year old patient diagnosed with a moderately differentiated endometroid adenocarcinoma who was diagnosed with para-aortic lymph node metastases in the infra-renal area. Results. The 63 year old patient presented for postmenopausal uterine bleeding and was diagnosed with a moderately differentiated endometroid adenocarcinoma in association with pelvic and para-aortic adenopathies. Surprisingly, the preoperative computed tomography described the presence of large adenopathic masses above the inferior mesenteric artery so we decided to extend the area of lymph node dissection. The patient was submitted to total hysterectomy with bilateral adnexectomy, pelvic and para-aortic lymph node dissection, the para-aortic resected lymph nodes including both the inframesenteric and the infra-renal group. The histopathological studies confirmed the presence of metastases in the infra-renal lymph node station. Conclusions. In patients with endometrial cancer infra-renal para-aortic lymph node stations might present metastatic cells; therefore, a close evaluation of these groups during preoperative workup as well as intraoperatively is mandatory.



#### **IM24. Incidence of echinococcosis in the Pleven region in the period 1998-2017 [ORAL]**

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**Introduction:** Echinococcosis is a chronic relapsing disease of medical, social and economic importance. Humans are accidental hosts of the *Echinococcus granulosus* tenia. The disease takes a severe course, frequent relapses, and sometimes results in severe complications and death. Bulgaria is among the countries with high prevalence of echinococcosis. This necessitated the introduction of a five-year national program for control of Echinococcosis in humans and animals. **Materials:** The study on echinococcosis in the Pleven region covers a 20-year period, divided in to two parts: before and after the introduction of the 5-year program for control (1998 – 2007 and 2008 – 2017). Data was collected from epidemiological records and histories of 255 cases of primary echinococcosis and 34 cases of relapses for the period. All patients underwent surgical, or puncture, aspiration, injection and re-aspiration (PAIR) therapy. **Results:** Incidence and major epidemiological characteristics were studied. A high incidence 5.27 ‰ was registered in the first period (1998 – 2007), reaching 8.14 ‰ in 1999 and 7.62 ‰ in 2000. During the following years (2008-2017) the incidence rate decrease to an average of 3.39 ‰. In 2017 it dropped to 2.42‰. The data analysis showed that the incidence was higher in the working-age population. However, the number of cases in the age group 5-19 was not negligible. Alongside with typical cases of liver and pulmonary echinococcosis, atypical primary localizations (breast, heart, kidney) and polyorganic forms were also diagnosed. We did not find significant gender-related differences. A map was made of the Pleven region, presenting the prevalence in the municipalities. **Conclusion:** The Pleven region has overcome the crisis regarding human echinococcosis prevalence. There are still isolated cases that require concrete therapy, prevention and organizational arrangements.

#### **IM25. Pneumonia “under cover”: a clinical case [FLASH]**

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**Introduction:** Pneumonia is a common infectious pathology which frequently has atypical clinical manifestations in elderly. **Case presentation:** A 82-year-old man, known with chronic viral C hepatitis and hypertension, non-smoker, with no occupational exposure to noxes, presented for rest dyspnea with orthopnea, installed progressively over the last 2 weeks, bilateral leg edema and productive cough with ineffective expectoration. The patient was a febrile and denied fever, chills or chest pain. **Physical examination:** bilateral leg edema, perioral cyanosis, vesicular sounds present but diminished basal bilaterally, with bilateral basal crackles, blood

pressure of 160/90 mmHg, a heart rate of 85 bpm. Paraclinical - mild leukocytosis with neutrophilia, respiratory alkalosis, hypercapnia and hypoxia. The ECG showed sinus rhythm, left ventricular hypertrophy and secondary terminal phase changes. The abdominal ultrasound revealed only bilateral pleural effusion. A clinical diagnosis of congestive heart failure syndrome was established, until the result of the thorax X-ray raised a high suspicion of a pulmonary tumor and a CT-scan was programmed. The CT scan examination infirmed the presence of a lung tumoral process and described an area of alveolar condensation with aeric bronchogram, the radiological aspect being highly suggestive of pneumonia. Under antihypertensive, antibiotic and mucolytic treatment, the patient had a favorable evolution, with symptom relief and radiological resolution. Conclusions: It is a case of a community-acquired-pneumonia in a non-smoker, immunocompetent, elderly patient, who had no fever, no chest pain and who presented with symptoms and clinical signs highly suggestive of cardiac failure. The initial imaging investigations were highly suggestive for a lung tumor. However, the CT scan revealed only a pulmonary condensation syndrome.

### **IM26. All oral antiviral treatment with paritaprevir/ ombitasvir/ ritonavir and dasabuvir in chronic HCV infection- real life experience [ORAL]**

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**Introduction.** All oral antiviral treatment in chronic HCV infection is one of the most important breakthroughs in hepatology. While clinical trials have revealed maximum efficacy with minor side-effects, its use in real life raises questions about drug-drug interaction and use in patients with comorbidities. **Methods.** We performed an observational prospective study on 442 patients who underwent treatment with OMB/PTV/r + DSV during December 2015- June 2018. Inclusion criteria were: patients with compensated liver cirrhosis (F4 fibrosis, clas Child A), patients with F3 fibrosis, patients with F2 fibrosis and HCV related comorbidities or indication for kidney transplant and patients with HCV relapse after liver transplant. Clinical and biologic parameters were evaluate at initiation of therapy, at the end of therapy and at 12 weeks after the end of therapy. **Results.** All patients have reached the end of treatment checkpoint and in 397 patients we determined presence of sustained virologic response. Four patients had detectable HCV-RNA at the end of treatment and three patients did not achieve SVR. Serious adverse events occurred in four cases (2 patients with B-cell lymphoma and hematologic decompensation died during treatment, one patient presented variceal bleeding and one patients presented acute pancreatitis). The most common adverse reactions were nausea and fatigue. None of the patients discontinued antiviral therapy. In patients with cardiovascular comorbidities, diabetes mellitus or autoimmune manifestations concurrent medication had to be adjusted. In patients after solid organ transplantation doses of tacrolimus were drastically reduced, with frequent monitoring of tacrolinemia. **Conclusion.** Real life experience with OMB/PTV/r + DSV proves its efficacy in achieving SVR in patients with compensated cirrhosis or chronic HCV hepatitis. We did not identify treatment-related adverse reactions. Close monitoring is required in patients with comorbidities and concurrent medication.

**IM27. The association between hydroxychloroquine use and frequency and severity of SLE flares in Molustudy: results from a prospective, observational study [FLASH]**

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Objectives: To determine if the use of Hydroxychloroquine (HCQ) is associated with a reduction of the frequency and severity of SLE flares over a 12-month period. Methods: Prospective, observational study of SLE patients (SLICC/ACR, 2012 classification criteria) receiving corticosteroid (CS) treatment with/without cytostatic drugs and not receiving HCQ. The patients were divided into two groups: basic SLE treatment without HCQ– G0 and basic SLE treatment plus HCQ 6,5mg/kg body weight – G1. The frequency and severity of SLE flares were assessed by SELENA/SLEDAI flare index. Results: The variables of G0 and G1 at baseline are shown in the table 1.

Parameter	G0, n=51 (mean±SD)	G1, n=46 (mean±SD)	p
Age (years)	46,2 ± 12,2	40,0 ± 13,9	>0,05
Female, n (%)	49 (96,1)	44 (95,7)	>0,05
Weight (kg)	66,3 ± 8,6	71,7 ± 7,2	>0,05
Disease duration (months)	110,0 ± 73,3	96,9 ± 82,9	>0,05
SLEDAI (points)	13,5 ± 7,2	13,0 ± 9,5	>0,05
SLICC/ACR DI (points)	1,3 ± 1,4	1,1 ± 1,1	>0,05
CS cumulative dosage	12,6 ± 11,9	10,0 ± 7,8	>0,05

We have determined that in G0 occurred 36 flares, including 10 cases of severe flares, vs G1, where only 19 flares were unregistered, including one severe flare (p<0,05). The relative risk (RR) for G1 vs G0 of flares is presented in the table 2.

	RR	95% CI	p
All types of flares at 6 months	0,5	0,25–0,98	0,04
All types of flares at 12 months	0,49	0,25–0,94	0,03
Severe flare at 6 months	0,15	0,01–1,12	>0,05
Severe flare at 12 months	0,12	0,01–2,20	

Conclusions: The use of Hydroxychloroquine was associated with a decrease of the frequency of SLE flares as assessed by SELENA/SLEDAI flare index (RR for flares at 6 months of HCQ use = 0,5, 95%CI=0,25–0,98, RR for flares at 12 months of HCQ use = 0,49, 95%CI=0,25–0,94).

### **IM28. Serotonin - the anti-aging neurotransmitter and degenerative chronic low back pain in older adults under balneal treatment [FLASH]**

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Introduction: Chronic low back pain is considered one of the major disabling health conditions among older adults. It affects almost 80% of the population over a lifetime. The prevalence of chronic low back pain increases with age and determine disability regarding quality of life. Pain is often associated with the risk of depression and anxiety symptoms. Neurotransmitter serotonin modulates many brain functions like emotions depression or anxiety, motor function and pain sensitivity. The aim of this study is to evaluate the variation of serotonin seric levels and the correlation with life quality parameters in senior patients with degenerative chronic low back pain, under specific balneal treatment. Methods: We evaluated patients over 60 years old, with degenerative chronic low back pain, hospitalized for rehabilitation treatment in Balneal and Rehabilitation Sanatorium of Techirghiol, Romania, for a 2 - week period of time. The patients were divided into 3 groups depending on the treatment: cold mud baths, hot mud baths, and no mud treatment (control group). All groups received electrotherapy, kinetotherapy and massage. The patients were evaluated paraclinical and clinical before and after the treatment. Results: There were significant differences of the values of serum levels of serotonin between the 3 groups of patients taking in consideration the age and gender of the patients. The group of patients with hot mud baths got higher increase of serotonin seric levels and improved the quality of life parameters compared to the other two groups of patients. Conclusions: Balneal treatment provides significant improvement of pain level on degenerative chronic low back pain and the biological parameters - serotonin seric levels.

### **IM29. Comorbidities in patients with type 2 diabetes mellitus: a report on 219 cases [ORAL]**

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**Introduction.** A great number of comorbidities is often registered in patients with type 2 diabetes mellitus (T2DM), increasing the costs associated with the management of this disease. Our objective is to describe the characteristics and comorbidities of a study group of 219 T2DM patients. **Methods.** 219 T2DM patients were selected to partake in this study (mean age = 69.04±10.79 years, range 37-93, 51.14% female). Patients were identified by a database search of diagnostic codes of all discharge diagnoses and medical data were retrieved from the Clinical Emergency Hospital of Bucharest records. **Results.** The following comorbidities were registered: 80.82% arterial hypertension, 47.95% dyslipidemia, 45.21% valvulopathy, 36.07% heart failure, 33.79% arrhythmia, 33.33% obesity, 32.88% chronic kidney disease, 16.44% anemia, 12.79% hepatic steatosis, 10.50% diabetic nephropathy, 9.59% peripheral arterial disease, 8.68% diabetic neuropathy, 8.67% chronic venous insufficiency, 7.77% dyselectrolytemia and 4.57% diabetic retinopathy. **Conclusions.** Our study clearly reinforces the need for a therapeutic approach centered not only on T2DM alone, but also on the T2DM-related and non-related comorbidities that increase the disease burden in diabetic patients and also the health-associated costs of this disease.

### **IM30. Peripheral arterial disease in patients with type 2 diabetes mellitus [ORAL]**

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**Introduction.** Peripheral arterial disease (PAD) is a vascular comorbidity that increases the burden of disease in patients with type 2 diabetes mellitus (T2DM) by influencing the evolution of foot ulcerations and the onset of the diabetic foot. Our objective is to describe the characteristics of T2DM patients with PAD and T2DM diabetics without PAD in a group of 219 T2DM patients. **Methods.** 219 T2DM patients were selected to partake in this retrospective study (mean age = 69.04±10.79 years, range 37-93, 51.14% female). Patients were identified by a database search of diagnostic codes of all discharge diagnoses and medical data were retrieved from the Clinical Emergency Hospital of Bucharest records. **Results.** PAD was present in 9.59% of T2DM patients. Dyslipidemia was registered in 57.14% cases of T2DM patients with PAD versus 46.60% in T2DM patients without PAD. The frequency of chronic kidney disease was similar in both groups: 39.29% in patients with T2DM and PAD and 38.22% in patients with T2DM and no PAD. **Conclusions.** In our study, the frequency of PAD in T2DM patients was lower (9.59%) than in other literature reports (50-55%). However, screening for this clinical entity can prevent the development of complications in T2DM patients.

## CARDIOLOGY

### **C1. Reno-vascular hypertension: the surgical approach [FLASH]**

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Introduction: Malignant hypertension is a rare disease, with an incidence rate of less than 1%, that consists in a sudden and rapid blood pressure growth, with possible severe vascular changes and potential lethal complications. This pathology is characterized by fibrinoid arteriolar necrosis with retinal hemorrhages, exudates and papillary edema. Objectives: The goal of this paper is to review the possible causes of malignant renal hypertension or reno-vascular hypertension and to underline the role of the surgical management for this pathology. Methods: Malignant hypertension is a medical emergency that implies a prompt management in order to prevent severe and potential deadly complications like cardiovascular and neurological events. This pathology requires a prompt and an adequate management in order to reduce the blood pressure levels and the risk of end organ damage, the most sensible organs being the brain, kidneys and retina. There are numerous factors and pathologies that can lead to malignant hypertension: renal artery sclerosis, renal artery compression by nearby tumors (renal, adrenal, retroperitoneal or abdominal tumors), retroperitoneal fibrosis, pheochromocytoma, aortic coarctation, hyperaldosteronism, hyperthyroidism as well as hypothyroidism, drugs (cocaine, amphetamine, beta blockers, oral contraceptives, and alpha stimulants), pregnancy. It is estimated that over 20% of all cases of malignant hypertension are related to chronic kidney disease. Conclusions: Over the years, the prognostic of patients with malignant hypertension has significantly improved due to the introduction of new antihypertensive drugs. Rarely, the pharmacological therapy can fail, the ultimate solution being the surgical management and even bilateral nephrectomy.

### **C2. Cellular, molecular and functional characterization of the endothelial cell migration associated pathways activated by reconstituted HDL containing human apoE3 [ORAL]**

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**Introduction:** Atherosclerotic coronary heart disease is a leading cause of death worldwide. HDL (High-Density-Lipoprotein) and apolipoprotein E (apoE) have atheroprotective properties and affect the functions of endothelial cells (ECs), although the exact molecular mechanisms are not yet fully characterized. Herein, we study the atheroprotective potential of reconstituted-HDL containing human apoE3 and phospholipids (rHDL-apoE3) at cellular, molecular and functional levels, focusing on EC migration. **Methods:** Human Aortic ECs (HAECs) were treated with rHDL-apoE3 or PBS (negative-control), and isolated total RNA was analyzed by whole-genome microarrays (Affymetrix) followed by bioinformatical ( $\pm 2$ -fold and  $\leq 0.05$  FDR thresholds) and high-throughput qRT-PCR analysis. Human Coronary Artery ECs (HCAECs) were treated with rHDL-apoE3 or PBS in the presence or absence of a specific inhibitor of PI3-kinase (LY294002) or DMSO, using rhVEGF as positive-control. The expression and activation of key EC migration-associated proteins was determined by western-blotting. Wound-healing assays were performed on HCAECs treated with rHDL-apoE3 or PBS or rhVEGF to measure cell migration. **Results:** rHDL-apoE3 induced significant expression changes in 198 genes of HAECs involved mainly in re-endothelialization and atherosclerosis-associated mechanisms. The most pronounced effect was observed for EC migration. In specific, 42/198 genes were involved in EC migration-related pathways: 1) PI3K/AKT/eNOS-MMP2/9, 2) Small RHO-GTPases, 3) RAS/C-RAF/MEK/ERK. Selected changes were validated by high-throughput qRT-PCR. At the protein level rHDL-apoE3 increased the expression of PIK3CG, EFNB2, FLT1 and ID1, as well as the activation of ERK1/2, AKT, eNOS and P38-MAPK in HCAECs compared to PBS-control. Consistently, rHDL-apoE3 stimulated HCAEC migration compared to PBS-control. Pre-treatment of HCAECs with the LY-inhibitor attenuated the rHDL-apoE3-induced AKT and eNOS activation. **Conclusion:** rHDL-apoE3 upregulates the RAS/C-RAF/MEK/ERK, PI3K/AKT/eNOS and PI3K/AKT/RAC1-GTPase/P38-MAPK pathways at transcriptional and protein levels in primary human ECs, and activates ERK1/2, P38-MAPK as well as AKT and eNOS through PI3K-phosphorylation. Through these changes, rHDL-apoE3 induces HCAEC migration suggesting an atheroprotective role in-vitro.

### **C3. The impact of Greek financial crisis in coronary artery disease burden [FLASH]**

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**Background:** Economic crisis poses an immense threat to public health worldwide and has been linked to cardiovascular morbidity and mortality. Greece is facing a distinctive recession over the recent years. However, the exact impact on coronary artery disease (CAD) burden has not been adequately addressed. **Methods:** Demographic, clinical and angiographic data of 3895 hospitalized patients were retrospectively studied. Patients were classified in those before crisis (2006-2007, n=1228) and those during crisis (2011-2015, n=2667). **Results:** All data before and during crisis were compared. During crisis, patients presented with less acute coronary syndromes (ACS - 45.5% vs 39.9%,  $p < 0.001$ ). Subsequently, there were more patients without

CAD (23.7% vs 35.1%,  $p < 0.001$ ) or one vessel disease (20.5% vs 23%,  $p < 0.001$ ). The prevalence of traditional risk factors decreased significantly or remained stable except obesity (26.3% vs 31.4%,  $p = 0.002$ ). A significant increase of the examined females (23.6% vs 26.7%,  $p = 0.04$ ) was also observed. Conclusions: The extend of CAD during financial crisis was partially affected. Even though the incidence of ACS was decreased, more women and more patients with no or single vessel disease were led for cardiac catheterization. In addition, the prevalence of traditional risk factors for CAD did not increase except obesity confirming the “obesity paradox”. It seems that the impact of traditional risk factors for CAD is not an immediate process and is somewhat related to living conditions or other exogenous and social factors.

**Table**

<b>Parameter</b>	<b>2006 - 2007</b> (n=1228)	<b>2011 - 2015</b> (n=2667)	<b>p-value</b>
Gender (% , males)	76.4	73.3	0.038
Obesity (%)	26.3	31.4	0.002
Smoking (%)	45.4	36.9	<0.001
Hypertension (%)	69.2	60	<0.001
Dyslipidemia (%)	59	48.1	<0.001
Diabetes (%)	28.4	27.2	0.438
ACS (%)	45.5	39.9	<0.001
Without CAD (%)	23.7	35.1	<0.001
1-vessel disease (%)	20.5	23.0	<0.001
Number of stented vessels	0.2±0.4	0.3±0.6	<0.001

#### **C4. Effects of reconstituted HDL particles on endothelial cell microRNA expression [ORAL]**

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Introduction: Atherosclerosis is a major contributing factor to the development of cardiovascular disease. Available evidence indicates that HDL exhibits atheroprotective effects on endothelial cells (ECs), although the exact molecular mechanisms are not yet fully elucidated. Ongoing efforts focus on reconstituted HDL (rHDL)-based therapeutics against atherosclerosis. Herein, we investigate the comparative effects of different types of rHDL on EC microRNA expression, aiming to identify microRNAs that could mediate the observed atheroprotective molecular changes. Methods: rHDL containing apolipoproteins A-I or E3, purified from an adenovirus system and phospholipids was produced. Human aortic ECs (HAECs) were treated with rHDL-apoA-I, rHDL-apoE3, or PBS (baseline-control), total RNA was isolated and microRNA expression was analyzed by microarray (miRNA2.0 GeneChip.Array/Affymetrix). Microarray



data were subjected to bioinformatical analysis using fold change  $\geq \pm 1.5$  and FDR  $\leq 0.05$  thresholds, followed by miRBase/miRWalk/TargetScan and Ingenuity Pathway Analysis, along with extensive PubMed data mining and in depth comparison with our teams previous whole genome expression data from HAECs treated with the same rHDL preparations. Results: rHDL-apoA-I induced expression changes in 8 microRNAs, 7 downregulated (miR-3188, miR-3185, miR-1231, miR-3195, miR-2861, miR-1915, miR-638) and 1 upregulated (miR-744). rHDL-apoE3 downregulated only miR-503. IPA analysis indicated these 9 microRNAs, affect cell cycle, inflammatory response and cellular growth and proliferation pathways. In depth data mining for these microRNAs revealed that they regulate several re-endothelialization/atheroprotective functions. Importantly, key genes regulating EC functions that were found to be differentially expressed by the two rHDL subpopulations, are among the validated/predicted targets of these microRNAs, such as genes: VEGFA, ANGPTL4, EFNB2, VIPR1 and LDLR. Conclusions: rHDLcontaining apoA-I or apoE3 significantly changed the expression of a specific subset of microRNAs in ECs, reported as associated with atheroprotection-related functions. These findings are currently being validated and functionally characterized to elucidate the molecular effects and atheroprotective potential of the different rHDL subpopulations.

### **C5. Quantitative and qualitative expression of leptin receptor in healthy offspring of hypertensive patients [FLASH]**

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Background: Data support that leptin might have a balanced effect on blood pressure (BP) through sympathetic activation along with nitric oxide (NO) release linking to leptin receptors (LR). In addition, LR gene polymorphisms seem to be related with elevated BP. The aim of this study was to calculate the total number of the human soluble LR (hsLR) along with the most common LR gene polymorphisms (Lys 109 Arg and Gln 223 Arg) in healthy offspring of hypertensive patients (HOH) and to compare these findings to those of healthy offspring of normotensive individuals (HON). Methods: In total 16 HOH and 24 HON matched for age, sex and body mass index (BMI) were studied. Human soluble LR number was measured by Elisa and Lys 109 Arg and Gln 223 Arg polymorphisms were determined by PCR-RELF on receptor gene. Results: The mean number of hsLR was significantly lower in HOH compared to HON. Conversely, the percentage of Lys 109 Arg and Gln 223 Arg was increased but not statistically different in HOH (Table). Conclusions: Healthy offspring of hypertensive patients seem to have less number of hsLR. This implication might play a role to the development of hypertension.

**Table**

	<b>HOH</b> n=16	<b>HON</b> n=24	<b>p-value</b>
Gender (men)	9	13	NS
Age (years)	17±3	17.5±2.8	NS
BMI (kg/m <sup>2</sup> )	21±2.5	21.5±2.7	NS
hsLR (IU/ml)	21.8±0.2	30.2±0.4	0.007

Lys 109 Arg (%)	43.75	37.5	NS
Gln 223 Arg (%)	47.9	34.1	NS

## C6. The role of remote ECG in prehospital medical care [FLASH]

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**Introduction:** The in-hospital mortality rate of ST Segment Elevation Myocardial Infarction (STEMI) is still high, due to lethal arrhythmias that are triggered by ischemic events, but it could be significantly reduced by the modern reperfusion therapy and improved secondary prophylaxis. Remote ECG support for diagnosis and therapy in acute coronary syndromes (ACSs) has been established in emergency medical services (EMS) as feasible and safe. **Objectives:** To evaluate the types and frequency of heart diseases, diagnosed by EMS dispatch using remote ECG. **Methods:** In a retrospective study were analyzed 25195 ECG's performed by paramedics, when called for a cardiovascular emergency, during 2016 - 2017. The recorded ECG signals were transmitted through mobile phone to emergency dispatch, where a PC-based ECG receiving station displayed them for remote analysis and evaluation by a cardiologist. **Results:** A total of 11449 (100%) ECG's were transmitted and remote analyzed in 2016 and 13746 (100%) – in 2017. A total number of 19135 (76%) ECGs were transmitted by emergency medical assistants and 6060 (24%) ECGs - by emergency doctors. Remote analysis permitted to diagnose 163 (0,6%) cases of STE-ACS, 600 (2,3%) of NSTEMI-ACS, 6901 (27,4%) of cardiac arrhythmias, 8723 (34,6%) of chronic changes during two years. Early recognition of 763 cases of ACS led to timely emergency hospitalization and appropriate treatment. **Conclusion:** Prehospital remote ECG, carried out by paramedics and supported by physicians significantly improved quality of diagnosis in ACS, time of admission and patient survival.

## C7. Clinical presentation of hypertensive crises in emergency medical services [ORAL]

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**Introduction:** Hypertensive crisis is defined as levels of systolic blood pressure >180 mmHg and/or levels of diastolic blood pressure >120 mmHg and is usually seen in patients with essential hypertension. In addition, hypertensive crisis is a severe clinical condition in which a sudden increase in arterial blood pressure can lead to acute vascular damage of vital organs, so timely detection, evaluation and adequate treatment are crucial to protect target organ function, ameliorate symptoms, reduce complications, and improve clinical outcomes. **Objectives:** The objective of this study is to evaluate the incidence and clinical presentation of hypertensive crises

in the emergency medical services in relation to age, sex, duration and severity of hypertension, as well as the prevalence of accompanying symptoms and clinical manifestations. Methods: The study was conducted between January and May 2016 and included 630 subjects of both sexes, aged 28-92 with a diagnosis of hypertensive crises. All subjects were divided into two groups: hypertensive urgencies (492 subjects) and hypertensive emergencies (138 subjects). Results: The study results indicate that female subjects were significantly over-represented compared to men (365-57.9% vs. 265 – 42.1%,  $p=0.007$ ). The average age of the male subjects was  $56,6 \pm 16,6$  years, while the female subjects' average age was  $68,4 \pm 12,6$  years. The majority of subjects belonged to the age group of 60-69 (36.4%) years of age: 28.8% urgency and 38.6% emergency. Hypertensive urgencies frequently present with headache (62,2%), epistaxis (16,4%), faintness (8%), and psychomotor agitation (10%) and hypertensive emergencies frequently present with chest pain (30,4%), dyspnea (28.6%) and neurological deficit (29.4%). Types of end-organ damage associated with hypertensive emergencies include cerebral infarction (26.4%), acute pulmonary edema (24.8%) and hypertensive encephalopathy (28.6%), as well as cerebral hemorrhage (4.5%) and congestive heart failure (12%). Other clinical presentations associated with hypertensive emergencies include aortic dissection (0.8%), and preeclampsia and eclampsia (2,6%), as well as acute coronary syndromes (20.4%). Conclusion: The total sample of 630 subjects was 57.9% female and 42.1% male. The largest number of subjects belonged to the age group of 60-69 (36.4%) years of age: 28.8% with hypertensive urgency and 38.6% with hypertensive emergency. Hypertensive urgencies were significantly more common than emergencies (78,1% vs. 21,9%,  $p<0.0001$ ). The average blood pressure in subjects with hypertensive crisis was 216.46/122.16 mmHg. The most common symptoms of hypertensive urgency were headache (62.2%), epistaxis (16,4%), faintness (8%), and psychomotor agitation (10%) while the most common symptoms of hypertensive emergency were chest pain (30,4%), dyspnea (28.6%) and neurological deficit (29.4%). Clinical manifestations of hypertensive emergency were cerebral infarction (26.4%), acute pulmonary edema (24.8%), hypertensive encephalopathy (20.6%), acute coronary syndromes (20.4%), cerebral hemorrhage (4.5%), congestive heart failure (12%), aortic dissection (0.8%), preeclampsia and eclampsia (2,6%).

### **C8. Atrial multifocal tachycardia in a patient with sequelae of stroke [FLASH]**

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Introduction: Residual radiological lesions may persist even after resolution of pulmonary diseases, such as tuberculosis. Case presentation. We present the case of a 72-year-old woman, admitted for dyspnea, fatigability, dizziness and diffuse abdominal pain. The patient was known with chronic heart failure NYHA class III, arterial hypertension, arrhythmia, type II diabetes mellitus treated with metformin, and ischemic stroke. The ambulatory treatment consisted of diuretics, such as furosemide and spironolactone, beta blockers (carvedilol), statin, angiotensin converting enzyme inhibitor and a benzodiazepine tranquilizer. The following exams were performed: ECG – multifocal atrial tachycardia 103 bpm, abnormal repolarization in DI and

aVF, atrioventricular block 2nd degree; echocardiography – ejection fraction 25%, mild aortic and mitral regurgitation; carotid ultrasound - important bilateral atheromatous plaques, without significant stenosis; thyroid ultrasound - multiple hypoechogenic nodules, suggestive for adenomas; chest X-ray - aortic dilatation, bilateral nodular opacities predominant in the superior lobes, the biggest one in the right pulmonary field. The ECG Holter monitoring revealed recurrent atrial flutter alternating with atrial tachycardia, with variable degree of atrio-ventricular block and isolated ventricular extra systoles. The cerebral CT scan showed multiple sequelae of cerebrovascular disease, enlargement of the ventricular system and atheromatous plaques of the basilar and internal carotid arteries. Conclusion: Multifocal atrial tachycardia is a rare type of arrhythmia that usually appears in patients with COPD. In our patient, the etiology of multifocal atrial tachycardia was related with the presence of thyroid nodules.

### **C9. The importance of cardiopulmonary testing in the rehabilitation of coronary patients [FLASH]**

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Introduction: Cardiopulmonary exercise testing represents the gold standard in functional capacity assessment, being a valuable method for cardiovascular diagnosis as well as in designing cardiovascular rehabilitation programs for each patient. Our study aimed to assess the usefulness of cardiopulmonary exercise testing for coronary patients with interventional or conservatory treatment, before the initiation of the specific program of cardiovascular rehabilitation. Methods: The study included 53 patients (43 men, 10 women) admitted to the Clinic of Cardiovascular Rehabilitation of Recovery Hospital Iasi, assessed before the initiation of cardiovascular rehabilitation program by cardiopulmonary exercise test, measuring the most important parameters such as: maximal oxygen uptake (VO<sub>2</sub> max), oxygen uptake at the level of anaerobic threshold (AT), respiratory exchange ratio (RER), oxygen pulse (OP), minute ventilation (VE), maximal work rate (Wmax), metabolic efficiency (slope of  $\Delta\text{VO}_2/\Delta\text{w}$ ). It was assessed the relation between the clinic-pathogenic profile and the ergospirometric parameters. Results: The average age of enrolled subjects was  $59 \pm 9$ , with history of arterial hypertension 66%, angina pectoris 66%, myocardial infarction 71%, interventional treatment 61% and conservatory treatment 39%. Patients with arterial hypertension associated significantly lower values for Wmax compared to those without arterial hypertension ( $p=0,022$ ). Also for the subgroup of hypertensive patients it was determined significantly higher values for the slope of VO<sub>2</sub> versus the work rate ( $\Delta\text{VO}_2/\Delta\text{WR}$ ), a parameter reflecting the impairment of metabolic efficiency ( $p=0.051$ ). Patients with history of myocardial infarction presented at the cardiopulmonary testing significantly higher values for VE ( $p=0,004$ ), in comparison to those without. For the patients with history off interventional treatment, the VO<sub>2</sub> max was associated with higher values, but the results were at the edge of statistical significance ( $p=0,065$ ). Conclusions: Cardiopulmonary exercise testing is an investigation of major importance in order to achieve a cardiovascular rehabilitation program individualized for each patient, considering the great variety of respiratory parameters changes in coronary diseases.

### **C10. Variation of blood pressure in adolescents population in Brasov district [FLASH]**

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**Introduction:** The increasing prevalence of hypertension in childhood population during last years justifies the interest of pediatricians in determination of the evolution trend of blood pressure in children. **Objective:** Our aim was to analyze the anthropometrical parameters and the value of blood pressure in adolescents. **Material and method:** we had performed a prospective study in 2017 (March – June) during adolescent population in Brasov district, aged between 14-18 years with measurement of weight, height, body mass index and blood pressure. **Results:** Our study group consists 398 children, 173 girls and 225 boys; 10,15% of girls had hypertension and 89,85% had normal BP; 13,5% of boys had hypertension, 3,5% had “high normal”BP and 83% had normal BP. Regarding BMI: 16,18 % of girls were overweight and 9,24% were obese; 21,77% of boys were overweight and 9,33% were obese. **Conclusions:** both in boys and girls the BMI tends to be higher than 50th percentile; regarding BP also the values both in boys and girls tend to be higher than 50th percentiles, boys had more often “high normal” BP then girls.

### **C11. Role of obesity and dyslipidemia in arterial stiffness in patients with diabetes mellitus [FLASH]**

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**Background:** Diabetes mellitus is a chronic disease with increasing prevalence, associated with great burden on health systems. Diabetic patients have an increased risk of developing atherosclerotic cardiovascular disease. **Methods:** We performed a retrospective study on a group of 54 patients (27 previously diagnosed with diabetes mellitus and 27 without diabetes mellitus or another cardiovascular disease), aged between 39-74 years old. We analyzed data from a family medicine office record database, between May-July 2017. Body mass index (BMI), blood pressure (BP), serum glucose and lipids were evaluated, as well as the finger-toe pulse wave velocity measured using a pOpmetre. **Results:** According to BMI values, 66.6% of the patients were obese and 13.3% overweight. In the group previously diagnosed with diabetes mellitus. Most of the patients are hypertensive, and just one third have controlled BP. 7.2% of all patients had diabetic retinopathy and 11.1% had diabetic nephropathy. Diabetic neuropathy was diagnosed in 26.6% of the patients. Diabetic arteriopathy was the most frequent complication, being present in 33.3% of the patients. 40% of the patients with hypertriglyceridemia associated at least one of the complications described above. Study compared ft-PWV in diabetic patients versus non-diabetic patients. We found an association between increasing arterial stiffness and obesity grade. 35.5% of patients with increased total cholesterol had diabetic complications, as

well as 40% of those with high LDL-cholesterol. Instead, 53.3% of patients diagnosed with diabetes in the last 1-5 years have already developed complications. 68.8% of those with diabetes onset in the last 5-10 years had at least one complication, as well as 60.5% of those with onset more than 10 years before. Conclusions: The study highlighted the correlation of obesity degree and lipids values with the presence of diabetic arteriopathy. Our study highlights the negative role of obesity and dyslipidemia over diabetes evolution and its complications.

### **C12. The 54-th Meeting of the European Society of Phlebectomy - the Romanian perspective [FLASH]**

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The traditional French-to Romanian cultural relationship, enhanced in 1968 by the historical visit of General Charles de Gaulle, as President of the French Republic, in Romania, reaches its climax in 2006 on the occasion of The Summit of The Francophony, held in Bucharest, Romania. The European Society of Phlebectomy, founded in 1987 in Paris, France, having as Founding President Jean-Marc Trauchessec, France, has the French as the first official language. The 54-th Meeting of The European Society of Phlebectomy organized, together with The Romanian Society of Phlebectomy, the 1-st of October 2016 at the Elisabeta Theatre in Bucharest, Romania, has two co-Presidents: Marina Jana Valentina Pacescu, Bucharest, the President of The Romanian Society of Phlebectomy and the National representative of Romania and Pierre-Louis Choukroun, Paris, France, The President of The European Society of Phlebectomy. The Scientific program includes fifteen speakers with twenty-one oral communications from three countries grouped in four Sessions with oral communications and discussions and two Symposia.

There are four Sessions with oral communications and this discussions including:

- three speakers with five oral communications from France;
- three speakers with three oral communications from Switzerland and
- seven speakers with nine oral communications from Romania.

Servier Symposium "The Chronic venous disease" includes three speakers with three oral communications from Romania; Alfa-Wassermann Symposium "The secondary prevention of the Deep venous thrombosis" includes one speaker with one oral communication from Romania.

The constant progress in the development of the co-operation among the health professionals from different countries, implicated in the diagnosis and in the treatment of the patients with venous diseases, representing the basis for new achievements in the science, education and practice in this domain of activity, is reflected in their contributions to the scientific events of the Francophone medical scientific societies.

### **C13. Managing atrial fibrillation in elderly - a continuous challenge [ORAL]**

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### 3. *Karl-Olga-Krankenhaus Stuttgart, Germany*

**Introduction:** Atrial fibrillation (AF) is the most common arrhythmia in clinical practice; its burden exponentially increases with age. Heterogeneity and incomplete understanding of the pathophysiology, dramatical increase in incidence with age and lack of response to antiarrhythmic medication transforms AF in a continuous and exponential challenge over time. The purpose of this study is to evaluate AF ablation combined with antiarrhythmic drug therapy as a strategy to rhythm control in patients over 65 years old with difficult to control AF. **Methods:** Twenty-seven patients with AF and no significant valvular disease were included in a prospective study between 2014 and 2018. Inclusion criteria: age  $\geq 70$ , persistent AF, failure of maintaining sinus rhythm with antiarrhythmic drug therapy, ejection fraction  $\geq 40\%$ , written consent for ablation. The mean age was  $75 \pm 3.2$ , 31.2% women. All patients underwent pulmonary vein isolation and ablation guided by fractionated electrograms in the left atrium. The endpoint was obtaining and maintaining sinus rhythm (SR). **Results:** Twenty-one patients (85.1%) maintained SR for a mean follow-up period of  $2 \pm 0.5$  years after ablation under continuous antiarrhythmic drug medication. Anticoagulation therapy was discontinued in 15 (71.4%) patients which maintained SR for a period of minimum 12 months evaluated by repeated 24h ECG monitoring and serial ECGs. The other 6 patients in SR continued anticoagulation therapy due to severely enlarged left atrium. No periprocedural complications were noticed. **Conclusion:** Atrial fibrillation ablation (substrate-based and pulmonary veins isolation) combined with antiarrhythmic drug therapy in patients in which the antiarrhythmic drug therapy alone failed, is a safe and effective strategy to maintain SR in elderly patients.

### **C14. Magnesium sulfate: effective drug for hypertension treatment [FLASH]**

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**Introduction:** MgSO<sub>4</sub> is a musculotrope vasodilator with direct action on arteries and veins and it is a unique calcium antagonist, because Mg is physiological calcium competitor. **Methods:** Retrospective meta-analysis of hypertensive emergencies from Moldova, clinical studies, literature and scientific publications, regarding the level of Mg in cardiovascular disease and hypertension treatment with MgSO<sub>4</sub>. **Results:** In 2017, Pre-hospital Emergency Medical Service of Moldova assisted 182.281 patients with hypertensive emergencies, most frequent being in ageing people. The results of the various study confirmed an inverse relationship between magnesium and blood pressure. The studies have shown that Mg decreases, or Mg deficiency is mostly evidenced in the elderly population, those with hypertension, diabetes, dyslipidemia, etc., also in antihypertensive treatment with diuretics and beta-blockers. The association of hypertension and hypomagnesaemia has considered established. Low intracellular Mg<sup>2+</sup> results in increased membrane permeability to Na<sup>+</sup> and Ca<sup>2+</sup>, increased angiotensin-2-mediated synthesis of aldosterone, the production of thromboxane and vasoconstrictor prostaglandins. In hypertension is altered intracellular Mg<sup>2+</sup> homeostasis and transport Mg<sup>2+</sup> across membranes

via the Na<sup>+</sup>/Mg<sup>2+</sup> and Mg<sup>2+</sup>/Ca<sup>2+</sup> exchangers, and the transient receptor potential melastatin 6 and 7 channels (TRPM6, TRPM7). Magnesium competes with calcium for binding sites, so is a unique, physiological Ca<sup>2+</sup>-antagonist and by decreasing voltage-operated calcium channels activity in vascular smooth muscle, Mg lowers intracellular calcium and inhibits Ca<sup>2+</sup> depolarizing effects and as a Ca<sup>2+</sup> channel blocker relieve vasospasm, promoting vasorelaxation, lowers peripheral and cerebral vascular resistance, and decrease arterial blood pressure. In patients with pregnancy-induced hypertension, MgSO<sub>4</sub> treatment significantly decreased circulating levels of angiotensin-converting enzyme. Conclusions: MgSO<sub>4</sub> alone or in association, can be an effective drug in the treatment of hypertension. As magnesium is a physiological calcium competitor, rapid intravenous (bolus) administration is prohibited as it can reduce blood pressure. An intravenous bolus dose of 1 g over 5 minutes is recommended.

### **C15. Arterial hypertension: new target values [ORAL]**

Diaconu CC

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Arterial hypertension has a prevalence of 30-45% in the general population and it is associated with a very high cardiovascular risk, being considered "the silent killer". Genetics plays an important role in hypertensive patients. Currently, there is a plethora of guidelines for arterial hypertension, sometimes creating confusion, due to different recommendations on blood pressure targets. According to the 2013 European Society of Hypertension/European Society of Cardiology Guidelines for the management of arterial hypertension, hypertension is defined as a systolic blood pressure value  $\geq 140$  mmHg and or diastolic value  $\geq 90$  mmHg. However, at the end of 2017, the new guidelines of the American College of Cardiology/American Heart Association have been published. These guidelines have brought a new definition of the high blood pressure, with different cut-off values. According to the American guidelines, stage 1 arterial hypertension is defined as a systolic blood pressure of 130-139 mmHg or diastolic 80-89 mmHg, and stage 2 as a systolic blood pressure  $\geq 140$  mmHg or diastolic  $\geq 90$  mmHg. This new definition of high blood pressure has an impact on the treatment strategies, due to the lowering of the blood pressure threshold to initiate treatment. A comparative analysis of the recommendations of the most important guidelines will be presented.

### **C16. Polypragmasie chez les patients agés [ORAL]**

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Les schémas de traitement du patient âgé comprennent souvent de nombreux médicaments en raison de multiples conditions, parfois graves. Cependant, les personnes âgées ont modifié leur pharmacocinétique et leur pharmacodynamie, ce qui peut poser des problèmes dans le traitement



de diverses maladies. Les patients âgés ont une fonction rénale et hépatique réduite (excrétion des médicaments altérée), une réduction des graisses (modification de la distribution des médicaments) et une déficience cognitive. Le terme polypragmasia définit l'administration d'un grand nombre de médicaments (généralement plus de cinq) ou l'utilisation de doses inappropriées. Les personnes âgées s'auto-administrent souvent des médicaments en vente libre ou des compléments alimentaires pouvant interagir avec les médicaments prescrits par le médecin. L'optimisation des schémas thérapeutiques des personnes âgées devrait être une priorité pour l'interniste. La polypragmasie augmente la possibilité de «cascades de prescription», lorsqu'un effet secondaire est interprété comme un symptôme d'une nouvelle affection pour laquelle un nouveau médicament est initié. Les critères de Beers sont les plus utilisés pour évaluer les médicaments d'ordonnance inadéquats chez les personnes âgées. La présentation inclura un certain nombre de cas cliniques illustratifs pour le concept de polypragmasia chez les personnes âgées.

### **C17. Association of coronary arteries restenosis with changes in purine [FLASH]**

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**Introduction:** The cardio-vascular diseases are the global problem having not only the medical but the social meaning. The percentage of coronary heart disease is about 43%, but according to the prognosis by 2020 year it will become the most widespread reason of the death. The prognosis of mortality directly is connected with immediate diagnostics, prevention of complications and myocardial revascularization on time. There is the risk of the development of complications in spite of the real progress in modern cardiology and cardio-surgery. More often these complications resulted in activation of inflammatory factors and progress atherosclerotic process in the stenting zone. Thus, the search of new biochemical markers of early diagnostics of complication after coronary revascularization is very actual. The aim - to estimate the diagnostic significance of catabolites of purine metabolism in coronary arteries restenosis development. **Methods:** Determination of intermediates of purine metabolism guanine, hypoxanthine, adenine, xanthine and uric acid in plasma was performed. 96 patients with acute coronary syndrome were examined (age 40-75). Metabolites of purine metabolism were determined in blood plasma by the method of direct spectrometry. **Results:** Statistically significant increase in the concentration of guanine, hypoxanthine, adenine, xanthine and uric acid in plasma in the 2nd and 4th groups compared with the control group were revealed. In plasma samples taken from the patients from the 2nd group (patients with acute coronary insufficiency on the third day after stenting) there was a tendency to fore-fold elevation of the guanine and hypoxanthine concentration (p value < 0.00001), three-fold elevation of adenine and xanthine concentration (p value < 0.0001), and elevation of uric acid concentration in 2 times (p value < 0.0001) relative to the upper limit of the physiological norm were revealed. In plasma samples taken from the patients from the 4th group (patients hospitalized again with acute coronary syndrome within 6 months after stenting with in-stent restenosis), there was also a tendency to statistically significant increase the concentration of

guanine more than 17 times (p value < 0.0004), hypoxanthine (p value < 0.0003) and adenine (p value < 0.0002) in 20 and 7 times respectively, xanthine in 5 times (p value < 0.0006) and two-fold increase of uric acid (p value < 0.001) concentration relative to the upper limit of the physiological norm were revealed too. Conclusion: Given the simplicity and accessibility of the determination of purines and their catabolites with direct spectrometry method, it is possible to use it in clinical practice to identify the association between changes in purine concentration and the possible development of restenosis after coronary artery stenting.

### **C18. Impact of ageing in metabolic syndrome [ORAL]**

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Introduction: Aging is a real global concern, elderly population being at its highest level in human history. The aging population transforms the world dramatically and very quickly. Distribution of the population by age categories has changed and will continue to change radically, given the long-term decline in fertility rates and the increase in life expectancy. Methods: We realized a retrospective study on 495 patients admitted in the Cardiovascular Rehabilitation Clinic from March to June 2016. Our patients were divided by age, body mass index according to WHO, blood pressure values, cholesterol, triglycerides, HDL-cholesterol according to the NCEP ATP III guidelines, gender. The range used for our studied parameters was from our laboratory. Results: In young people under 35 years old, the addressability of the doctor is higher in male patients (73,3%) and over time the ratio equals and even reverses so that between 75-84 years the female patients predominate (63,6%). As we expect, first degree obesity is most common in the 55-64 age group (42,8%), regardless of the sex of the patient. In the same age range, there is the maximum number of patients with diabetes - a fact revealed by high HbA1c values (29,8%), hypertensive (with left ventricular hypertrophy – 8,7%), hypercholesterolemia (48%), hypertriglyceridemia (41,5%) and decreased values of HDL cholesterol (21,2%). Conclusions: Metabolic syndrome can be considered a disease that affects active people. Within our group in the age range of 55-64 years were diagnosed a high percentage of patients with comorbidities like: hypertension, diabetes mellitus, mixed dyslipidemia, obesity.

### **C19. Relationship between age and clinico-biological parameters in obstructive sleep apnea and diabetes [ORAL]**

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**Introduction:** Obstructive sleep apnea (OSA) causes oxidative stress, sympathetic nervous system activation and overstimulation of the renin-angiotensin-aldosterone axis, being a frequent comorbidity in patients with cardiovascular disease. **Methods:** Our study included 30 patients with OSA and other cardio-metabolic comorbidities, 23 patients with type 2 diabetes but without OSA and 25 non-diabetic, non-apneic controls. All patients underwent oscillometric assessment of arterial stiffness, clinical examination and routine blood tests. **Results:** Mean age was 61.87 years, 59.16 years and 57.63 years in our diabetes, control and OSA groups, respectively. Age was correlated with aortic pulse wave velocity (PWV) ( $p=0.032$ ,  $r=0.310$ ), hemoglobin ( $p=0.028$ ,  $r=-0.321$ ) in our non-apneic subjects, but not in our OSA group. We also found a positive association between PWV and total cholesterol and uric acid levels ( $p=0.05$ ,  $p=0.01$ , respectively) in non-apneic patients. Age was negatively associated with glomerular filtration rate in both non-apneic patients and OSA subjects ( $p=0.000$ ,  $r=-0.591$  and  $p=0.005$ ,  $r=-0.502$ , respectively). Surprisingly, in our OSA group, age was negatively correlated to AHI ( $p=0.05$ ) but showed a positive correlation with minimal nocturnal O<sub>2</sub> saturation ( $p=0.05$ ). Age was also significantly correlated to brachial and aortic Aix ( $p=0.01$ ), and DRA, a marker of coronary perfusion ( $p=0.004$ ,  $r=-0.527$ ) and glomerular filtration rate ( $p=0.005$ ,  $r=-0.502$ ) in our OSA group. We found positive associations between AHI and resting and 24-h medium heart rate ( $p=0.01$ ,  $p=0.00$ , respectively), inflammation markers (erythrocyte sedimentation rate:  $p=0.01$ ; C reactive protein  $p=0.02$ ), LDL ( $p=0.02$ ), total cholesterol ( $p=0.01$ ), brachial and aortic augmentation index (Aix) ( $p=0.03$  and  $0.003$  respectively). **Conclusion:** OSA is associated with higher heart rate, subclinical inflammation and LDL cholesterol. Aging induces increased aortic PWV in non-apneic subjects and increased brachial and aortic Aix in patients with moderate-severe OSA. Although age was negatively associated with AHI, it was negatively correlated with minimal nocturnal O<sub>2</sub> saturation.

## **C20. Beta-blockers in the treatment of chronic heart failure: did gender make a difference? [ORAL]**

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**Introduction.** The purpose of the study was to describe the clinical characteristics of patients diagnosed with chronic heart failure in two tertiary hospitals and to investigate whether gender differences between men and women exist with regard to the treatment of chronic heart failure with beta-blockers. **Methods.** We conducted a retrospective study of 103 patients (mean age

70.77 ± 9.57 years, range 38-92 years), consecutively hospitalised for chronic heart failure during 2017 (95.15% with reduced ejection fraction and 4.85% with preserved ejection fraction). The study group consisted in 50.49% women (52 cases, mean age 72.69 ± 9.57 years, range 52-92 years), and 49.51% men (51 cases, mean age 68.80 ± 9.78 years, range 38-86 years). Results. Beta-blockers were prescribed in 89 cases (86.41%): 47 men (92.16%) and 42 women (80.77%). Beta 1-selective antagonists were prescribed in 66 cases (74.16%) and non-selective agents in 23 cases (25.84%). The most common chosen beta-blocker for men was metoprolol (23 cases, 45.10%), followed by carvedilol (16 cases, 31.37%) and bisoprolol (7 cases, 13.73%). Nebivolol was prescribed in one case only (1.96%). Women were given metoprolol as the medication of choice in 23 cases (44.23%), followed by carvedilol (7 cases, 13.46%), bisoprolol (5 cases, 9.62%), and nebivolol (5 cases, 9.62%). In one case, the choice of beta-blocker was unspecified (1.92%) and betaxolol was prescribed in one case only (1.92%). Conclusions. In our study, a higher number of male patients (92.16%) vs. female patients (80.77%) received beta-blockers for the treatment of chronic heart failure. Beta 1-selective antagonists were far more prescribed (74.16%) than non-selective agents (22.33%), yet men received a higher proportion of non-selective agents (31.37%) than women (13.46%). Metoprolol was prescribed similarly irrespective of gender (45.10% in men vs. 44.23% in women). Carvedilol was chosen for more men (31.37%) than women (13.46%). The same statement applies for bisoprolol: 13.73% of men were given bisoprolol vs. 9.62% of women.

### **C21. Anticoagulation therapy in chronic heart failure: did we treat women differently? [FLASH]**

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Introduction. The purpose of the study was to describe the prescription rates of anticoagulation therapy in patients diagnosed with chronic heart failure from two tertiary hospitals and to investigate whether gender differences between men and women exist with regard to the anticoagulant treatment. Methods. We conducted a retrospective study of 103 patients (mean age 70.77 ± 9.57 years, range 38-92 years) consecutively hospitalized for chronic heart failure during 2017 (95.15% with reduced ejection fraction and 4.85% with preserved ejection fraction). The study group consisted in 50.49% women (52 cases, mean age 72.69 ± 9.57 years, range 52-92 years), and 49.51% men (51 cases, mean age 68.80 ± 9.78 years, range 38-86 years). Results. 61 patients (59.22%) with chronic heart failure had atrial fibrillation. Anticoagulation therapy was prescribed in 54 cases (52.43%): 29 men (53.70%) and 25 women (46.29%). Vitamin K

antagonists were prescribed in 37 cases (68.51%), low molecular weight heparins in 1 case (1.85%) and novel oral anticoagulants in 16 cases (29.60%). The novel oral anticoagulants prescribed were: rivaroxaban (9 cases, 16.65%), apixaban (4 cases, 7.40%) and dabigatran (3 cases, 5.55%). Men received vitamin K antagonists in 20 cases (37.03%) and novel oral anticoagulants in 9 cases (16.66%). Novel oral anticoagulants were prescribed in the following order: apixaban (4 cases, 7.44%), rivaroxaban (3 cases, 5.55%) and dabigatran (2 cases, 3.72%). Women were anticoagulated in 25 cases (46.29%): vitamin K antagonists (17 cases, 31.48%), novel oral anticoagulants (7 cases, 12.96%) and low weight molecular heparins (1 case, 1.85%). Women received primarily acenocumarol (17 cases, 31.48%), followed by rivaroxaban (6 cases, 11.11%) and dabigatran (1 case, 1.85%). Conclusions. In our study group, anticoagulation treatment was prescribed more frequently in male patients. The most common prescribed anticoagulant was a vitamin K antagonist, acenocumarol (68.51%), yet men received acenocumarol more often than women. Novel oral anticoagulants were also administered less frequent in women than in men. Rivaroxaban was more prescribed in women (11.11%) than in men (5.55%), whereas apixaban was only given to men. The prescription rate of dabigatran was also in favour of men (3.72% vs. 1.85% in women).

## **C22. Dyslipidaemia and statin therapy in chronic heart failure: differences between men and women [FLASH]**

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Introduction. The purpose of our study was to identify the rate of dyslipidaemia in a group of chronic heart failure patients consecutively hospitalised in 2 tertiary hospitals during 2017 and to investigate whether gender differences between men and women exist with regard to the prescription patterns of statin therapy. Methods. We conducted a retrospective study of 103 patients (mean age  $70.77 \pm 9.57$  years, range 38-92 years) hospitalised for chronic heart failure (95.15% with reduced ejection fraction and 4.85% with preserved ejection fraction). The study group consisted in 50.49% women (52 cases, mean age  $72.69 \pm 9.57$  years, range 52-92 years), and 49.51% men (51 cases, mean age  $68.80 \pm 9.78$  years, range 38-86 years). Results. Dyslipidaemia was found in 56 patients (54.37%) of the study group: 24 males (42.86%) and 32 females (57.14%). Dyslipidaemia was present in 24 out of 51 males (47.06%) and in 32 out of 52 women (61.54%). Obese patients accounted only for 31 (30.10%) members in the evaluated group: 12 men (38.71%) and 19 women (61.29%). Statin therapy was prescribed in 44 cases (78.57% of the dyslipidemic group) and the prescribed medication consisted in: atorvastatin (28

cases, 63.64%), rosuvastatin (14 cases, 31.82%) and simvastatin (2 cases, 4.84%). Statin therapy was chosen for 23 (95.23%) of the 24 men with dyslipidaemia. Atorvastatin was the first choice in statin therapy (16 cases, 69.57%), followed by rosuvastatin (6 cases, 26.09%) and simvastatin (1 case, 4.34%). The female patients had dyslipidaemia in 32 cases and received statins in 21 cases (65.62%). The prescription pattern was atorvastatin (12 cases, 57.14%), rosuvastatin (8 cases, 38.10%) or simvastatin (1 case, 7.76%). Conclusions. In our study group, dyslipidaemia was more frequent in women than in men. The female group consisted of more patients with dyslipidaemia (32 cases, 61.54%) than the male group (24 cases, 47.06%). Statin therapy was prescribed for more men (23 cases, 95.23%) than women (21 cases, 65.62%), although more women suffered from dyslipidaemia than men. Atorvastatin was the first statin chosen for both groups, followed by rosuvastatin and simvastatin. The prescription rates of atorvastatin were higher in men (16 cases, 69.57%) than women (12 cases, 57.14%), but the prescription rates of simvastatin and rosuvastatin were higher in women (8 cases, 38.10%; 1 case, 7.76%, respectively) than in men (6 cases, 26.09%; 1 case, 4.34%, respectively).

## RESPIRATORY DISEASES

### **R1. Subclinical vascular alterations in chronic obstructive pulmonary disease (COPD) [FLASH]**

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**Introduction.** Atherosclerotic vascular disease is very common in aged patients with COPD, systemic inflammation being an important pathogenic mechanism, shared by the two disorders. However, vascular pathology frequently develops silently and is often under diagnosed. The purpose of this study was to identify subclinical vascular alteration in COPD patients and to describe the relation between vascular modifications and respiratory clinical and functional profile. **Methods.** We performed a prospective, case-control study, comparing a group of 23 patients with COPD without known vascular pathology and a group of 24 healthy subjects, matched by age and gender. Arterial stiffness was assessed using a brachial cuff-based oscillometric device, measuring the following parameters: brachial and aortic augmentation indexes (AIXbr, AIXao), aortic pulse wave velocity (PWVao), central pulse pressure (PPao), central systolic blood pressure (SBPao), brachial pulse pressure (PPbr), heart rate (HR). Carotid intima-media-thickness (IMT) was assessed by carotid ultrasound. Lung function was assessed by spirometry testing. The 6 minute walking test was performed to determine COPD related exercise capacity alteration. Blood lipidic profile and smoking status were also determine. **Results.** Old patients with COPD presented a significant elevation of arterial stiffness, revealed by higher values of PWVao, PPao, SBPao, PPbr, than control group. In line with arterial stiffness alteration, COPD group associated a higher mean value for carotid intima-media thickness. Significant correlations of the cardiovascular and respiratory alterations were identified in COPD patients: arterial stiffness parameters (AIXao, PPao) and carotid IMT correlated with heart rate; SBPao, significantly correlated with smoking status (pack-years). Ventilatory function and exercise capacity did not correlate with vascular parameters. **Conclusions.** In elderly, COPD associates structural and functional arterial alterations (increased vascular stiffness and increased intima-media thickness). Vascular impairment does not correlate with airflow obstruction but correlates with smoking status in COPD patients.

### **R2. Inhaler influence on asthma and COPD patients' disease management [ORAL]**

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**Introduction:** An important aspect of the good management of COPD and asthma is the proper application and compliance with the inhaled drugs. A variety of inhaler devices are available on the market, including pressurized metered-dose inhalers (pMDIs), dry powder inhalers (DPIs), and nebulizers. The present study is a prospective, observational study aiming to assess patient satisfaction with the marketing authorized inhalers for administration of medication for asthma and COPD, applying the Feeling of Satisfaction with Inhaler questionnaire (FSI-10). **Methods:** The observational period was between July and September 2017 with patients diagnosed with asthma and COPD, recruited from pharmacies. The international standards for the forward and backward translation approach were followed for FSI-10. **Results:** The assessed group comprised 32 participants (19 female and 13 male). The highest results are given to the questions concerning the education on the inhaler and its preparation for use. The lowest - to the question on the patient's total satisfaction with the inhaler. **Conclusion:** Inhaler satisfaction is very important aspect of the management of asthma and COPD. Knowing patients' preference and satisfaction with their inhaler device can help the manufacturers and can be a factor for better adherence and good treatment outcomes. Unfortunately, the results from the performed study show that the Bulgarian patients are not satisfied with their inhalers. This fact emphasizes the need of better education and application of better constructed inhalers for the patients that suffer from these chronic diseases.

### **R3. Screening of lung cancer [ORAL]**

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Given that survival in lung cancer decreases with disease progression, the diagnosis at early stages is essential. Base on the known risk factors, several algorithms were created in order to identify the potential to develop lung cancer. And so patients at risk can benefit from screening programs. Chest X-ray was the first screening tool used, but failed to show an improvement in survival. Low dose computer tomography (LDCT) was the most studied method. It was first used in 1990. Compared to chest X-ray, it has a bigger sensitivity and it can detect pulmonary nodules under 2 mm in diameter. Since 2015, LDCT in used in patients between 55-74 years old with a history of at least 30 PA or at least 50 years old and a history of 20 PA and one additional risk factor: personal history of cancer/ chronic obstructive pulmonary disease/ pulmonary fibrosis, occupational exposure to carcinogens or family history of lung cancer. The patients should be monitored every year until reaching the maximum age of inclusion criteria or have stopped smoking for at least 15 years or until other comorbidities prevent them from benefiting from LDCT. There have not been any proves regarding the role of blood or air biomarkers in lung cancer patients. This presentation was supported by the FDI grant no. 0547/2018, funded by National Council for Higher Education, Ministry National Education”



#### **R4. Corticosteroids versus macrolides in the treatment of cryptogenic organizing pneumonia [FLASH]**

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Cryptogenic organizing pneumonia (COP) is a type of organizing pneumonia which affects the bronchioles and the alveoli. It is a rare lung condition that has unknown cause. Although the name includes pneumonia, it is not an infection. Males and females are equally affected, with a mean age of developing the disease of 50 to 60 years old. Clinical manifestations of COP usually begin gradually, like a prodrome of a flu-like illness, with low-grade fever, dry cough, malaise, anorexia, weight lose, mild dyspnoea. Occasionally, dyspnoea may be severe, even at rest, in case of rapidly progressive disease. In rare cases, patients may have uncommon manifestations such as chest pain, arthralgia, night sweats, and haemoptysis. At physical examination, we can find pulmonary crackles, but physical exam may be almost normal in some patients. The diagnosis may be often delayed to several weeks, because the symptoms are nonspecific. In order to diagnose COP, we should perform laboratory test, a chest radiography, a computed tomography which shows bilateral areas of alveolar condensation, a spirometry that reveals a restrictive ventilatory dysfunction, a bronchoscopy with bronchoalveolar lavage which shows a mixed pattern (increase of lymphocytes, neutrophils, eosinophils). A pulmonary biopsy with histopathological exam is mandatory in order to diagnose COP that reveals the presence of buds of granulation tissue formed of fibroblasts, myofibroblasts and connective tissue. Corticosteroids are the first line treatment, resulting in rapid clinical and imaging improvement, but several studies concluded the macrolides can be used in COP therapy, due to their anti-inflammatory effects. Macrolides, such as clarithromycin, may be used especially in patients with a good clinical status, in addition of corticosteroids or as an alternative treatment, with the advantage of avoiding the side effects of long-term corticosteroid therapy.

#### **R5. Is there a relationship between heart rate and RDW in patients with OSAS and arrhythmias? [ORAL]**

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Introduction: Obstructive sleep apnea syndrome (OSAS) is the most common respiratory sleep disorder, with increasing prevalence. Nowadays, the association of obstructive sleep apnea syndrome with cardiovascular and metabolic pathology is more and more recognized. Methods: We performed a prospective, interventional study, in order to evaluate the correlation between heart rate and systemic inflammation, assessed by a surrogate marker, the red cell distribution width (RDW), in patients with OSAS and arrhythmias. The study has started in June 2013 (ongoing) and included 52 patients diagnosed with OSAS and cardiac arrhythmias. We also

assessed the effect of continuous positive airway pressure (CPAP) on systemic inflammation in these patients. Results: The model is statistically significant ( $F_1; 9 = 9,488$ ,  $\text{sig} = 0,013$ ), indicating that when the heart rate increases by 4,247 u.m, the RDW increases by 1%, ( $t = 3,080$ ,  $\text{sig} = 0,013$ ). The constant is statistically significant and shows that the minimum heart rate for the patients analyzed is 71,095 beats/minute. There is also a decrease of RDW values in patients using CPAP ( $p\text{-value} < 0.05$ ). Conclusion: Increased heart rate is associated with a higher degree of systemic inflammation. CPAP therapy reduces systemic inflammation associated with OSAS, assessed by RDW analysis, leading to cardiovascular risk reduction.

## **R6. Cytological examination of bronchoscopies and correlation of lung cancer types with smoking: a 1-year retrospective study [FLASH]**

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Introduction: Worldwide, lung cancer is the most common malignancy among men (1.241.600) and the first cause of death (1.098.700). Among women it is the third most common malignant disease (583.100) and the second cause of death (491.200) after breast cancer. The treatment of lung cancer and patient survival is based on the knowledge of both the extent of the disease and the type of carcinoma. Our objective was the evaluation of 503 results of bronchoscopy specimens for the detection of the incidence of lung cancer types and their correlation with smoking. Methods: Retrospective study of the year 2016, the results of bronchoscopy specimens from 503 patients. The average age was 62.7 years (30-85 years). The specimens were processed with the liquid-base cytology technique (Thin Prep®) and stained with Papanicolaou stain. The type of tumors was classified according to their morphological and immunocytochemical criteria. Results: Out of 503 cases, 323 were negative for malignancy. In 129 (73.3% men) cases the diagnosis was malignancy and more specifically: squamous carcinoma in 38 (29.4%) related to 32 active or former smokers, adenocarcinoma in 22 (17%) related to 12 active or former smokers, small cell carcinoma in 18 (14%) related to 10 active or former smokers, non-small cell carcinoma in 41 (31.8%) related to 25 active or former smokers, 10 (7.8%) were metastatic carcinomas (3 active or former smokers). In 51 cases the diagnosis concerned atypical cells or cells suspected of malignancy (24 active or ex-smokers). Conclusion: From our results, it seems that in bronchoscopy specimens, the most common type of lung cancer is squamous cell carcinoma and concerns three out of four active or ex-smokers followed by adenocarcinoma and small cell carcinoma which account for about half of active or ex-smokers.

### **R7. Cytological results of TBNA specimens: retrospective study of one year [FLASH]**

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**Introduction:** TBNA technique helps diagnose both neoplasms and benign diseases. Although its diagnostic value is high, in Greece remains an underused technique and only 21% of the pulmonologists reporting its use. Its diagnostic value depends on tumor type, size and location of the lymph node (the studies place the sensitivity to 32-84% and the specificity to 98-100%). Our aim was the evaluation of 313 cytological results of TBNA samples in order to highlight the incidence of lung cancer types. **Methods:** Retrospective study of the year 2016, the cytological results of TBNA specimens from 313 patients. The average age was 62.7 years (45-71 years). The smears were processed by the conventional method and stained with Papanicolaou stain. The type of tumors was classified according to their morphological and immunocytochemical criteria. **Results:** Out of 313 cases, 198 were negative for malignancy. In 87 (71.1% men) cases the diagnosis was malignancy and more specifically: adenocarcinoma in 38 (43.7%), squamous carcinoma in 19 (21.8%), small cell carcinoma in 4 (4.6%), non-small cell carcinoma in 20 (23%), while 6 (6.9%) cases were metastatic carcinomas. In 28 cases, the diagnosis concerned cells atypical or suspected of malignancy. **Conclusion:** From our results, it seems that adenocarcinoma is the most common type of lung cancer followed by squamous and small cell carcinoma. Additionally, we would like to add that TBNA remains an important technique in the diagnosis and staging of lung cancer and that the expertise of a cytopathologist is obligatory for reaching high levels of sensitivity and specificity.

### **R8. Cytologic examination of bronchial washings and correlation of lung cancer types with smoking: a 1-year retrospective study [FLASH]**

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**Introduction:** Worldwide, lung cancer is the most common malignancy among men and the first cause of death. Among women, it is the third most common malignant disease and the second cause of death after breast cancer. Bronchoscopy, like most invasive methods, has contraindications, so it is not always possible to obtain cell samples with a bronchial brush or a tissue biopsy. Our objective was the evaluation of 518 results of cytological examination of bronchial washing samples in order to highlight the incidence of lung cancer types and their

correlation with smoking. Methods: Retrospective study of the year 2016, the results of bronchial washing samples from 518 patients. The average age was 62.6 years (19-86 years). The specimens were processed with the liquid-base cytology technique (Thin Prep®) and stained with Papanicolaou stain. The type of tumors was classified according to their morphological and immunocytochemical criteria. Results: Of the 518 cases, 420 were negative for malignancy. In 62 (71.1% men) cases the diagnosis was malignancy and more specifically: squamous carcinoma in 20 (32.2%) related to 16 active or former smokers, adenocarcinoma in 15 (24.2%) related to 7 active or former smokers, small cell carcinoma in 4 (6.5%) related to 2 active or former smokers, non-small cell carcinoma in 20 (32.2%) related to 13 active or former smokers, while 3 (4.9%) cases were metastatic carcinomas (1 active or former smoker). In 36 cases, the diagnosis concerned cells atypical or suspected of malignancy (19 active or former smokers). Conclusion: From our results, it appears that in bronchial washing samples, the most common type of lung cancer is squamous cell carcinoma and concerns about three out of four active or ex-smokers followed by small cell carcinoma and adenocarcinoma which account for about half of active or former smokers.

## ENDOCRINOLOGY - DIABETOLOGY

### ED1. Some bioethics aspects on therapeutical approach of third age obesity [ORAL]

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Ethics is the science of morality. The definition of "ethics" means a complex of issues which reflects the pluralism of our living, the multitude of point of views and the variety of moral norms, legal, cultural and social concept that includes them. Obesity is a major health problem: a high incidence (especially in industrialized countries); an impairment of life duration and quality; promote a pathology of cardiovascular, respiratory, rheumatology, endocrinal-metabolically (mortality of 1.5 - 4 times higher than in normal weight); increased risk of an operator; a psychosocial consequences. Bioethics should act both at individual and society level and has to consider obesity as major diseases and not as a stigmat. Such programs should target not only weight but also increased the reintegration into the society, moral support, decisive initialization and success of treatment. These techniques used individual therapy, group therapy, in which the family psychologist and psychotherapist is very important. Efficiency increases when behavioral therapy includes the whole family. The therapy must act for cognitive restructuring - helping patients with answers to their negative attitudes. All physicians must undertake a nutrition education, dietetics and culinary diet based on scientific, non-harmful, as appropriate needs, balanced principles, practical and effective.

### ED2. The contribution of fasting and postprandial blood glucose increments to endothelial function in type 2 diabetes and stable angina pectoris [FLASH]

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Introduction: Both fasting and postprandial hyperglycemia are independently associated with deteriorating endothelial function and atherosclerosis in patients with dyslipidemia and diabetes mellitus. Aim: Evaluation of contributions of fasting and postprandial blood glucose increments on endothelial function in patients with stable angina pectoris (SAP) and diabetes mellitus type 2 (T2DM) was evaluated. Material and methods: 90 T2DM patients (62 with SAP and 28 without SAP) treated with metformin and/or sulphonylurea were enrolled in cross-sectional nested case-control clinical study. The areas under the sixpoint daily glucose curve above the fasting glucose

concentrations (AUCpp) and over 5.5 mmol/L (AUCbg) were calculated to determine postprandial (AUCpp) and fasting (AUCbg-AUCpp) glucose increments. Malondialdehyde (MDA), protein carbonyl group (PCO), and nitric oxide (NO) were determined. Results: AUCbg-AUCpp 58.2 (95%CI 41.2–75.7) was higher in SAP group compared to non-SAP 35.1 (95%CI 24.1–51.1) mmol\*h/L. They had significantly higher NO (mean  $\pm$  SD)  $30.50 \pm 12.1$  vs.  $21.8 \pm 8.4$  nmol and MDA  $15.7 \pm 4.6$  vs.  $12.9 \pm 3.8$   $\mu$ mol/g plasma proteins, but similar PCO concentration. AUCpp positively correlated with MDA ( $r=0.42$ ) and NO ( $r=0.37$ ) in the presence of SAP. AUCbg-AUCpp positively correlated with PCO ( $r=0.47$ ) in the absence of SAP. The analysis revealed that AUCpp over turning point of 0 mmol\*h/L was associated with high MDA and NO concentration in diabetics with SAP. Conclusion: In T2DM patients with stable SAP, AUCpp at any point, significantly contributes to increasing of MDA and NO concentration.

### **ED3. Teriparatide treatment in patients with severe osteoporosis based on Romanian protocol [ORAL]**

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Introduction: Teriparatide (TPT) is an anti-osteoporotic drug designed for selected severe cases and prescribed based on national protocols. We introduce a cohort treated in accordance to Romanian protocol for TPT (the drug is indicated in severe cases of osteoporosis as those with high fracture risk of prevalent fragility fractures, as well as glucocorticoid osteoporosis in accordance to specific criteria of T-score and medical history). The drug administration includes (as generally recommended): daily 20  $\mu$ g, subcutaneous injections for 24 months with self administration (specific device), once in life (non- repeatable). Method: This is an observational descriptive study with cross-sectional and longitudinal results (12, 24 months) on TPT patients according to national protocol criteria, conducted between 2013-2018 at a tertiary centre of endocrinology on patients with informed written consent. Statistical significance:  $p<0.05$ . Results: 50 patients were enrolled; 50% reached the first of two years and, except one patient, further therapy for one more year as recommended based on protocol. Mean age was 77 yrs (majority: menopausal women). Half had upper digestive tract conditions that contraindicated oral bisphosphonates. One tenth had current/recent glucocorticoid exposure. 15% of patients used TPT as first-line therapy for osteoporosis. Prior specific medication for osteoporosis exposure was between 1 and 14 years. An average number of prior fractures were 3 (more than 80% of vertebral site). Conclusion: TPT was introduced based on Romanian protocol applied for this studied cohort, in severe patients with long time estrogen deprivation since menopause; the majority of them have a long history of other anti-osteoporotic drugs exposure while the number of first time TPT uses is rather low.

#### **ED4. Menopause: apparently healthy versus patients with adrenal incidentaloma confirmed with non-functioning pattern [ORAL]**

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**Introduction.** Non-functional adrenal tumours detected as incidentaloma (NATI) are age-related and mostly display a poorly symptomatic pattern. If co-morbidities, especially bone- related and metabolic anomalies in menopausal females, are more prevalent is the objective of the current study. **Method.** Retrospective, observational, case-control study on patients admitted on a Tertiary Romanian Centre of Endocrinology. **Inclusion criteria:** menopause, confirmed NATI, informed written consent. **Exclusion criteria:** prior specific drugs for osteoporosis. **Assessments:** medical history of cardio-metabolic disease, panel of osteoporosis investigations. **Statistical significance:**  $p < 0.05$ . **Results:** 165 women: 1/3 represents the studied (S) group (NATI+ve), the others (NATI negative)- control (C) group with similar age (58 yrs) between groups. **Metabolic complications:** more prevalent in S group (high blood pressure: 75 vs. 60%, hyperlipemia: 65 vs. 60%, altered glucose profile: 30 vs. 25%); body mass index higher in S group ( $p < 0.05$ ). Osteocalcin (15 vs. 25ng/mL,  $p = 0.005$ ), CrossLaps (0.3 vs. 0.4ng/mL,  $p = 0.03$ ), 25OHD:  $15 \pm 6$  vs.  $20 \pm 9$  ng/mL ( $p = 0.01$ ), parathormone: 40 vs. 50pg/mL ( $p > 0.5$ ). **Bone Mineral Density at lumbar Dual-Energy X-Ray Absorptiometry (DXA):** 1.03 vs. 1.02g/sqcm ( $p > 0.05$ ); 40% had osteoporosis on both groups. Plasma morning cortisol was higher in S group ( $p < 0.05$ ) and shower statistical significant lower suppression after 1 mg overnight of dexamethasone (1.8 vs. 1.1  $\mu\text{g/dL}$  (normal  $< 1.8 \mu\text{g/dL}$ ) while morning plasma ACTH levels (Adrenocorticotropic hormone) were lower in S group (13 vs. 18 pg/mL,  $p < 0.05$ ). **Conclusion.** NATI, an age-related expected conditions, associate a higher prevalence of cardio-metabolic diseases, slightly modified plasma cortisol-ACTH axe while lumbar DXA might not introduce a statistical significance difference between the NATI positive and negative menopausal subjects, opposite to bone turnover markers.

#### **ED5. Ovariectomized rats as a model of postmenopausal osteoporosis: confirmation and applications [FLASH]**

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**Objective:** Osteoporosis is a common disorder characterized by reduction in bone mass and increased risk of fracture. The aim of this in vivo study was to analyze the tissue reaction after

induced estrogen-deficient osteoporosis in female Wistar rats. We aimed to assess the effect of ovariectomy on bone turnover and degradation, to evaluate whether ovariectomized (OVX) rats could be an experimental model of postmenopausal osteoporosis. Materials and Methods: We used 20 female Wistar rats of reproductive age-2 months, which were divided into 2 groups: Group (G1)-10 ovariectomized animals (ovx) and Group (G2)-10 sham-operated animals (sham). The effect of ovariectomy on bone regeneration was assessed by using immunohistochemical and ELISA method. Changes in expression of matrix metalloproteinase-9 (MMP-9), osteonectin (SPARC) and collagen type 1 (COL-1) were observed in the epiphyseal zone of the femur. The serum concentrations of alkaline phosphatase (ALP) and MMP-9 were determined eight weeks after the operations. Results: Our results showed that bone turnover significantly increased and bone mass significantly decreased 8 weeks after ovariectomy. We found that the expression of MMP-9 in osteoclasts significantly increased in the group with osteoporosis – G1 compared to G2. The expression of SPARC and COL-1 significantly decreased in the group with osteoporosis – G1 compared to G2, ( $p < 0.05$ ). The results showed the values of ALP and MMP-9 in rats of G1 statistically significantly increased compared to G2 ( $p < 0.05$ ). Conclusion: Increased expression of MMP-9 in G1 confirms that estrogen deficiency leads to the development of osteoporosis by stimulating the expression of MMP-9 from the osteoclasts. Activated osteoclast increase the resorption of bone collagen. Thus, we propose that the ovariectomized rat model could be considered a reproducible and reliable model of osteoporosis. The survey is a project of MU-Pleven № 5 / 2016 and № 12/2014.

#### **ED6. Anthropometric indices and thyroid cancer risk factors [FLASH]**

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Introduction: Thyroid cancer is a frequent endocrine neoplasia with an increasing incidence over the last decades. There is still controversy over the relation between anthropometric indices and thyroid cancer. Materials and methods: The study group included 20 female patients, aged between 16 - 68 years, with thyroid cancer (follicular carcinoma, papillary carcinoma, medullary carcinoma and lymphoma). Age, age of menarche, weight, height, body mass index (BMI), body surface were evaluated. Results: The patients included in the study had the mean age of menarche 11,7 years; the weight was between 50 and 82 kg with a mean of 62,2 kg, the height was between 157 and 173 cm with a mean of 167,2 cm, BMI had values between 17,2 and 29,07 kg/m<sup>2</sup> with a mean of 22,29 kg/m<sup>2</sup>. The body surface values were between 1,53 and 1,99 m<sup>2</sup> with a mean of 1,70 m<sup>2</sup>. Conclusions: 50% of the patients were younger than 35 years of age when the thyroid cancer diagnosis was confirmed by histopathology. 90% of the patients had the age of menarche between 11 and 12 years of age. 90% of the patients included in the study had height values higher than 160 cm. BMI was lower than 18,5 kg/m<sup>2</sup> in 30% of the patients and body surface was higher than 1,6 m<sup>2</sup> in 60% of the patients.



### **ED7. Endocrine changes during pregnancy [FLASH]**

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**Introduction:** A number of thyroid parameters changes during pregnancy. In women with chronic autoimmune thyroiditis with hypothyroidism under therapy increased L-Thyroxine dose is required. Maternal hCG levels peak at approximately 12 weeks resulting in a high-normal or elevated FT4 and a suppressed TSH. Failure to recognize normal pregnancy-induced alteration in endocrine function can lead to unnecessary diagnostic tests and interventions that may be detrimental to mother and fetus. **Materials and methods:** The study group included 20 pregnant patients, with thyroid disease (chronic autoimmune thyroiditis), aged between 24 – 41 years. TSH, FT4, glucose, weight, height, body mass index (BMI) were evaluated during the first semester of pregnancy (1 - 12/14 weeks) and during the second semester of pregnancy (14 – 28 weeks). **Results:** During the first semester of pregnancy TSH values were between 0,01 and 14,8  $\mu$ UI/ml, FT4 levels were between 0,8 and 1,53 ng/dl, glucose levels were between 82 and 102 mg/dl and BMI values were between 19 and 34 kg/m<sup>2</sup>. During the second semester of pregnancy TSH values ranged between 0,1 and 8,8  $\mu$ UI/ml, FT4 levels were between 0,32 and 1,3 ng/dl, glucose levels were between 79 and 105 mg/dl and BMI was between 22 and 39 kg/m<sup>2</sup>. **Conclusions:** During the first semester of pregnancy 20% of the patients were with subclinical hyperthyroidism, 20% of the patients were with subclinical hypothyroidism and 10% were with clinical hypothyroidism; during the second semester of pregnancy, under therapy, 20% of the patients had subclinical hyperthyroidism, 10% had clinical hypothyroidism and 10% had subclinical hypothyroidism. All patients had normal glucose levels in both semesters of pregnancy.

### **ED8. Glucose metabolism changes in hyperprolactinemic patients [FLASH]**

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**Introduction:** Diabetes mellitus mainly occurs in individuals with underlying defects in insulin secretion; hyperglycemia typically resolves when the hormone excess is corrected. Hyperprolactinemia was associated with obesity, reduced sensitivity to insulin and diabetes mellitus.

**Materials and methods:** The study group included 30 female patients, 15 patients with hyperprolactinemia and 15 patients with normal prolactin levels. Prolactin (PRL), weight, height, body mass index (BMI) and glucose were evaluated. **Results:** In hyperprolactinemic group, with

patients aged between 17 - 46 years, PRL levels had values between 27 and 1182 ng/ml with a mean of 127,07 ng/ml; glucose levels were between 67 and 165 mg/dl with a mean value of 94,2 mg/dl and BMI was between 18 and 49 kg/m<sup>2</sup> with a mean value of 27,63 kg/m<sup>2</sup>. In normoprolactinemic group glucose levels were between 62 and 120 mg/dl with a mean of 89,47 mg/dl and BMI was between 26 and 34 kg/m<sup>2</sup> with a mean value of 29,5 kg/m<sup>2</sup>. Conclusions: Both groups had normal mean value of glucose; only one patient, with hyperprolactinemia had diabetes mellitus and 4 patients - two with hyperprolactinemia and two with normal prolactin levels -had impaired fasting glucose. Increased BMI was observed in 63,3% of the patients; 5 patients with hyperprolactinemia had normal BMI values.

### **ED9. Primary hyperparathyroidism with systemic involvement [FLASH]**

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Introduction: Primary hyperparathyroidism is a syndrome characterized by parathyroid hormone hypersecretion in the absence of stimulation through hypocalcemia. It is the third endocrinopathy by frequency, after diabetes and thyroid dysfunctions. The most common complications are: osteoporosis, cardiac complications and renal lithiasis. Case presentation: A 66-year-old patient, diagnosed 30 years ago with primary hyperparathyroidism, presented for severe dyspnea. Clinical examination revealed a height of 1.32 m, postoperative scars (surgical intervention for pectum carinatum), fingers stick drummer, articular system: cervical spondylosis, thoracic kyphosis, lombar lordosis, mandibular bone dysplasia, clavicle fracture, respiratory system characterized by polypnea, with diminished vesicular murmur, bilateral wheezing and crackles, cardiovascular system: rhythmic cardiac sounds, a blood pressure of 120/60 mmHg, heart rate 95 / min. Biological: severe respiratory acidosis, increased blood urea nitrogen, hyperglycemia, HbA1c 6.1%, elevated serum phosphorus. Chest X-ray: thoracic kyphoscoliosis, sternal cerclage. Thoracic CT scan with contrast substance: chest with severe thoracic kyphosis, deformed, with T6 peak and appearance of the spring rib clogged III, IV, V, VI, bilateral; severe demineralization of bone segments, with geodes in the humerus, sternum and vertebrae; small bilateral pleurisy; emphysematous changes in both upper lobes; condensation processes in the postero-basal segment in the right lower lobe and the left basal pyramid; right adrenal adenomatous nodule of 17/12 mm. Noninvasive ventilation was used, with unfavorable evolution to death. Conclusions: Patients with secondary restrictive ventilatory dysfunction due to primary hyperparathyroidism are at risk for pulmonary infections, which can exacerbate the chronic respiratory failure, with fatal evolution.

### **ED10. 25-Hydroxy Vitamin D evaluation in patients with metabolic syndrome [FLASH]**

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**Introduction:** Vitamin D deficiency is associated with an increased risk of developing diabetes, high blood pressure, atherosclerosis and the risk of cardiovascular events.

**Methods:** The purpose of this study is to highlight the levels of serum 25-hydroxy vitamin D and serum TNF- $\alpha$  in patients of the test group diagnosed with metabolic syndrome. The test group consists of 39 patients (24 females and 15 males) with BMI more than 30 kg/m<sup>2</sup>. Determination was performed by electrochemiluminescence detection (ECLIA) immunochemical method. The results of this study indicate statistically significant pT ( $\alpha < 0,05$ ) decreased levels of serum 25-hydroxy vitamin D and statistically significant increased levels of serum TNF- $\alpha$  in the test group subjects compared to the control group. **Conclusions:** High serum levels of TNF- $\alpha$  constitutes a marker for systemic inflammatory response, being involved in the occurrence of the insulin resistance mechanism, developing major cardiovascular events in correlation with vitamin D depletion.

### **ED11. Cost-effectiveness analysis of noninsulin health technologies for treatment of diabetes mellitus type 2 in Bulgaria [FLASH]**

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**Introduction:** The treatment of Diabetes mellitus type 2 /DMT2/ includes drugs with various mechanisms, adverse effects and costs. Given diabetes high prevalence and health care expenditures, it is important to identify which therapeutic alternatives offer the best value for their costs. This study performs modelling cost and health benefits of Dipeptidyl peptidase-4 inhibitors /DPP-4i/, Sodium-glucose cotransporter 2 inhibitors /SGLT2i/, Thiazolidindiones /TZD/ and Glucagon-like peptide 1 agonists /GLP-1ag/. An indirect comparison of therapeutic alternatives for the second and third treatment line was performed. Cost-effectiveness analyses were conducted in the Bulgarian setting from a public perspective in accordance with guidelines of Bulgarian HTA Agency. **Methods:** Identification and analysis of published data from health technology assessment for treatment of DMT2 in other countries (2006-2016).

Network meta-analysis, including also modelled data of health utilities and costs of DPP-4i vs SGLT2i vs TZD vs GLP-1ag, discounted at 5%. The Markov model was applied with time horizon of 5 years. The indirect comparison includes the four types of drugs plus Insulin and sulphonylurea. **Results:** In the group of patients with DMT2 Canagliflozin dominates Liraglutide and is with better efficacy and lower costs than Sitagliptin, and Pioglitazone: Cana vs Sita (ICER 13464,22BGN/QALY), Cana vs Pio (ICER 21 2844,94BGN/QALY). Liraglutide is cost-effective in comparison with Sitagliptin with ICER 10187,47BGN/QALY, Exenatide than Pioglitazone (ICER 23228,71BGN/QALY) and Sitagliptin than Pioglitazone (ICER 1554,71BGN/QALY). All results are below defined in Bulgaria reimbursement act cost-effectiveness threshold. **Conclusion:** DPP-4i, SGLT2i and GLP-1ag are cost effective health technology in comparison with existing therapeutic alternatives for treatment of DMT2 in Bulgaria. These results suggest that adding these groups of drugs to dual and triple therapy versus insulin and sulphonylurea in patients inadequately controlled with Metformin would be a more efficient use of health care resources in the Bulgarian setting.

## **ED12. Mass spectrometry MALDI-TOF for microorganisms' identification in patients with diabetic foot syndrome (DFS) (FLASH)**

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**Introduction.** The number of patients with diabetes is increasing year by year. One of the most common complications of this disease is diabetic foot syndrome (DFS). A priority task of modern microbiology is identification of microorganisms. Actually microorganisms are best identified using 16S rRNA and 18S rRNA gene sequencing. Matrix-assisted laser desorption ionization–time of flight mass spectrometry is an alternative to 16S rRNA gene sequencing using for identification of bacterial strains. **Methods.** The purpose of the study was to identify microorganisms by MALDI-TOF mass spectrometry in patients with diabetic foot syndrome. For the study, microscopy of the wound sample with Gram staining has been used. Wound contents were cultured also on mannitol salt agar, meat-peptone agar, Saburo agar, blood agar. 72 patients with DFS were investigated between 2013-2015. The comparison group consisted of 30 patients with chronic purulent inflammatory diseases of the lower extremities not suffering from diabetes mellitus. The average age of patients was  $54 \pm 3,8$  years and they were on treatment in the surgical department of "Karaganda City Hospital №1" and "Regional Medical Center" Kazakhstan. **Results.** The results of MALDI-TOF spectrometry showed up microorganisms in patients with DFS. Gram-positive microflora was represented primary by *Staphylococcus aureus* and *Staphylococcus haemolyticus*. Among the Gram-negative bacteria, prevailed enterobacteria as *Escherichia coli*, *Enterobacter cloacae*, *Proteus mirabilis* and non-fermenting Gram-negative bacteria. *Pseudomonas aeruginosa* was also isolated. The dominant microorganism was *Staphylococcus aureus* (37%) coagulase-negative. Monocultures prevailed in 22 patients. **Conclusion:** The dominant microorganism in patients with diabetic foot syndrome is *Staphylococcus aureus*, Gram-positive bacteria, which occurred mostly as monoculture. Gram-negative bacteria are represented by enterobacteria and also non-fermenting bacteria.

## NEUROLOGY

### **N1. Rapamycin: a new hope in tuberous sclerosis treatment? [ORAL]**

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**Introduction:** Tuberous sclerosis (TSC) is a genetic disorder caused by heterozygous mutations in the TSC1 or TSC2 genes. Recent findings, in animal models, show that restoration of the underlying molecular defect can improve neurological dysfunction in several of these models, even if treatment is initiated in adult animals, suggesting that pathophysiological processes in the mature brain contribute significantly to the overall neurological phenotype in these models. **Case presentation:** We are presenting the case of a 7-year-old patient, known with tuberous sclerosis complex and delayed neuro-psychomotor development, who presented for polymorphic epileptic seizures. Her condition became symptomatic when she was 2 years old, with 4-5 episodes of spastic contractions a day. The neuromotor rehabilitation program and cognitive therapy were initiated and sustained during a period of 6 months, but no improvement was noted. The annual MRI showed tuberous cortical lesions and typical subependymal nodules. At the ultrasound examination of the heart there could be seen certain hyperechogenic areas of the interventricular septum and the right ventricular apex. At the moment of admission, the patient's level of consciousness is altered, with a return to epileptic seizures that are pharmacologically resistant and exacerbated by an acute infectious respiratory episode. Last year, mTOR inhibitor-based treatment was started, showing good results. **Conclusions:** The data from animal models of TSC show that a sizeable proportion of the neurological phenotypes associated with pathogenic mutations is caused by altered mTOR signaling and can be corrected using mTOR inhibitor-based treatment approaches, even if treatment is initiated in adult animals. This treatment can lead to an increase in the quality of life of patients with tuberous sclerosis and to better control of epileptic seizures.

### **N2. Description of a patient with parasellar meningioma [FLASH]**

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The aim of the current investigation was to describe the clinical history of a patient; that have been treated in Clinic of Neurology of UMHAT „D-r G. Stranski” – Pleven. He was admitted after consideration with his GP. **Material and methods:** The patient was in good condition, with dyslopia, lesion of the left trochlear and oculomotor nerves, headache, nausea, ataxia,

pyramidal symptoms at the contra laterall side of the brain tumor. Complete anamnesis data were taken. MRT and CT scan of the brain, ECG, ultra sound of the abdomen and heart, X-ray and CT of the lungs, EEG, biochemical, immunological, serologic tests were performed. The patient was discussed with neurologist, neurosurgeon, cardiologist, ophthalmologist, and anesthesiologist. Coagulation test were provided. Antiepileptic treatment was started and continued successfully individually for this patient. The patient was discharged in good condition. He refused operative treatment. Results: The analysis of the received results and data of the dynamic clinical neurological examination, laboratory investigations, revealed therapeutic challenges and alternatives concerning the clinical interpretations, diagnosis and differential diagnosis. Conclusions: The preliminary patient's diagnosis was ischemic stroke in the brainstem. It's necessary to be provided more investigations and long term neurological observation for the correct final diagnosis.

### **N3. Clinical presentation of acute stroke in emergency medical services [FLASH]**

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Introduction. Stroke is one of the leading causes of morbidity and mortality worldwide. Globally, Cerebro-Vascular Accident (CVA) or stroke accounts for about 10% of all deaths, two-thirds of which occur in low income countries. According to the WHO, stroke is a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal and at times global (applied to patients in deep coma and those with subarachnoid hemorrhage) loss of cerebral function with symptoms lasting more than 24 hrs or leading to death, with no apparent cause other than that of vascular origin. Among the stroke subtypes, cerebral ischemia and infarction constitute about 85-90% of the total stroke subtypes in western countries with only about 10–15% patients with cerebral hemorrhage. Objectives. The objective of this study is to evaluate the clinico – epidemiological profile and clinical presentation of acute stroke in relation to age, sex, as well as, the prevalence of accompanying symptoms and clinical manifestations. Methods. The study was conducted between January 2016 and December 2016 and included 880 subjects of both sexes, aged 30-86 with a diagnosis of stroke. All consecutive cases attending the study site were enrolled and studied with predesigned questionnaires after obtaining ethical clearance for this observational study. Predesigned pretested questionnaire was used to assess demographic profile, behavioral risk factor, all the patients were assessed clinically through detailed history and clinical examination. From the history, various demographic variables were collected including age, sex, history of transient ischemic attack/stroke, hypertension, diabetes mellitus, coronary artery disease, prestroke disability, smoking, and family history of stroke. After the availability of the results of all investigations, ischemic stroke patients were grouped according to the TOAST subtypes. Inclusion criteria: 1. Subjects aged older than 20 years. 2. The diagnosis of acute stroke (ischemic/hemorrhagic) based on clinical evaluation and imaging (computed tomography [CT]-head/magnetic resonance imaging [MRI] brain). Exclusion criteria: 1. Patients with stroke-like conditions due to systemic diseases such as infections and trauma. 2. All hemorrhagic stroke patients who have posttraumatic, drug-induced (e.g., anticoagulant-induced), and those with bleeding diathesis-related etiologies will be excluded. 3. Patients in whom the

whole investigation protocol was not possible. All the data were fed on excel spreadsheet, and statistical analyses were made using Epi Info version 3.3.2. Results. A total of 880 cases of strokes were enrolled, out of 916 CVA and the response rate is 96%. The age of the participants ranges from 30-92 years with an average of  $68.3 \pm 17.7$  years. Majority of the study participants 584 (66.36%) were between 50–69 years and presented with ischemic CVA (725 - 82.4%), while 155 (17.6%) had hemorrhagic CVA. Clinical signs and symptoms of ischemic and hemorrhagic CVA showed significant difference in symptoms like change in consciousness ( $p = 0.001$ ), weakness in face/limb ( $p = 0.002$ ), dysphagia ( $p = 0.002$ ), headache ( $p = 0.002$ ), diabetes ( $p = 0.001$ ), tobacco consumption ( $p = 0.002$ ) and alcohol consumption ( $p = 0.001$ ). During occurrence of current event symptoms occurs at home in 82.6% while 8.9% were in workplace and 8.5% other places. Ambulance services were availed by 89.6% of the sufferers for transportation, while 10.4% travelled by privately hired vehicle. Thus, using TOAST classification, it was observed that 381cases (43.6%) had large vessel atherothrombotic disease, 188 cases (21.4%) had small vessel disease (lacunar infarcts), 117cases (13.4%) had cardioembolic strokes, and 194 cases (22.04%) had stroke of undetermined etiology Among ischemic stroke patients, 464 (64.2%) patients were hypertensive, 180 (23.44%) patients were diabetic, and 309 (42.7%) patients were smokers. Conclusions. Stroke is an important cause of morbidity and mortality and has an increasing trend in the Emergency Medical Services Ischemic CVA constitutes a larger percentage of stroke subtypes 82.4% and using TOAST classification, it was observed that 381cases (43.6%) had large vessel atherothrombotic disease, 188 cases (21.4%) had small vessel disease (lacunar infarcts), 117cases (13.4%) had cardioembolic strokes, and 194 cases (22.04%) had stroke of undetermined etiology Among ischemic stroke patients, 464 (64.2%) patients were hypertensive, 180 (23.44%) patients were diabetic, and 309 (42.7%) patients were smokers.

#### **N4. Clinical descriptions of patients with epileptic status with diagnostic and differential diagnostic alternatives [FLASH]**

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The aim of the current investigation was to describe the clinical history of four patients; treated in the Clinic of Neurology of UMHAT „D-r G. Stranski” – Pleven. They were admitted from the emergency department with epileptic status. Material and methods: The patients were in severe condition, with generalized tonic clonic epileptic status. Complete anamnesis data were taken. Twice brain MRT and CT scan, ECG, ultra sound of the abdomen and heart, X-ray and CT of the lungs, EEG, biochemical, microbiological, immunological, serologic and genetic tests, lumbar puncture were performed. The patients were discussed with neurologist, neurosurgeon, cardiologist, ophthalmologist, anesthesiologist and infectionist. Coagulation tests were provided. The antiepileptic treatment was continued successfully individually for each patient. The patients were discharged in good condition without motor deficit and epileptic symptoms. Results: The analysis of the received results and data of the dynamic clinical neurological examination, laboratory investigations, revealed therapeutic challenges and alternatives concerning the clinical interpretations, diagnosis and differential diagnosis. Conclusions: It's necessary to be provided

more investigations in the genetic and molecular pathology and microbiology laboratories for the correct final diagnosis.

## **N5. Recognition and treatment of stroke at the pre-hospital stage in Republic of Moldova [FLASH]**

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**Introduction:** Stroke is the second leading cause of death (WHO) and the leading cause of long term disability. Hypertension is the most important risk factor for stroke. In stroke, there are numerous treatments that save lives. With regard to the pre-hospital stage, the guidelines state that: "Rapid identification of patients with acute stroke and immediate hospitalization in a hospital with a stroke unit are important to provide optimal emergency treatment, including thrombolysis". **Materials and methods:** The data presented here are collected from records of emergency care, through National Centre of Prehospital Emergency Medicine, Chisinau, between years 2016-2017. **Results:** In 2017 of the Emergency Medical Service Care served 182 281 patients with hypertension emergencies and EMSC served 11 786 patients of them was with cerebrovascular disease: 5175 (43.9%) urban and 6611 (56.1%) rural population. The 10 211 (86,6%) were hospitalized. The ischemic stroke were 7223 and 6417 (88.8%) were hospitalized. Patients with hemorrhagic stroke were 782 patients (6.6%) and 78,0% were hospitalized, transient ischemic attack 2319 patients (19.7%) and were hospitalized 85,3%. Up to the age 40 were registered 281 patients, 40-50 years were 593 patients and 50-70 years 6111 patients, and 238 patients aged 70 years. **Conclusion:** In emergency treatment of stroke, time is of the essence for the outcome. Current guidelines give rise to a loss of time that restricts the opportunities for effective treatment. To save lives and health, pre-hospital interventions must be included as an active part of the treatment chain. The ambulances should be equipped with a CT scanner for telemedical transfer of CT images for diagnostics at the nearest stroke unit.

## **N6. Biochemical changes in children with autistic spectrum disorder [FLASH]**

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Although research on autism has advanced, we still study the causes of this disorder. The term "autism" appears to have been used for the first time by a Swiss psychiatrist named Eugen Bleuler for the purpose of naming a group of symptoms of schizophrenia. Induced immunosuppression during pregnancy makes a woman more susceptible to infection, and the fetus becomes more immunologically vulnerable. Children born from older parents have a greater risk of autism. Both the use of antidepressants during pregnancy and the prevalence of



autism spectrum disorders have increased in recent years. The average concentration of erythrocytes below the limit may reveal the presence of lead intoxication. In the case of autism, the presence of heavy metals in the body is a widely debated theory that can be supported by the result of my research. Using the case study method, serum ionic calcium below normal limits may result in paraesthesias (false numbness / tingling sensation) which may also represent a loss / disorder of general sensitivity characteristic of all autistic people. It is not a novelty that among children with Autistic Spectrum Disorder sexual hormones play an extremely important role because they do not show any interest in the opposite sex. This does not mean that biologically they do not work normally, but this instinct is rudimentary.

#### **N7. Aggressiveness in children with autism [FLASH]**

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The increased level of aggression towards one's own person and around people or objects is common in people with autistic spectrum disorders. Using the case study method, we intend to demonstrate the influence of heavy metals on people with autistic spectrum disorders. The presence of lead and cadmium in excess of the maximum allowed may be one of the causes of these violent reactions. After the laboratory analyzes that we determined, we tried to find a solution to solve this situation. The reactions of autistic children may vary from child to child. The increased lead level is an eloquent indicator of autistic spectrum disturbance, there are studies trying to match the diagnostic to the presence of this metal in the blood, but we can also consider the idea of joining the lead in aggressive behavior. It is very important to begin recovering the baby immediately after diagnosis and to take into account the maximum rhythm, determined according to each case in order to give good results and to get the best possible prognosis. Autistic children, even they are different, may feel the same as all children.

## ONCOLOGY - HEMATOLOGY

### **OH1. Multifocal metastasis of renal cell carcinoma: a case report [ORAL]**

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**Introduction:** Renal cell carcinoma is a renal cortical tumor typically characterized by malignant epithelial cells with clear cytoplasm and a compact-alveolar (nested) or acinar growth pattern interspersed with intricate, arborizing vasculature. The stroma is reduced, but well vascularized. The tumor grows in large front, compressing the surrounding parenchyma, producing a pseudocapsule. A variable proportion of cells with granular eosinophilic cytoplasm may be present. In patients with metastatic renal cell carcinoma, the surgical removal of metastases, complete metastasectomy, is associated with significantly longer overall survival compared with incomplete metastasectomy. **Case presentation:** A 60-year-old patient with important cardiovascular risk factors (smoking, severe hypertension, hypercholesterolemia, insulin-dependent diabetes mellitus) is admitted in the hospital after he was diagnosed with a left kidney tumor. The imaging exams reveal the presence of a left kidney tumor, bilateral adrenal gland tumor, pulmonary and hepatic lesions, all of which are highly suspicious of being distant metastasis. He also had part of the 10th right rib removed two weeks before the presentation (the pathology and immune-histo-chemical tests prove the renal origin). The conduit suitable in this case is the combined surgical, endocrinological and oncological management. The first step undertaken was the removal of the left kidney and adrenal gland, which proved to be difficult. **Conclusion:** Clear cell renal cell carcinoma is an aggressive pathology, with a high metastatic potential. The early surgical treatment of the renal tumor and of the resectable metastasis can extend the survival rate. The surgical and interdisciplinary management of this patient is the key for survival.

### **OH2. Rare pathology: chronic kidney failure due to neglected penile cancer [FLASH]**

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**Introduction:** Penile neoplasia is a rare pathology, with the latest epidemiological data showing an incidence of 1/100,000, approximately 95% being squamous cancers. Classical presentation includes ulceration or a penile, painless, vegetative formation. The evolution of the untreated penile neoplasm is inevitably bleak. There is a specific psychological term within the specialized literature: "false shame". This material aims to highlight the effects this "false shame" may have on a patient with a neglected penile cancer. We also reviewed the literature in terms of presentation forms and therapeutic approach. **Case presentation:** We present the case to a 64-year-old patient, who complained of the impossibility of micturition. The clinical examination revealed a large size vegetative tumor at the level of the glans, with the destruction of the urethral meatus. Ultrasound revealed upper and lower urinary distention, with important changes in renal function. **Conclusions:** Penile cancer is one of the rare pathologies of the urinary system. Surgery is still the "gold standard" for treatment, but complementary methods - chemo and radiotherapy are gaining more and more ground. Neglecting such a disease leads to a bad prognosis for the patient in terms of survival and quality of life.

### **OH3. Molecular genetic testing in haemophilia A: where do the Balkans stand? [FLASH]**

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**Introduction.** Although molecular genetic testing is not required in the diagnostic approach of haemophilia A, the procedure has an important clinical value. Its applications include: genetic counselling, prenatal diagnosis for at-risk pregnancies, carrier testing, prognostication, and others. **Methods.** We performed a comprehensive review, using several major databases as well as the European Association for Haemophilia and Allied Disorders (EAHAD) Coagulation Factors Variant Database, regarding the implementation of molecular genetic testing in haemophilia A in member countries of the Balkan Medical Union. **Results.** Molecular genetic testing has already been performed in the following countries: Albania, Bulgaria, Croatia, France, Greece, Italy, Macedonia, Moldova, Serbia, Slovenia and Turkey. **Conclusions.** Molecular genetic testing in haemophilia A has been implemented in most member countries of the Balkan Medical Union. However, information is lacking whether some member countries have employed such techniques so far or have only failed to publish their scientific findings with respect to this particular topic. **Acknowledgements.** This work received support through the research grant competition for students of the Society of Students in Medicine of Bucharest (SSMB), contract no. 231/29.03.2017.

#### **OH4. Evolution of immunophenotypic and immunologic pathogens in older patients diagnosed with Non-Hodgkin's lymphoma [FLASH]**

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Non-Hodgkin's lymphoma (LNH) is an uncontrolled clonal proliferation of immature lymphoid precursors that lose their differentiation capacity and cause hypertrophy of the lymphatic organ that hosts them. Studying and analyzing the evolution of immunological and immunophenotypic parameters according to the applied treatment regimens demonstrates their predictive values for improving the long-term survival rate and recognizing optimal treatment regimens in order to reduce acute and late complications. Peripheral blood research in patients aged  $\geq 61$  years of onset of disease with assessment of humoral homeostasis indices and assessment of lymphoma phenotype by monoclonal antibody monoclonal antibody (AcM) labeling showed the predominance of cell line B antigens compared to cell line T. In addition to these features, AcMs are particularly important for the success of therapy. The use of chimeric or human AcM reduces immune rejection, facilitating effective clinical action. Each Ac specifically recognizes a particular antigenic determinant or epitope to which it binds to a portion having a complementary structure to the epitope. Cyclical monitoring of immunological parameters after each stage of therapeutic protocol termination determines their tendency to decrease and contributes to diminishing the immune response of the host organism. The slightly increased percentage of CD19, CD20 for the given age group determines a sufficiently high density on the target cell will support the effect of obtaining more effective therapeutic response in both monotherapy and combined therapies. Since most AcM-based treatments are dependent on these characteristics, and the immunological characteristics show that with the increase in the number of therapeutic cycles, the immune response of the host organism is reduced, which will induce attenuation of the anti-tumor defense mechanisms.

#### **OH5. The promising role of Geriatric Assessment (GA) in the treatment of cancer [FLASH]**

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Introduction: There is no doubt that we are leaving in an era where the number of elder patients with cancer has increased dramatically, as predicted by the founders of geriatric oncology. Approximately 60% of new cases of cancer occur in patients  $\geq 65$  years of age. Despite the high incidence of cancer in this group, there is less evidence regarding the risks and benefits of cancer treatment in this age, mostly because older people have been underrepresented in clinical trials. Chronologic age alone cannot determine our treatment decision because there is a wide heterogeneity among patients with the same age. A geriatric assessment (GA) seems to be a promising tool in oncologists' hands. GA is a multidimensional evaluation tool focused on determine a frail older person's medical, psychological and functional capability in order to

develop an integrated plan for treatment and follow-up. Methods: The International Society of Geriatric Oncology composed by experts in 2014 developed consensus statements upon the impact of GA in treatment-related complications, overall survival (OS), final therapeutic decision and much more. Results: GA can identify age-related problems which are not detected in patient's history and physical examination, predict severe treatment-related toxicity and OS in many types of tumors and influence a Tumor Board's decision. Experts concluded that the following domains should be included in GA: functional status, comorbidity, cognition, mental health status, fatigue, social status and support, nutrition and presence of any geriatric syndrome. Conclusion: Oncology teams should integrate GA findings into treatment decisions in order to weigh the pros and cons of chemotherapy treatment as well as to make rationale interventions to potentially decrease that risk. Because data on the utility of GA has been recently started to grow, more studies should be made to strengthen the validity of this promising tool.

### **OH6. Kit Therapy: a new approach ahead [FLASH]**

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Introduction: KIT gene is a proto-oncogene, which encodes a transmembrane kinase which is related to the receptors for colony-stimulating factor type 1 and platelet-derived growth factor, as well as to the immunoglobulin superfamily, use of which has been proven sufficient especially in stromal tumors. Imatinib mesylate is a 2 - phenylaminopyrimidine tyrosine inhibitor which has specific activity for ABL, platelet derived growth factor receptor, c -kit and Albeson -related gene, the pharmacokinetics of which are extensively described. Methods: Our review includes a wide understanding of molecular cancer therapies in GI Cancers, highlighting the pharmacological efficiency of imatinib, which has been proven by crystallographic studies. Preclinical data both in vitro and in vivo has indicated a tremendously efficient selective activity of imatinib mesylate on cells which express c -kit protein. Also, we review other mechanisms and mediators that might be potential targets of new therapies, such as sunitinib. Results: In terms of Gist treatment, imatinib molecularly targets the BCR-ABL, PDGFR $\alpha$  and Kit paths by preventing tyrosine autophosphorylation and thus "switching off" the downstream signaling pathways which promotes carcinogenesis. Regardless the exact mutation at every case, imatinib is used as a first-line treatment for metastatic, resilient and recurrent Gist. The value of surgery in cases of Gist metastasis is limited. Practically, the initial starting dose of imatinib is 400 mg/day per os, being compared with a starting dose of 800 mg/day, but still remaining the standard therapeutic plan. However, characterizing the molecular profile of the tumor and applying a personalized therapy requires a holistic approach by different specialties. Conclusion: The archived results with imatinib mesylate are spectacular, but follow up will always be necessary. It should be noted that in patients with complete cytogenetic remission alternative strategies are suggested. New bibliographic evidence suggest that GIST cells have the ability to get out of the control of KIT and PDGFRA $\alpha$  through the activation of alternative pathways .Under the framework of molecular research, our call is further investigation in the discovery of new signaling pathways like AXL , MET , IGF -R , that might contribute in the evolution of the disease.

### **OH7. Rare case of mucinous lung adenocarcinoma in a nonsmoker patient [ORAL]**

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**Introduction:** Between lung cancers histological types', adenocarcinoma is the most frequent. Though, the primitive mucinous variant is rare and has an atypic presentation, requesting attention in the diagnostic process. **Case presentation:** 78 years old female patient presents with chronic cough for more than a year with mucous sputum and dyspnoea with orthopnoea. Radiographic exam of the chest depicted extensive condensation processes bilaterally. CT thoracic scan showed condensation processes and nodules bilaterally with aeric bronchogram. Also, there was identified a possible tumoral process in the inferior left lobe. Bronchoscopy with broncho-alveolar lavage did not offer diagnostic features. So, the diagnostic was stated through surgical lung biopsy and was of mucinous adenocarcinoma. The paraclinical panel of investigations excluded, also, an extrapulmonary origin of the pathology. **Conclusion:** An atypical presentation can hide rare diagnoses, but is very important to pay attention to details and to undergo a complete panel of investigation, in order not to delay the diagnostic moment and in order to exclude other etiologies, like interstitial lung disease or an infectious cause.

### **OH8. Comparison of axillary imaging techniques in breast cancer staging [FLASH]**

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**Introduction:** Axillary node pathological status is one of the most important prognostic factors of breast cancer, but even replacing axillar dissection by sentinel lymph node biopsy still has a 20% complication rate. Improving clinical examination by using the best imaging technique may substantially reduce invasivity and complications. This must be correlated to risk factors and site-related probability. **Methods:** This presentation is an in-depth review and up-to-date study based on literature scientific papers and multicentric studies concerning the role axillary imaging techniques in breast cancer staging. The lymph node metastases' development favours ultrasound morphological depiction, but the vascularity study using ultrasound and MRI is of no less importance. **Results:** Ultrasound-guided fine needle aspiration (FNA) or core needle biopsy (CNB) reaches specificity of up to 100%, challenged by MRI with ultra-small paramagnetic iron oxide (95%) or diffusion-weighted imaging (DWI) (92%). The sensitivity of these methods is between 88-97% for ultrasound guided biopsy and 80-96% for MRI using USPIO or DWI. Discrimination between N0 and N+ is easier than between N1 and N2 or N3.

Conclusion: Comparing costs harm, degree of sophistication and time consumption, ultrasound is by far the best option for axillar basin evaluation. Considering intrathoracic nodes, the preference may favour MRI or PET-CT.

### **OH9. Our experience with the rare lymphoepithelioma-like cervical carcinoma [FLASH]**

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Introduction: Lymphoepithelioma-like carcinoma (LELC) of the uterine cervix is a rare type of squamous cell carcinoma (SSC). It is more common in Asian women– 5.5% than in Caucasians– 0.7%. It affects mostly younger women and has a lower frequency of regional lymph node metastasis and recurrence and better the 5-year survival than the common SCC. It is considered that LELC is associated with Epstein–Barr virus (EBV) infection in Asians and with Human papilloma virus (HPV) or no infection in Caucasian patients. The aim of this study was to determine the frequency of LELC in Caucasian patients and to examine the frequency of lymph node metastasis, recurrence and the survival rate of these patients. Materials and methods: A retrospective study has been done for a period of eight years on 775 female patients, who have been operated for cervical cancer in the Clinic of Gynecologic Oncology of University Hospital "Dr.GeorgiStranski"-Pleven. A group of 17 women with LELC have been identified by clinical and morphological data. All patients were clinical monitoring till now. Results: LELCs were 2.19% of all patients with cervical cancer and this is three times more often than the literature results. Three of the patients were with lymph node metastasis – 17.64% and two were with recurrence – 11.76%. Four of them died – 23.53%. Conclusion: LELC of uterine cervix is more often in Caucasians than it was thought and has no lower frequency of regional lymph node metastasis and recurrence. It has no better prognosis than the common squamous cell cervical cancer.

### **OH10. Perceived quality of life, health locus of control in patients with cancer: the impact of demographic variables [ORAL]**

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**Introduction:** Cancer is a serious life threatening illness that may influence on patient quality of life (QoL) and well-being. Optimal QoL has become a goal in health care. It can be argued that the improvement of QoL should be a primary goal of cancer care. Another important variable that may have influenced QoL is an individual perception of the degree of control the individual has over his life and health. **Methods:** This study evaluates the relation between perceived quality of life, Health Locus of control (HLOC) beliefs and tries to expand knowledge regarding the correlation between them. 115 oncology outpatients who have been submitted in pain therapy in the Pain Unit of an Oncological Hospital - Greece were administered the World Health Organization QoL instrument (WHOQOL-BREF) the Multidimensional Health Locus of Control scale (MHLC) and WHO (10 items) Well-Being Index. The present study is a cross-sectional, descriptive, correlational research design. **Results:** This study suggests that male patients well-being scores were significantly higher and reported also higher scores in the psychological and environmental domain of QoL but less in the external dimension of Health locus of control. Older cancer patients reported lower levels on the well-being and more on the external dimension of health locus of control and also lower scores on the QoL in the physical, psychological and social relationships domains. More educated patients reported significantly higher scores in the psychological and environment domains of QoL but less in the external attributional style of health locus of control. **Conclusions:** Findings provide evidence that demographic variables such as being male, younger more educated relate to a more preserved QoL. QoL has a significant correlation with internal health locus, doctors and important others. There is also a significant correlation between internal HLOC and well-being ( $r=.57$ ,  $p=.001$ ). It seems that cancer patients who use internal health locus beliefs appear to have a better well-being in comparison with those who use external attributions styles.

### **OH11. Comparative study of platelets between haematological analyzer - microscopic observation and role of plateletcrit [ORAL]**

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**Purpose:** Aims of this study is a comparison between platelet counts of hematologic analyzer and microscopic observation (count) per field. We studied platelet parameters in 111 samples of women with low platelet counts, increased MPV, and plateletcrit within the range 0.06-0.18% (normal range 0.15-0.35%) were examined. Plateletcrit is the percent count of platelet per unit of blood volume. From this study were excluded, Bernann Soullier, Absent radii, Mediterranean Thrombocytopenic, X-Linked Thrombocytopenia, as well as schistocytosis, metal valve cases, vascular grafts, and hemolytic anemias (Harris syndrome). **Material:** The study included samples of patients who came to the hospital as outpatients, internal patients of obstetrics and gynaecological clinics in the maternity hospital, and oncological patients. We collected platelet parameters from EDTA anticoagulated blood samples. All samples were collected by venipuncture and processed within an hour of collection in the Sysmex 5000 automated analyzer. The study was conducted with samples of March 2018. **Discussion:** This study attempts to link the number of low platelet counts with increased MPV and low Plateletcrit values. Currently studies, focus only on low platelet counts and elevated MPV, ignoring blood platelet aggregation



as a factor in haemostasis and its possible role. PCT is the volume occupied by platelets in the blood as a percentage and calculated according to the formula  $PCT = \text{platelet count} \times MPV / 10,000$  (25-27) its role in haemostasis is catalytic. The analyzer results, gave low platelet counts which obtained a range between 50K / uL - 149K / uL. MPV range was higher than 9.3fL (normal range 6-9fL) and plateletcrit range of 0.06% -0.19%. In the microscopic observation the overwhelming majority of samples showed a platelet count of more than 150 K / uL, but in five samples the platelet count remained lower than normal but above 50 K / ul, the antiplatelet therapy cut off. The results of the 111 samples examined microscopically, were: In 17 samples were found giant platelets (PLT larger than one erythrocyte), in 21 samples were found large platelets, in 24 samples were found clumps platelets, and in 2 samples were found platelet dissociations. We grouped our cases in to five categories: First group with haematological analyzer platelet count **50K/uL- 100K/uL**. Second group with haematological analyzer platelet count **101K/uL- 120K/uL**. Third group with haematological analyzer platelet count **121K/uL- 130K/uL**. Forth group with haematological analyzer platelet count **131K/uL- 140K/uL**. Fifth group with haematological analyzer platelet count **121K/uL- 149K/uL**. In total of **12** samples with haematological analyzer values of 50 K / uL to 100 K / uL, plateletcrit (PCT) range was **0.06% - 0.12%** whereas microscopic observation gave a platelet count of between 90 K / uL and 200 K / uL , while clumps platelets were observed in 3 samples, in 3 samples were observed large platelets, while giant platelets were observed in 1 sample. In total of **20** samples with analyzer values of 101 K / uL to 120 K / uL, plateletcrit (PCT) range was **0.10% - 0.15%**, while microscopic observation gave a platelet count between 150 K / uL - 400 K / uL ,in 6 samples were found clumps platelets, in 4 samples were observed large platelets , and in 2 samples giant platelets were found. In **19** samples with analyzer values of 121 K / uL -130 K/uL , plateletcrit (PCT) range was **0.12% - 0.17%**, while microscopic observation gave a platelet count between 150 K / uL and 300 K / uL, clumps platelets were observed in 3 samples, in 4 samples were observed giant platelets, while in 5 samples we observed giant platelets. In **27** samples with analyzer values of 131 K / uL -140 K / uL, plateletcrit (PCT) range was **0.13%- 0.18%**, while microscopic observation gave platelet counts between 150 K / uL and 300 K / uL, clups platelets were observed in 7 samples, in 4 samples were observed large platelets and in 5 samples we observed giant platelets. In **33** samples with analyzer values of 141K / uL - 149K / uL, plateletcrit (PCT) range was **0.15% - 0.20%.**, microscopic observation gave a platelet count between 150K / uL - 250K / uL, in 7 samples were observed clumps platelets, in 7 samples we saw large platelets, while in 4 samples giant platelets were observed and in 2 samples platelet dissociation.

**Table 1: MEAN OF PLT BETWEEN HAEMATOLOGICAL ANALYZER/ MICROSCOPIC OBSERVATION, IN ANALYZER VALUES 50 K/UI- 100 K/uL**

<b>Number of samples</b>	<b>12</b>	<b>Mean of Plateletcrit</b>	<b>Mean hematological analyzer PLT</b>	<b>Mean PLT</b>
<b>Giant PLT:</b>	<b>1</b>	<b>0,08%</b>	<b>79K/uL</b>	<b>138,2K/uL</b>
<b>Large PLT:</b>	<b>3</b>			
<b>Clumps PLT:</b>	<b>3</b>			
Dissociation of PLT:	<b>0</b>			

**Table 2:** MEAN OF PLT BETWEEN HAEMATOLOGICAL ANALYZER/ MICROSCOPIC OBSERVATION, IN ANALYZER VALUES 101 K/UI- 120 K/uL

<b>Number of samples</b>	<b>20</b>	<b>Mean of Plateletcrit</b>	<b>Mean hematological analyzer PLT</b>	<b>Mean PLT</b>
<b>Giant PLT:</b>	<b>2</b>	<b>0,12%</b>	<b>112,7K/uL</b>	<b>187,5K/uL</b>
<b>Large PLT:</b>	<b>4</b>			
<b>Clumps PLT:</b>	<b>6</b>			
Dissociation of PLT:	0			

**Table 3:** MEAN OF PLT BETWEEN HAEMATOLOGICAL ANALYZER/ MICROSCOPIC OBSERVATION, IN ANALYZER VALUES 121 K/UI- 130 K/uL

<b>Number of samples</b>	<b>19</b>	<b>Mean of Plateletcrit</b>	<b>Mean hematological analyzer PLT</b>	<b>Mean PLT</b>
<b>Giant PLT:</b>	<b>5</b>	<b>0,14%</b>	<b>125K/uL</b>	<b>200K/uL</b>
<b>Large PLT:</b>	<b>4</b>			
<b>Clumps PLT:</b>	<b>3</b>			
Dissociation of PLT:	0			

**Table 4:** MEAN OF PLT BETWEEN HAEMATOLOGICAL ANALYZER/ MICROSCOPIC OBSERVATION, IN ANALYZER VALUES 131 K/UI- 140 K/uL

<b>Number of samples</b>	<b>27</b>	<b>Mean of Plateletcrit</b>	<b>Mean hematological analyzer PLT</b>	<b>Mean PLT</b>
<b>Giant PLT:</b>	<b>5</b>	<b>0,15%</b>	<b>136,3K/uL</b>	<b>185K/uL</b>
<b>Large PLT:</b>	<b>4</b>			
<b>Clumps PLT:</b>	<b>7</b>			
Dissociation of PLT:	0			

**Table 5:** MEAN OF PLT BETWEEN HAEMATOLOGICAL ANALYZER/ MICROSCOPIC OBSERVATION, IN ANALYZER VALUES 141 K/UI- 149 K/uL

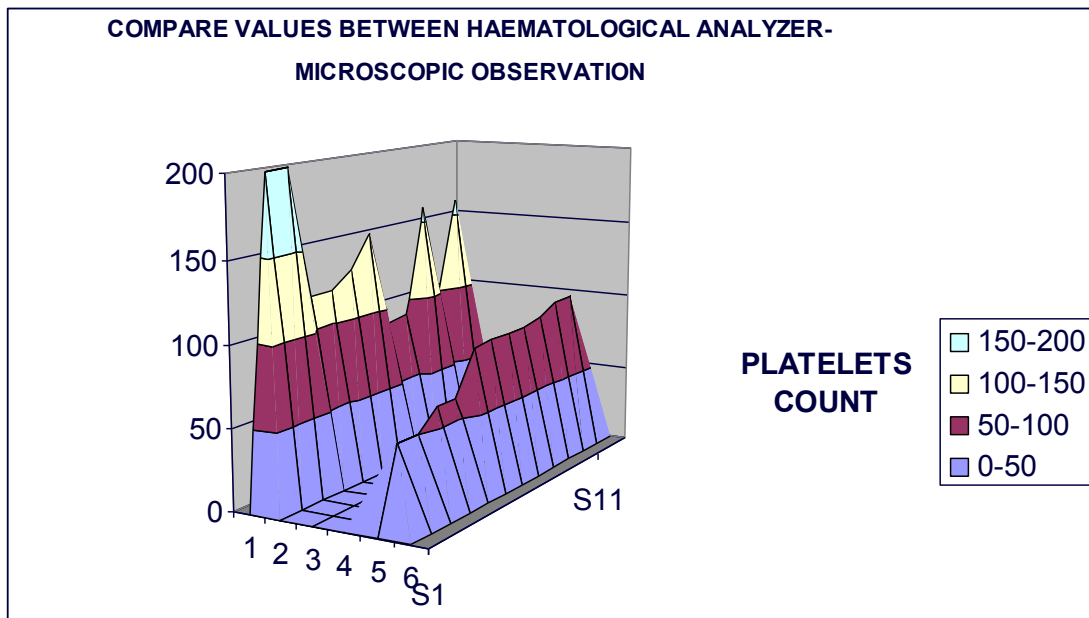
<b>Number of samples</b>	<b>33</b>	<b>Mean of Plateletcrit</b>	<b>Mean hematological analyzer PLT</b>	<b>Mean PLT</b>
<b>Giant PLT:</b>	<b>4</b>	<b>0,16%</b>	<b>146,4K/uL</b>	<b>190,3K/uL</b>
<b>Large PLT:</b>	<b>7</b>			
<b>Clumps PLT:</b>	<b>7</b>			

Dissociation of PLT:	2		
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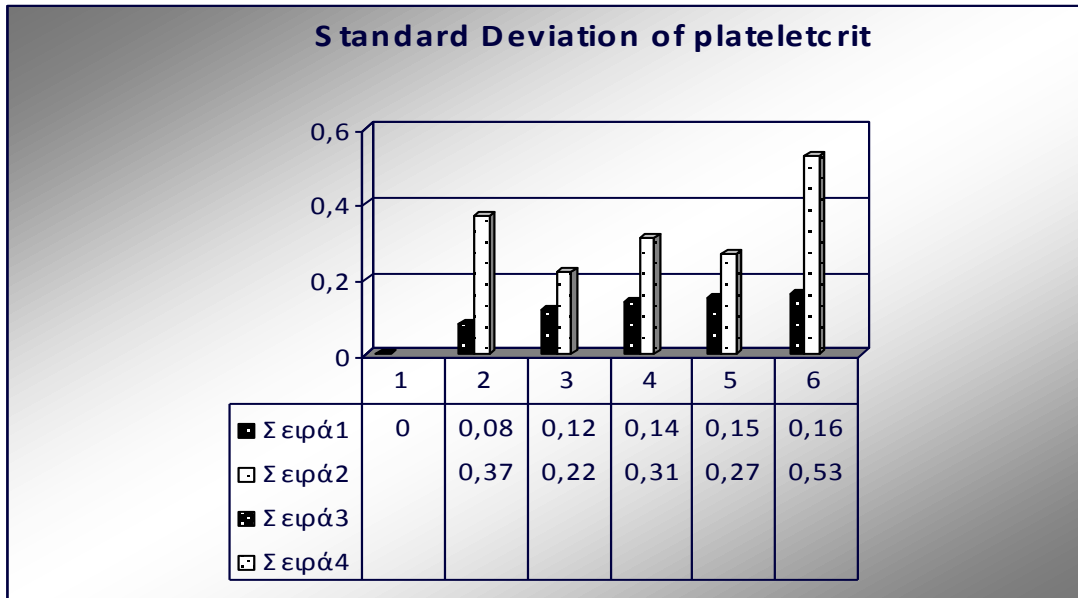
**Table 6:** MICROSCOPIC OBSERVATION OF ALL SAMPLES

Number of samples	Giant PLT	Large PLT	Clumps PLT	Dissociation of PLT:
111	17	21	24	2

**Table 7:** COMPARE VALUES BETWEEN HAEMATOLOGICAL ANALYZER – MICROSCOPIC OBSERVATION



**Table 8:** STANDARD DEVIATION OF PLATELETCRIT



For the above samples, there was no clinical information on bleeding. According to relevant studies at international level, the above platelet counts when accompanied by increased MPV are indicative of satisfactory haemostasis when immune disorders (HIT, antiplatelet antibodies, sepsis, extensive surgical procedures and wounds, as well as diffuse intravascular coagulation in progress). The administration of antiplatelet drugs based on the above values did not indicate a clinical hazard for the patients as evidenced by the therapeutic experience of our hospital, especially in cases of new antiplatelet drugs such as clopidogrel, which makes the above values safer. We do not know the behaviour of these drugs, combined with the research values in paediatric patients, since there are no polycentric studies. Conclusion: From the above, it is concluded that plateletcrit is an independent platelet-counting parameter. As a lower normal platelet count range, 140 K / uL is determined and is not affected by platelet- distribution (clumps platelets-dissociation) and corresponded to 0.15% plateletcrit.

## DERMATOLOGY

### **D1. Application of fruit acids of natural origin as hypopigmentation agents: in vivo investigation [ORAL]**

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Introduction: Fruit acids of natural origin have been used as good and safe hypopigmentation agents in many dermocosmetic products in the treatment of skin changes or for lightening of dark spots appearing on the skin due to oxidative stress and/or photodamage. Therefore, the aim of this study was in vivo investigation of hypopigmentation potential of dermocosmetic cream with standardized oil extract of wild apple fruit (*Mali sylvestris fructus*, (L.) Mill., Rosaceae), containing 2.62% of fruit acids. Methods: Dermocosmetic cream was made with 6% of wild apple fruit oil extract (obtained by digestion and sunflower oil as solvent), as a source of fruit acids and polyphenols, and stabilized by two natural biodegradable mixed emulsifiers. In vivo estimation of hypopigmentation efficiency after 7 days of application of cream, after artificially induced skin hyperpigmentation (induced by dihydroxyacetone), was investigated employing the biophysical methods on the skin of healthy volunteers (by measuring melanin index-MI and erythema index-EI). Results: In vivo investigation revealed good hypopigmentation potential of cream with 2.62% of fruit acids. Application of cream with fruit acids, as active exfoliation agents, after artificial hyperpigmentation induced significant decrease of MI ( $-16.00 \pm 11.40$  after 3 days and  $-27.75 \pm 12.15$  after 7 days). Decrease of EI after 7 days of cream application after artificial skin hyperpigmentation was  $-39.00 \pm 25.88$ . Conclusion: Formulated dermocosmetic cream with fruit acids from wild apple fruit oil extract demonstrated good lightening and anti-irritating effects on human skin after cream application after artificially induced skin hyperpigmentation, beside lower concentration of fruit acids (2.6%), probably due to the synergistic effects with the polyphenols which concentration was 7% in extract. Therefore, cream with fruit acids of natural origin, as active hypopigmentation agents, might be suitable for possible usage as dermocosmetic product for lightening of skin hyperpigmentation.

### **D2. Physical stability of emulsion creams for dermatological application containing methanol extracts of *Morus alba* L. and *Morus nigra* L [ORAL]**

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**Introduction:** Since cosmetic products are applied to the skin of various parts of the body, it is necessary that they are resistant to temperature influence and stable over a longer period of time. The physical stability of cosmetic products for application to the skin must be tested. It was shown in other studies, that formulated O/W emulsions with fruits extracts of *Morus alba* and *Morus nigra* reduce irritation, restore the protective barrier of the skin, and have more positive effects on skin hydration compared with the emulsion base itself. **Methods:** For the purpose of preliminary assessment of physical stability, measurements of the pH and electrical conductivity of the formulated phytopreparations of O/W emulsions 7, 45 and 90 days after preparing, were made using a pH meter (HI 8417, Hanna Instruments, Woonsocket, RI, USA) and conductometer (Hi 98311 Hanna Instruments). Samples were stored for 3 months in primary packaging (plastic baths) at room temperature. **Results:** Results of study are shown in table 1.

Table 1. pH and electrical conductivity values for O/W type emulsions with fruit extracts of *M. alba* and *M. nigra* 7, 45 and 90 after preparation

Sample	pH	Electrical conductivity ( $\mu\text{S}/\text{cm}$ )
MAE	5.48; 5.18; 5.35	128.2; 145.1; 148.9
MNE	5.31; 5.43; 5.38	113.5; 114.1; 115
EB	5.9; 5.94; 5.98	19; 19.2; 19.2

\* MAE (emulsion with *Morus alba* extract); MNE (emulsion with *Morus nigra* extract), EB (base of emulsion)

**Conclusion:** Based on the results of this study, formulated creams for dermatological use on the skin with extracts of fruits of *M. alba* and *M. nigra* are physically stable.

### D3. An overview of skin metastases [FLASH]

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3. Emergency University Hospital of Bucharest, Romania

Cutaneous metastases are an insufficiently studied, taking into account the fact that the skin is not the most frequent area of tumor spread. Almost any type of cancer can disseminate through lymphomatous, hematogen or contigue way and display abnormalities to the skin, usually the internal organs, such as lungs or liver, are the first site where metastases occur. There are a few similarities between their characteristics, skin metastases varying from papulae, to nodules or ulcerations, and from pale skin-coloured lesions to dark red spots. The metastatic tumors have different appearance from nodular lesions, inflammatory, to sclerodermoid, and histologic traits from adenocarcinoma, squamous cell carcinoma to undifferentiated lesions. Although there are uncertainties about the incidence of cutaneous metastasis, a meta-analysis published by Krathen in 2003 has found a percentage of 5.3%. Patients with melanomas, lymphoma or leukaemia were not included in this study; breast cancer (24%) had the highest incidence of secondary

determinations (most frequently to the chest wall), whereas the prostate cancer had the lowest one (of only 0.7%). Certain types of cancer seem to have a predilection for skin areas: the renal cancer for the scalp, adenocarcinoma for lymphedema of the face, breast cancer to carcinoma erysipelatoides. Usually, the primary tumor is followed by the appearance of cutaneous metastases, and rarely skin determinations occur at the same moment or before the original cancer site was diagnosed. The distribution follows sometimes the nearest region to the primary tumor, or has a certain predilection: kidney cancer for the scalp and face, breast cancer for the chest, lung cancer for the back, etc. The treatment consists of treating the primary tumor whenever it is possible, but when metastases had occurred the cancer might need only palliative care, being untreatable.

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#### **D4. The most common dermatological conditions in elderly population [FLASH]**

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Introduction: Aging is an inevitable and continuous process with a variable spectrum of manifestations of all organ systems including the skin. Geriatric dermatoses are a challenging job for the physician in terms of diagnosis, management, and follow-up. Since skin of the elderly population is going through a lot of changes from both an intrinsic and extrinsic point of view, it is imperative for the physician to have a better understanding of the pathophysiology of geriatric skin disorders and their specific management, which differs slightly from an adult population. In aging, a decline in the regular functions of skin is observed and as a result, some inevitable changes, such as roughness, wrinkling, and laxity of the skin, and atypical presentations of dermatologic diseases are observed. The incidence of skin diseases in this age category is increasing worldwide rapidly, mainly due to early or lifelong UV-over exposure. Methods: In our presentation we collected data from the international bibliography. Our purpose was to analyze the pathophysiological aspects of skin disorders in elderly and the description of some common geriatric skin disorders and their management. Results: Overall, the most frequent dermatological problems include eczematous dermatitis, with contact dermatitis, neurodermatitis and seborrheic dermatitis being an issue of great interest. Viral infections, particularly herpes zoster, occur frequently in old age secondary to impaired immune function. Drug eruptions and nutritional disorders are indisputably age-related skin problems and consist an urgent topic for immediate treatment. Both benign and malignant neoplasms have been noticed in the elderly population with increased frequency. Conclusion: Dermatological problems in the elderly population are very common. They are visible and can often add to the psychological stress in the geriatric population. The skin is not only the largest organ of the body but also a strong part of the immune system that protects us from the external environment. It bears the brunt of aging from both the external and internal environments, resulting in pathological processes that can ultimately affect the health and quality of life of older patients. In order to transform this

demographic change into a chance of a better understanding of the pathomechanisms of these diseases, an early diagnosis and therapy are essential steps. In addition, a joint effort to raise public awareness, patient education, preventive measures and consistent monitoring of high-risk groups is of great importance.

#### **D5. Romanian medicinal herbs as a green approach to new anti-ageing product formulations [ORAL]**

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This work was coordinated by Prof. Cerasela Gîrd and Assoc. Prof. Teodora Balaci, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Considering that the dermatocosmetics market is continuously developing and that more and more medicinal plants are being used in anti-ageing products, the aim of this research is to present our results about finding optimal formulations for: cleansing emulsion, serum, cleaning gel, day hydrating cream and night nourishing cream. This might ensure both maintenance and treatment of dehydrated and devitalized skin over a long time. There have been used some of the most relevant vegetal materials coming from Romanian flora with very good deterative (Saponariae radix), emollient (Altheae radix, Calendulae flores), vitaminizing (Hordei immature herba, Myrtillifructus, Vitis viniferae oleum, Vitis vinifera sap) and calming effects (Rosae flores, Lavandulae flores). Qualitative chemical analyses of vegetal materials were focused on identification of saponins, flavonoids, mucilage, volatile oil and oligo elements. The vegetal extracts were obtained through lyophilisation and quantitatively analyzed. Antioxidant action was evaluated by DPPH and ABTS methods. In order to be used in the most convenient, pleasant and efficient way, our multiple active principles extracts were processed in external use-only formulations for topical administration and local effect. We have selected suitable additives and tried several modern procedures in order to obtain high quality dermatocosmetics that might ensure superior skin maintenance and care. Thus, the specific determinations (pH, rheological studies and hydrating properties) confirmed both quality and stability of the products. Following our results, there were obtained anti-ageing pharmaceutical formulations using vegetal materials from Romanian medicinal herbs which were tested and proven to be efficient in care or treatment of multiple skin conditions.

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## **D6. The new approach to the treatment of solar lentigo [FLASH]**

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2. *Clinical Emergency Hospital of Bucharest, Bucharest, Romania*

**Introduction:** Solar lentigo (SL), also known as a sun-induced freckle or senile lentigo, is a hyperpigmentation that occurs increasingly with age in sun-exposed areas, such as the face, forearms, back, and the dorsal sides of hands. Solar lentigo is characterized by macular lesions exhibiting epidermal hyperplasia combined with hyperpigmentation. The underlying mechanisms responsible for the occurrence and maintenance of these spots are not yet completely defined. **Case presentation:** A female patient, aged 35 years, has suffered from pigmentation on the face and the neckline. After examination and history, the diagnosis was solar lentigo. Due to asymmetrical shape, irregular borders, color variation, and a diameter greater than 5 mm, differential diagnosis was made with melanoma using dermatoscopy. For the treatment, the following combinations were applied to the dermis: ion+, massage and led blue light followed by ion-, ultrasound, massage, led red light, then ion-, massage, led green light. As the base, the serum stabilized with 25% vitamin C was used. The results were visible after 2 weeks of treatment with 3 sessions per week. Each session lasted 15 minutes. **Conclusions:** In just 2 weeks of treatment, depigmentation of the affected areas was visible. Repigmentation of the same areas may occur over time, especially if sunscreen protection is not used.

## **D7. Cutaneous metastases in gynecologic malignancies [FLASH]**

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3. *Ponderas Academic Hospital, Bucharest, Romania*

**Introduction:** cutaneous metastases have been rarely reported in gynecologic malignancies, being most often a sign of disseminated recurrence. In rare cases these lesions present as oligometastatic disease and can be suitable for surgery. **Methods:** we present a case series of three patients with cutaneous metastases from gynecologic malignancies. **Results:** the first case was the one of a 54 year old patient who was diagnosed with a hemorrhagic ulcerated lesion on the right arm; the biopsy raised the suspicion of a metastatic lesion while the computed tomography demonstrated the presence of multiple liver metastasis as well as a breast tumor. due to the presence of local hemorrhage and necrosis, the cutaneous metastasis was resected with palliative intent. The second case was the one of a 66 year old patient diagnosed with previous history of surgically treated endometrial cancer and who was diagnosed with an oligometastatic lesion in the anterior abdominal wall invading the skin. The lesion was resected with curative intent while the histopathological studies confirmed the metastatic character of the lesion. The third patient was known with previous history of surgically treated cervical cancer and was diagnosed with a large subcutaneous metastasis invading the skin. In the meantime a large pelvic

unresectable recurrence was seen at magnetic resonance, so the patient was proposed for palliative oncologic treatment. Conclusions: cutaneous metastases from gynecological cancer are rarely found as oligometastatic disease, being in this way suitable for surgery with curative intent.

#### **D8. Quality of life and psychosocial consequences in patients with psoriasis [FLASH]**

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2. *Clinical Emergency Hospital of Bucharest, Romania*

Introduction: Psoriasis is well known as having a negative impact on the quality of life. Patients with psoriasis, progressively, depending on severity, experience problems in adapting to the workplace, lowering self-esteem, problems in human interaction, difficulty in having sex, etc. When patients suffer from rejection associated with psoriasis, they may feel stigmatized and it may have additional adverse effects on their emotional and occupational life. These patients require special attention because in some cases the problems can lead to suicide. Method. This study included 208 patients diagnosed with vulgar psoriasis over the age of 18 years. The patients responded to a specially designed questionnaire to determine the impact of psoriasis on their lives. Among other things, the number of years of illness, its evolution and the therapy followed were included in the study questionnaire. Results. The results of the study show that all participants in the study had a degree of psychosocial impairment, this degree increases proportionally to the severity of psoriasis. Quality of life and self-esteem are also affected by this condition. Conclusions. An early approach is needed both from the point of view of treatment and from the point of view of the psychological approach. The psychological approach is needed at the onset but also in the case of exacerbations. In some cases of severe psoriasis, psychiatric intervention may be necessary.

## GYNECOLOGY

### **G1. Can transvaginal ultrasound scan be used as a screening method for endometrial cancer in postmenopausal women? [FLASH]**

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- 2. Medical and Surgical Specialities Dept., Faculty of Medicine, Transilvania University of Brasov, Romania*

**Objective:** to assess the efficiency, feasibility and cost benefits of the TV ultrasound scan in post menopausal asymptomatic women in order to detect endometrial anomalies. **Material and Method:** We routinely scanned 239 women in a period of 1 year women were seeking medical advice in two centers for different complaints other than metrorrhagia. Main complaints were associated with menopause. Standard sections were obtained, endometrial thickness cut off was set at 4 mm, overall uterine wall aspect, vascularization, pathological mass, Douglas pouch aspect were noted. A chart was completed for each woman and in case of anomalies the result was discussed, follow up organized. We divided the patients in two groups: one with borderline endometrial thickness (5-8) and the other one with frankly abnormal endometrial thickness (over 9 mm). Patients with borderline anomalies were scheduled for follow up at 3 months, PAP smear and uterine ultrasound scan. Patients in the second group underwent D&C. **Results:** 36 women had abnormal endometrial thickness, some had endometrial polyps, other insignificant findings as myomas, uterine cavity fluid with thin endometrial cysts of the cervix and one had even an abnormal cervical circulation. We performed 7 DC with 3 endometrial hyperplasia with atypia, 1 uterine ADK and 1 uterine polyp and 2 hyperplasia without atypia. Patients with pathology underwent surgery. 12 patients had borderline abnormal endometrium and only 2 needed D&C after the second examination. **Conclusion:** The examination is cheap, noninvasive, and acceptable and proved to be efficient in detection of endometrial abnormalities and can be offered as a screening method for endometrial cancer.

### **G2. Postmenopausal vulvovaginal atrophy - a systematic review of a public health problem solved with CO2 Laser therapy [ORAL]**

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**Introduction:** Vulvovaginal atrophy is a condition which affects 40-57% of postmenopausal women and it is associated with a decreased level of estrogen in the vaginal tissue. The aim of this study is to illustrate the efficiency of CO2 Laser therapy in treating vulvovaginal atrophy. **Method:** After a systematic review, ten articles were considered from the databases for this study. We used the key words vaginal atrophy, postmenopausal sexual function, CO2 Laser and genitourinary syndrome and selected the studies including postmenopausal women with vaginal atrophy that was treated with laser therapy. Breast cancer survivors with vulvovaginal atrophy were excluded. **Results:** The women included in the studies aged between 51.6 and 66.8 years old. The symptoms included vaginal dryness, vaginal burning, itching, dyspareunia and intercourse bleeding, dysuria and urge incontinence. Objective questionnaires and analogue scales were used (VHI, VAS, QoL, and FSFI). The laser settings have been the same: 30 Watts, 1000 microseconds and 1000µm spacing. The women received 3 laser applications at monthly interval. The results are encouraging for this therapy: all the patients recorded improvements of the symptomatology (84% satisfaction), QoL improved in 91.7 % of cases, 85 % regained the sexual function, 85.71 % of the cases had alleviation of dyspareunia, normal flora of the vagina-Lactobacillus increased from 30% to 79%, vaginal pH decreased from a mean of 5.9 +/- 0.8 to 4.7+/- 0.5 and VHI, VAS for vulvovaginal atrophy and FSFI recorded major improvements. Only one study obtained significant worsening of sexual-related pain (P = 0.04). **Conclusion:** CO2 Laser is a useful tool in treatment of postmenopausal vulvovaginal atrophy but further researches should be conducted to assess the short-term and long-term effects of the laser procedure.

### **G3. Uterus didelphys at the limit between fertility and infertility: a case report [FLASH]**

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Uterine malformations such as double, didelphys, unicornuate or septate uterus, associated or not with abnormalities of the vagina (double, atrophic or septal vagina), can appear during the embryogenesis of the female genital organs from the Müllerian ducts, due to incomplete (total or partial) fusion, poor development or partial ducts resorption. Uterus didelphys is a variety of third class MDAs, consisting of a complete duplication of the uterine body and cervical canals, with no communication between them. Encountered up to 20% of the total MDAs, uterus didelphys is a common cause of infertility, in most cases one or both hemi-uteri being rudimentary. The existence of the uterus didelphys favors ischemic cervical incontinence, spontaneous abortion, pre-term labor, fetal malposition, abnormal presentation, fetal intrauterine growth retardation or placental insertion pathology. The diagnosis consists of transabdominal and transvaginal ultrasound. In case of pregnancy, delivery is most frequently premature and performed through C-section. In the present paper, the case of a young woman diagnosed with uterus didelphys, whose reproductive function was not affected, but rather preserved on each of the hemi-uteri, will be presented. With four previous deliveries, one C-section on the left hemi-uterus and three spontaneous births, the patient is a particular and rarely encountered case in the

specialty literature. The preservation of the reproductive function is explained due to the two hemi-uteri being approximately of equal sizes, close to the size of a normal uterus, the proper function of the adjacent annex (tuber, ovary) and the preserved cervical continence on both sides.

#### **G4. Laparoscopy and in vitro fertilization for sterility caused by endometriosis [FLASH]**

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**Introduction:** Endometriosis is a recognized cause of infertility and laparoscopy is the gold standard in diagnosis and treatment of this condition. Although surgery is aimed at removing lesions, relieving symptoms, and restoring or preserving fertility, it does not succeed as a reproductive method. Therefore an important contingent of these patients will use assisted reproduction. **Methods:** This presentation is an in-depth review and up-to-date study based on literature scientific papers and multicentric studies concerning the role of laparoscopy as treatment for endometriosis followed up by in vitro fertilization (IVF) as a standard sequence in endometriosis caused sterility. **Results:** Causes of infertility are complicated in endometriosis, being both fallopian and ovarian involvement. Since ovarian endometriomas are destructive lesions for the ovarian reserve, there is controversy over the best way to solve this pathology. Studies show, however, that excision surgery has better outcomes in terms of improved fertility versus ablation and drainage after which recurrence can occur. Studies have shown a reduction of ovarian reserve after surgical treatment of endometriomas. It is unclear whether this reduction is due to surgical ablation or affection itself. Controversy also exists with regard to the benefits of postoperative medical treatment gonadotrophin analogues prior to IVF, the general agreement being that a 3-month limited treatment could be beneficial. Another highlighted aspect of the correlation between IVF and endometriosis is the possibility that ovarian stimulation has a “flare up” effect on endometriosis. Several studies have shown that there is no evidence to support worsening or recurrence of endometriosis after IVF. **Conclusion:** The cure for infertility in which endometriosis is incriminated would benefit from using both laparoscopic procedure and then IVF.

#### **G5. Detection of cytomegalovirus DNA in women with pregnancy loss [FLASH]**

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**Introduction:** The cytomegalovirus (CMV) infection during pregnancy is a frequent and serious threat to the fetuses of pregnant women. In primary infection which become for the first time during pregnancy, the chance of passing the virus to fetus is much higher. Among women which are previously infected there's about a 30 to 50 percent chance that the baby will become infected in the womb. The rate of susceptibility to CMV is between 50% and 80% according different studies. The objective of this study was to determine frequency the detection of CMV DNA in abortive samples in women with pregnancy loss. **Methods:** Cross sectional study was designed to examine in women with pregnancy loss. For six months, an abortive sample of 40 women hospitalized in Clinic of obstetrics and gynecology, University hospital-Pleven, Bulgaria were examined. By DNA-sorb-AM-AmpliSens DNA extraction was performed. The detection of cytomegalovirus DNA was performed by AmpliSens CMV – Eph PCR kit. From the participants a demographic, data was collected by a questionnaire. The study protocol was approved by ethics committee of the university. **Results:** CMV DNA was detected in 16/40 (40%) of the women. In women up to 20 years of age (n=12), two positive samples were found. In women aged between 21 and 30 years of age, (n=12), six positive samples were found. The highest number of positive samples – 8 was found in women over 30 years of age (n=16). In the surveyed group, 18 (45%) were from minority groups, 32 (80%) were pregnant, low social status was found in about 80% of women. **Conclusion:** Our results indicate that a high frequency of CMV DNA in abortive samples from women who lost their pregnancy. Routine serologic screening for CMV of pregnant women will be advance in understanding of CMV infection among pregnant women and its prevention.

## **G6. Cervical viral infections among asymptomatic Bulgarian women [FLASH]**

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**Aim:** Although sexually transmitted viral infections are significant and increasing public health concern, little is known about their prevalence among Bulgarian women. The aim of this study was to investigate cervical viral infections in asymptomatic women **Methods:** The study group included 52 randomly selected asymptomatic female volunteers from Bulgarian border town Kardzhali. Cervical specimens were tested by real-time PCR for human papillomaviruses (HPV), herpes simplex virus (HSV) types 1 and 2, cytomegalovirus (CMV), Epstein-Barr virus (EBV), and human immunodeficiency virus (HIV). **Results:** The investigation demonstrated a high rate (61.5%) of infection with one or more viruses of uterine cervix of participating women considered at low risk. The most prevalent was HPV, found in 32.7% of all women. The genotyping of high-risk (HR) HPV positive specimens showed that HPV16 was the most prevalent HR type. HSV prevalence (30.8%) was almost as high as that of HPV and most women were HSV1 infected. 9.6% and 5.8% of all specimens were positive for EBV and CMV, respectively. **Conclusions:** Our results indicate that women from Kardzhali region, involved in this study, might be at risk for development of genital tract pathology, including cervical cancer, and for transmission of virus infection sexually and perinatally.

### **G7. Digestive tract resections as part of debulking surgery for advanced stage endometrial cancer [FLASH]**

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Introduction: endometrial cancer remains one of the most common gynecologic malignancies reported worldwide, with good chances of cure especially diagnosed in early stages. However, certain cases are diagnosed in advanced stages of disease, when disseminated lesions are already present. In these cases it seems that the best therapeutic approach remains debulking surgery of all visible lesions; therefore, multiple visceral resections might be needed. Methods: we present a case series of 7 patients diagnosed with advanced stage endometrial cancer in which digestive resections were needed in order to maximize the debulking effort. Results: the most commonly performed resection was rectosigmoidectomy (in four cases), followed by total colectomy in two cases and right ileocectomy in one case. In all cases other visceral resections consisted of total hysterectomy, bilateral adnexectomy and omentectomy as well as pelvic and para-aortic lymph node dissection. In cases in which total colectomy was performed terminal ileostomy was also associated while in cases in which less extensive resections were needed, the continuity of the digestive tract was re-established via intracorporeal anastomosis. In all cases debulking to no residual disease was achieved. Postoperatively a single patient developed a colorectal leak and necessitated reoperation. Conclusions: digestive tract resections can be safely associated as part of debulking surgery for advanced stage endometrial cancer in order to maximize the debulking effort.

### **G8. Urinary tract resections as part of debulking surgery for advanced stage endometrial cancer [FLASH]**

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Introduction: patients diagnosed with advanced stage endometrial cancer will associate in a significant number of cases extended pelvic lesions necessitating performing extended pelvic resections in order to maximize the debulking effort. The most commonly involved viscera include the rectosigmoidian loop and the urinary tract Methods: we present a case series of three patients diagnosed with advanced stage endometrial cancer in which urinary tract resections were

needed in order to maximize the debulking effort Results: in two cases partial cystectomy was needed while in the third cases a total cystectomy was performed. Cases in which partial cystectomy was performed were therefore submitted to cystoraphy alone or cystoraphy with ureteral reimplantation while in the case in which a total cystectomy was needed the two ureters were exteriorized in terminal ureterostomy. Other visceral resections included rectosigmoidectomy in two cases and total colectomy in one case. In all cases maximal cytoreductive surgery was achieved. Conclusions: urinary tract resections can be safely performed as part of debulking surgery for advanced stage endometrial cancer

### **G9. Patterns of lymphatic spread in ovarian cancer [FLASH]**

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Introduction: ovarian cancer remains one of the most frequently encountered gynecologic malignancies, being diagnosed in an important number of cases in advanced stages of the disease. In this situation the only therapeutic option remains maximal cytoreductive surgery. The most commonly seen patterns of spread are represented by the peritoneal, lymphatic and hematogenous route. However, although most cases are diagnosed with pelvic and para-aortic lymph node metastases, in certain cases inguinal lymph node metastases might be seen from the beginning. Methods: we present a series of 21 patients submitted to lymph node dissection for advanced stage ovarian cancer. Results: among these cases 19 patients presented pelvic lymph node metastases, three of the 19 patients with pelvic lymph node metastases associated para-aortic lymph node metastases and other two cases were diagnosed with inguinal lymph node metastases; among these two cases, a single patient associated both pelvic and inguinal lymph node metastases. Conclusions: lymphatic spread is frequently encountered in advanced stage ovarian cancer, the most frequently affected lymph node groups being represented by the pelvic and para-aortic stations. However, in certain cases inguinal lymph node metastases might be seen even in the absence of pelvic lymph node metastases.

### **G10. Compartment based surgery in endometrial cancer [FLASH]**

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**Introduction:** the technique of compartment based radical hysterectomy, implemented by Hockel in early stages of endometrial cancer, has been recently implemented in patients with endometrial cancer too. The technique consists of en bloc resection of the mesometrium in association with pelvic and para-aortic lymph node dissection in order to achieve a good local control of the disease. **Method:** we present a case series of five patients in which the principles of compartment based radical surgery were successfully applied. **Results:** the mean age of patients introduced in the current study was 57 years (range 48- 64 years), all cases being diagnosed with FIGO stage I or II endometrial cancer. The mean operating time was 110 minutes (range 90-150 minutes) while the mean blood loss was 250 ml (range 100-400ml). Histopathological studies revealed the presence of intermediate or high risk lesions in four cases while in the fifth cases the tumor was considered as a low risk one. Postoperatively one patient developed a venous thrombosis and necessitated administration of chronic anticoagulant treatment. **Conclusions:** compartment based surgery is feasible in patients with endometrial cancer, providing in this way a safe therapeutic option especially in cases with high risk lesions.

### **G11. Debulking surgery for relapsed uterine sarcomas [FLASH]**

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**Introduction:** uterine sarcomas remain one of the most aggressive gynecologic malignancies being associated with a high capacity of relapse. Whenever relapse is diagnosed, it seems that the best therapeutic approach in order to control the disease remains debulking surgery. **Methods:** we present a case series of eight patients diagnosed with relapsed uterine sarcomas which were successfully submitted to debulking surgery. **Results:** visceral sacrifice in order to achieve a good control of the disease was needed in all but one case. The main associated visceral resections included rectosigmoidian resection, partial cystectomy and segmental enterectomy. The median operation time was 180 minutes (range 100-210 minutes) while the median blood loss was 500 ml (range 200-750ml). Postoperatively one patient developed an anastomotic fistula which needed reoperation. The histopathological studies revealed the presence of uterine carcinosarcomas in four cases and endometrial stromal sarcomas in two cases. after a median follow up of 12 months one patient has been diagnosed with disseminated lesions and is submitted to palliative chemotherapy **Conclusions:** debulking surgery is safe and effective in treating relapsed uterine sarcomas.

### **G12. Douglas peritonectomy versus rectosigmoidian resection in advanced stage or relapsed ovarian cancer [FLASH]**

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Introduction: the peritoneal route remains one of the most commonly incriminated pathways of spread in ovarian cancer. However, depending on the depth of invasion of the peritoneal nodules of carcinomatosis, these lesions can be resected by stripping peritonectomy or by performing a segmental colorectal resection. Methods: we present a series of 17 patients diagnosed with advanced stage or relapsed ovarian cancer with peritoneal carcinomatosis of the Douglas pouch who were submitted to surgery with curative intent. Results: Douglas peritonectomy was feasible in two patients (one case diagnosed with stage IIIC ovarian cancer and one case with relapsed ovarian cancer) while in the other 15 cases colonic resections were needed. Among these cases rectosigmoidian resection was performed in 13 cases, rectosigmoidian resection in association with right colectomy was imposed in one cases while in another cases total rectocolectomy was needed. Postoperatively one patient developed an anastomotic leak and necessitated reoperation. None of the cases in which Douglas peritonectomy was performed experienced postoperative complications. Conclusions: Douglas peritonectomy can be safely associated as part of debulking surgery in selected cases. However, in patients presenting penetrating lesions, segmental colonic resections should be performed in order to minimize the risk of postoperative complications.

### **G13. Inguinal lymph node metastases in relapsed endometrial cancer – a case report [FLASH]**

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Introduction: the most common pathways of lymphatic spread in endometrial cancer is via the pelvic and para-aortic lymph nodes. However, in rare cases metastases in the inguinal lymph nodes might occur. Methods: we present the case of a 65 year old patient with previous history of surgically treated endometrial cancer who presented for the apparition of a groin mass 18 months after surgery. Results: at the time of the initial surgery the patient was submitted to total hysterectomy with bilateral adnexectomy, pelvic and para-aortic lymph node dissection. The histopathological studies demonstrated the presence of a poorly differentiated endometroid endometrial cancer with lymph node metastases in three of the 18 resected pelvic lymph nodes; in the meantime none of the resected para-aortic lymph nodes presented any sign of tumoral invasion. Postoperatively the patient was submitted to six cycles of adjuvant chemotherapy; 18 months after surgery she presented for the apparition of a large inguinal mass at the level of the left groin. The biopsy confirmed the metastatic character of the adenopathic inguinal mass while the computed tomography excluded the presence of any other local or distant recurrent lesions. The patient was resubmitted to surgery, a left inguinal lymph node dissection being performed. Six months later the patient is free of any recurrent disease. Conclusions: although it represents a

very scarce eventuality, inguinal lymph node metastases might occur in patients with previous history of endometrial cancer.

#### **G14. Total vulvectomy with bilateral groin lymph node dissection for vulvar [FLASH]**

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Introduction: vulvar sarcomas represent extremely rare gynecologic malignancies, which might be misdiagnosed for a long period of time and treated as Bartholin's cysts or abscesses. However, once the right diagnostic is established, surgery remains the only potential curative therapeutic option. Methods: we present the case of a 54 year old patient who presented for vulvar pruritus associated with the apparition of a tumoral mass on the left hemivulva. At the time of presentation the lesion measured 4/6 cm, the biopsy demonstrating the presence of a vulvar sarcoma. Results: the patient was initially submitted to surgery, a radical vulvectomy with bilateral groin lymph node dissection being performed. The postoperative course was uneventful, the patient being discharged in the sixth postoperative day. The histopathological studies confirmed the sarcomatous origin of the tumor, the final diagnostic being the one of a carcinosarcoma. Three of the resected lymph nodes presented metastases, this fact being explained by the association of a carcinomatous component to the sarcomatous one. Conclusions: although are rare eventualities, vulvar sarcomas should be suspected in patients presenting chronic vulvar lesions associated with pruritus. Once the diagnostic of sarcoma is established, wide resection is recommended in order to control this biological aggressive disease.

#### **G15. Laterally extended endopelvic resection for locally advanced vaginal cancer – a case report [FLASH]**

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Introduction: compartment theory of locoregional spread of gynecologic malignancies proved to be valid not only in patients with cervical cancer but also in patients with vaginal cancer. Therefore, it has been successfully implemented in patients with tumoral recurrences or persistent disease after irradiation for vaginal cancer. Methods: we present the case of a 63 year old patient, with previous history of vaginal cancer; at that moment she was submitted to radiation therapy. However, when ending the radiation therapy she was diagnosed with persistent disease, so she was submitted to surgery. Results: the patient was submitted to a laterally extended endopelvic resection in association with pelvic and para-aortic lymph node dissection.

The postoperative course was uneventful, at two years follow up the patient being free of recurrent disease. Conclusions: laterally extended endopelvic resections offer a good control of the disease in patients with previous history of persistent to radiotherapy vaginal cancer.

### **G16. Pelvic exenteration for locally advanced vulvar cancer [FLASH]**

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Introduction: the overall incidence of vulvar cancer has increased in the last decades while the age at diagnostic reported a decreasing trend, this malignancy being more often diagnosed in patients less than 60 years of age. Therefore, attention has been focused in obtaining a good local control of the disease by performing resection with curative intent. Methods: we present a case series of seven patients diagnosed with advanced stage vulvar cancer in which pelvic exenteration was needed due to the local extent of the disease. Results: in all cases pelvic exenteration was associated with pelvic, para-aortic and lymph node dissection. in regard of the extent of the pelvic exenteration, anterior pelvic exenteration was performed in four cases, posterior pelvic exenteration was performed in two cases and total pelvic exenteration was needed in one case. Postoperatively the patient submitted to total pelvic exenteration experienced a wound dehiscence in the right inguinal area which necessitated a prolonged time (of one month) in order to heal. In all but one case an R0 resection was achieved. Conclusions: in certain cases diagnosed with advanced stage vulvar cancer pelvic exenteration might be needed in order to control the disease.

### **G17. Anterior pelvic exenteration as salvage therapy for locally advanced cervical cancer with vesico-vaginal fistula: a case series of two patients [FLASH]**

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Introduction: although screening tests have been widely implemented, a significant number of women are still diagnosed with advanced stage cervical cancer, when the tumoral process has destroyed the compartmental borders and has invaded the surrounding viscera. In such cases neoadjuvant treatment should be taken in consideration in order to provide tumoral regression. Unfortunately some patients develop serious complications such as fistulas so radiotherapy has to be stopped. Methods: we present a case series of two patients diagnosed with locally advanced cervical cancer with urinary bladder invasion submitted to neoadjuvant radiation therapy and

who developed an extensive necrosis followed by the apparition of vesico-vaginal fistulas. Results: in both cases radiation therapy was immediately ended and the patients were submitted to surgery, anterior pelvic exenteration with pelvic and para-aortic lymph node dissection being performed. The postoperative course was uneventful in both cases. Conclusions: although radiation therapy is the standard of care in patients diagnosed with locally advanced cervical cancer, certain cases might develop serious complications (such as tumoral fistulas with the surrounding viscera), therefore imposing performing per primam surgical treatment.

### **G18. The significance of PTEN expression in endometrial carcinomas [FLASH]**

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Introduction: Uterine cancer in most developed countries is the second most common cause of mortality from gynecological cancer after ovarian cancer. It is clear today that cytomorphology alone is not often sufficient to provide an accurate diagnosis, but additional techniques such as immunocytochemistry are required to solve differential diagnostic problems. Our aim was the value of PTEN expression in endometrial carcinomas since the PTEN gene belongs to the category of tumor suppressor genes that regulate the cell growth and proliferation and are consequently involved in apoptotic cell processes (promote apoptosis). Methods: Endometrial samples freshly resected from 126 women who underwent total abdominal hysterectomy were studied. The mean age of the patients was 68.3 years with a range from 37 to 82 years. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues and stained with Papanicolaou stain and PTEN antibody (clone 6H2.1, dilution 1:80, DAKO). Results: Out of 126 (100.0%) cases, 102 were endometrioid (81.0%) and 24 nonendometrioid carcinomas (19.0%). High expression of PTEN was more frequent in type I (41.1%) comparatively to type II (25.0%) adenocarcinomas ( $p=0.840$ ). In addition, high expression of PTEN was found to be related to less advanced and aggressive clinical stage of disease (stage I: positivity 51.9%, stage II: 38.5%, stage III: 10.5% and stage IV: 6.7%) ( $p=0.350$ ) as well as in low grade (grade 1: 61.9%, grade 2: 35.1%) comparatively to high grade (grade 3: 29.7%) ( $p=0.02$ ) carcinomas. Conclusion: Immunocytochemical findings from PTEN stain, in addition to cytomorphologic features, appeared to be useful for the diagnosis of endometrial carcinoma in endometrial cytology with imprint smears and may help to organize the appropriate therapeutic strategy for the survival of these patients.

### **G19. The contribution of BCL-2 oncogene in endometrial carcinomas [FLASH]**

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**Introduction:** Endometrial carcinoma is the most common malignant tumor of the female genital tract and the fourth most common female cancer in the developed countries followed by breast, colon and lung cancer. It is clear today that cytomorphology alone is not often sufficient to provide an accurate diagnosis, but additional techniques such as immunocytochemistry are required to solve differential diagnostic problems. Our aim was the value of Bcl-2 expression in endometrial carcinomas since this oncogene has predominant role in regulating the inhibition of cellular apoptosis and prolonging cell survival, thereby inducing the concentration of genetic mutations. **Methods:** Endometrial samples freshly resected from 126 women who underwent total abdominal hysterectomy were studied. The mean age of the patients was 68.3 years with a range from 37 to 82 years. The cytological diagnosis was confirmed by pathologists. Cytological imprint smears were obtained by touching the cut surface of fresh cancer tissues and stained with Papanicolaou stain and Bcl-2 antibody (clone 124, dilution 1:50, DAKO). **Results:** Out of 126 cases, 102 were endometrioid (81.0%) and 24 nonendometrioid carcinomas (19.0%). Positivity of Bcl-2 stain was observed only in type I (21.5%) comparatively to type II (0.0%) adenocarcinomas ( $p=0.100$ ). In addition, positive expression of Bcl-2 was found to be related to less advanced and aggressive clinical stage of disease (stage I: positivity 22.8%, stage II: 30.8%, stage III: 0.0% and stage IV: 0.0%) ( $p=0.410$ ), and high expression of Bcl-2 stain was observed only in low (42.8% grade I and 7.1% grade II) ( $p=0.00$ ) than in high grade carcinomas (0.0%). **Conclusion:** Our study showed that in cytological specimens the expression of Bcl-2 in quantitative level alone cannot contribute substantially to the diagnosis and differential diagnosis of endometrial carcinomas. However, it was observed that expression of Bcl-2 is associated with a more favorable differentiation of tumor cells.

## **G20. The congenital uterine anomalies and their clinical significance [FLASH]**

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The real role of the uterus as an organ is to achieve the creation of an environment that will accommodate the development of an embryo, the creation of a new life for the successful continuation of the species and evolution. Therefore, congenital uterine anomalies have a distinct position in the appearance and repercussion of congenital abnormalities of the female genital tract. They constitute the result of abnormal development of the Müllerian ducts during the fetal life and they are usually perceived immediately after a woman enters reproductive age, causing gynecological and obstetrical disorders, like primary amenorrhea, chronic pelvic pain, dysmenorrhea, repeated abortions, bleeding during pregnancy, high risk of preterm labor and abnormal fetal positions. The frequency of their appearance is estimated to be 3-4% of women in the general population, 4% in infertile women and 15% in women with repeated miscarriages. Treatment of congenital uterine abnormalities, where feasible, is generally surgical and aims at restoring, as far as possible, a normal intrauterine cavity and improving reproductive capacity.

Thus, various surgical techniques have been developed from time to time, more or less successful, but in most cases the restoration is mostly personalized.

## **G21. Urinary tract infections in pregnancy – etiology and treatment options [FLASH]**

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**Introduction:** Pregnancy causes numerous changes in the woman's body that increase the likelihood of urinary tract infections (UTIs). Urine culture is the standard method for evaluating for UTI during pregnancy. Antibiotic selection should be based on urine culture sensitivities. Often, therapy must be initiated on an empirical basis, before culture results are available. This requires clinical knowledge of the most common organisms and their region-specific sensitivities to medications. The aim of this study was to evaluate the prevalence and the antimicrobial resistance profiles of bacteria responsible for UTIs among Bulgarian pregnant women, in order to establish appropriate empirical treatment. **Methods:** One hundred pregnant women with confirmed UTI were included in the study. The presence of bacteria in their urine specimens was detected using a technology based on light scattering (HB&L, Alifax, Italy). Each positive sample was cultured on CHRO Magar Orientation Medium and Columbia Blood Agar. Further identifications were performed by phenotypic methods. Susceptibility testing for ampicillin, ampicillin-sulbactam, amoxicillin-clavulanic acid, cefuroxime, cefixime, fosfomycin, gentamicin, amikacin, nalidixic acid, trimethoprim-sulfamethoxazole, ciprofloxacin and levofloxacin was conducted, using the disc diffusion method. **Results:** *Escherichia coli* was the most common cause of UTI, accounting for approximately 60% of cases. Other pathogens include the following: *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Streptococcus beta-haemolyticus*, *Staphylococcus spp.*, and *Myroides spp.* Considering all detected bacterial species, the most active antimicrobial agents against infectious bacteria were fluoroquinolones, amoxicillin-clavulanic acid and amikacin. Almost all isolates of *E. coli* and *E. faecalis* were susceptible to fosfomycin. **Conclusions:** The etiological spectrum of UTIs among Bulgarian pregnant women corresponds with that reported in the literature. Fosfomycin exhibits excellent activity against the most frequent species *E. coli* and *E. faecalis*. Amoxicillin-clavulanic acid should be considered as another treatment option. Data on susceptibility patterns of local uropathogens are important to support empirical therapy.

## **SURGERY - TRAUMATOLOGY**

### **ST1. The glabellar flap for naso-canthal angle defects correction, in three evolutive stages of its design, in our clinical practice [ORAL]**

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Although the classic glabellar flap remained one of the most efficacious surgical alternatives in the correction of the tissue defects in the nasocanthal angle, again our attention was focused on three esthetic postoperative problems, which were: a. The evident skin folds in the flap base caused from a great axis of rotation ( $\alpha \geq 150^{\circ}$ ). b. The evident decreasing of inter-supraciliary distance from the tissue complex transposition. c. The esthetic problems in the nasocanthal angle from the thickness of the corrective flap. For the resolving of these issues, we present here, a three stage modification of the glabellar flap: Stage I: A bilobed design of this flap is used to decrease the axis of rotation and to minify the tissue bulk in frontonasal angle. Although, the reduction of the rotation axis in  $\alpha \leq 120^{\circ}$  decreased the skin folder in the flap base, it was remained in the postoperative view: a. The diminution of the distance between two eyebrows, and the b. the tissue thickness in the nasocanthal angle. Stage II: The evolution of the glabellar flap design from bilobed in the threelobed flap was done to protect the distance between two eyebrows. This type of flap had the same angle of rotation with the bilobed flap ( $\alpha \leq 120^{\circ}$ ) with its postoperative esthetic problems in the skin of frontonasal angle, but with its third lob, it kept the normal distance between the eyebrows. It was remained problematic the tissues thickness of the corrective tissue complex in the cantho-nasal angle. Stage III: To minimize the tissue thickness in the naso-canthal angle, we displaced the corrective lob of the three-lobed glabellar flap, from its primary position over the eyebrow in a new position under the eyebrow. (It's understood, this is done when the defect lets the opportunity of this lob rising under from the skin under the eyebrow.) Esthetically, the corrective tissue comes from the skin orbicular area and has the same tissues characteristics with the recipient defect. On the other hand, the displacement of the corrective lobe under the eyebrow reduces the rotation axis in  $90^{\circ}$ , decreasing in maximum the skin folder of rotation. As conclusion, it may be said, that this flap remains an efficacious surgical alternative in the correction of the tissue defects in the nasocanthal angle, when the defect after the neoplasia excision allows the sub-supraciliary position of the corrective lobe of the three-lobed glabellar flap.



## **ST2. History of damage control management in the politrauma patient [ORAL]**

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Damage control is a new term first used by the United States Navy during World War II to describe emergency measures for control of flooding that threatens to sink a ship. Central goal is to ensure survival of the ship until it reaches a port where definitive repairs can be safely performed. The term “Damage control” was introduced by Rotondo and Schwab in 1992 and outlined a three phased approach: a) Part one (DC-I) consists of immediate exploratory laparotomy with control of bleeding and contamination, abdominal packing and abbreviated wound closure; b) Part two (DC-II) consists of the ICU resuscitation; immediate endpoints include physiological and biochemical stabilization. A tertiary exam should be performed at this time to identify all injuries; c) Part three (DC-III) consists of re-exploration and definitive repair of all injuries. Coagulopathy observed in trauma patients was thought to be a resuscitation-associated phenomenon. The replacement of lost and consumed coagulation factors was the mainstay in the resuscitation of hemorrhagic shock for many decades. Recently, better understanding of the pathophysiology of coagulopathy in trauma patients has led to the logical opinion that we should directly address this coagulopathy during major trauma resuscitation. Damage control resuscitation (DCR), the strategic approach to the trauma patient who presents in extremis, consists of balanced resuscitation, haemostatic resuscitation, and prevention of acidosis, hypothermia, and hypocalcemia. The term “lethal triad” was used to describe the physiologic derangement observed in these patients and refers to the triad of the deteriorating status of acute coagulopathy, hypothermia, and acidosis of exsanguinating trauma patients. Recently, injury itself is reported to cause early coagulopathy, which is known as “trauma-induced coagulopathy” or “acute traumatic coagulopathy (ATC). ATC is an obvious early coagulopathy and occurs prior to significant dilution, within 30 min of injury, and affects a quarter of the patients with severe trauma. The patients with this coagulopathy have higher mortality than those with normal clotting function. Damage control surgery is defined as the planned temporary sacrifice of normal anatomy to preserve the vital physiology. This is a concept in which the initial surgery becomes part of the resuscitation process rather than part of the curative process. It consists of 3 parts including the initial abbreviated laparotomy, ICU resuscitation and subsequent reoperation for definitive resuscitation. Damage control surgery is a surgical strategy aimed at restoring normal physiology rather than anatomical integrity. Only when the patient has become physiologically stable is the final therapeutic surgery embarked on. This process serves to limit the physiological exposure to an unstable environment, allowing better resuscitation and outcome in the critically ill trauma patients. Conclusions: Damage Control Resuscitation represents the most important advance in trauma care. DCR strategy is the measure that directly addresses trauma-induced coagulopathy. Although several concerns, such as the plasma to RBCs ratio, the method of achieving balanced resuscitation, and the administration of other coagulation factors it is now the most beneficial measure for treating trauma-induced coagulopathy, and it can change the treatment strategy of trauma patients. The effect of the reversal of coagulopathy in the massively hemorrhagic patient may shift the operative strategy from one of DCS to definitive surgery. Damage control philosophy is based on

the principal that outcome after major trauma is determined by the physiological limits of the patient, rather than by the effort of anatomical restoration by the surgeon.

### **ST3. The vermilion flap – an accompanying flap in transversal advanced approaches for the lip reconstructions, to avoid the postoperative contraction in the suturing line [ORAL]**

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The inferior lip remains a fragile morphologic region with serious requests in its partial, or total reconstruction, for its own anatomical position, as a region very exposed toward the aggressiveness of the trauma, and for its own biologic characteristics, which have transformed it in a region highly vulnerable for the malignity. What has attracted our attention in our clinic practice is the dominance of the advanced transversal techniques, which create a perpendicular sutured line, with high risk of postoperative contracture and its functional or esthetic sequel. This risk is presented from a direct suture after a simple cuneiform excision, till in broad excision with Schucardt, or other flap reconstructions. Although, in the early period, these surgical techniques expose minimal deformation of the lip linearity, in the long term follow up postoperative period, we have encountered esthetic discontent, or functional discomfort of the patients, due to the postoperative fibrosis resulting in a lip contracture. This is consequence of an esthetic awareness and cultural evolution of the people. The cause of these postoperative complaints is the fibrotic contraction of postoperative cicatricial tissues. This pathological process in the level of surgical incision causes the traction of the lip and depression of the vermilion along the postoperative cicatrix, accompanied with not only esthetic problems, but sometimes and with functional ones. Therefore, in this presentation, we proposed a combination of the transversal advanced reconstructive approaches, with the advanced vermilion flap over the suturing line to break the retraction forces of the perpendicular cicatrix. The postoperative results and the following up of the lip linearity during these years of the application of this techniques combination are optimistic and guarantee the complete elimination of the retraction complication in the postoperative period of the cuneiform excision. In no one case of our application of this approach, we haven't seen the deformation of the vermilion linearity and the cicatrix retraction of the lip in the line of suturing, giving not only long term postoperative functional safety, but and satisfactory long term esthetic results.

### **ST4. Bladder neck sclerosis - approach and repercussions [FLASH]**

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**Introduction:** Bladder neck sclerosis is a well-known pathology that can occur following prostate-related surgery. We refer in this case to both malignant and benign prostatic pathology. The problem of this type of illness is the frequency of relapses and the difficulty of their progressive approach and the implications that this type of illness can have at a distance. **Methods:** Bladder neck contracture is one of the most frequent complications of prostatic related surgery. We wanted to evaluate the correction methods and the impact that this pathology may have at a distance. **Results:** The spectrum of therapeutic approaches varies greatly from simple dilatation, which is often sufficient to sophisticated reconstructive procedures. The treatment of this pathology unfortunately requires a personalized approach for each patient, the guidelines having only an orientation role. They retain their importance and the basic indication to be respected, a gradual approach being most often indicated. **Conclusions:** Bladder neck sclerosis is an underestimated pathology in most cases. The implications of its neglect can be disastrous at a distance, sometimes implying renal failure and / or dialysis.

#### **ST5. First time performed in Albania immediate breast reconstruction using prosthesis and biological mesh and sentinel lymph node biopsy using isotope mapping [FLASH]**

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**Objective:** To report the first case done in Albania of Sentinel Lymph Node Biopsy (SLNB) using isotope mapping and Nipple Sparing Mastectomy (NSM) with immediate breast reconstruction with prosthesis and biological mesh (ADM). **Methods and results:** Patient H.D, female, 49 years old, presented at the ambulatory of breast surgery near the Hygeia Hospital Tirana (private hospital) on 10 October 2014 for a nodule in her breast. Fine Needle Aspiration shows C5 (mammary carcinoma); at palpation of the right breast it was evident one mass of 2 cm on the upper outer quadrant, without skin retracing in that area, and a mobile nodule of 1 cm in right axillary region. The patient was diagnosed with right breast cancer T2 N1 Mx clinically. All the laboratory and imaging examinations were normal; this case was selected to be submitted to surgical procedures: right nipple sparing mastectomy (NSM) and immediate breast reconstruction, using prosthesis and biological mesh and Sentinel Lymph Node Biopsy, during a live surgical course on 25 October 2014 at Hygeia Hospital Tirana. Lymphoscintigraphy with technetium was performed, surgery started with Sentinel Lymph Node Biopsy that revealed isolated tumour cells (ITS) and to be followed by Nipple Sparing Mastectomy with immediate reconstruction using prosthesis and biological mesh (ADM). The definitive biopsy of the nodule in the breast resulted: infiltrative carcinomatous subtype medullar, pT1c N0(i+)Mx; IHC: ER 0%, PR 0%, Her-2/neu 0, Ki67 60%. The post operatory period was normal without problems

and the patient left the hospital 3 days after surgery, patient has done the chemotherapy: Doxorubicin 50 mg 2 fl and Endoxan 500 mg 2fl per day therapy for 4 cycles every 3 weeks follow by Doxetaxel 80 mg 2 fl per day therapy every 3 weeks for 4 cycles. The patient has done the periodic clinical visit, there were no problems with the aesthetical situation, and she feels very happy for booth facts: treatment of the oncological problem and avoidance of breast disfigurement. She has a very good psychosocial situation, as evaluated by the psychosocial service made during patient's interview. Conclusion: This case has is of high importance in our experience of surgical breast cancer treatment. For the first time it was possible to perform the Sentinel Lymph Node Biopsy using isotope mapping and immediate reconstruction of the breast with prosthesis and biological mesh, avoiding to the woman patient in matter two very morbid conditions such as unnecessary axillary dissection and disfigurement of her body image and it was all resolved timely through only one surgical procedure.

### **ST6. Thyroid cancer incidence in surgery of thyroid gland [FLASH]**

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Background: There was performed a prospective study for follow-up according to a medical register model: "Thyroid goiter and its variations. Diagnosis, post-operational complications". Materials and methods: From 1 January 2002 to 31 July 2005, we selected a total of 279 patients who were operated on thyroid gland at the Third Clinic of General Surgery in University Hospital Center "Mother Theresa" in Tirana. Results: 250 of the 279 patients in this study were women (89.61%) and 29 there were men (10.39%), female-male ratio was 1:8.93 (in literature 1:5.4%). In 189 patients (66.67%) the group-age was from 26-50 years old. When the intervention was done, all the patients were hormonally balanced (euthyroidian) and without biochemical alterations. The multinodular non-toxic goiter was the most common observed disease 63.8% (women were 161 or 64.4% and men 17 or 58.62%). The common operation to be performed was the subtotal thyroidectomy, 51.60%. The histo-pathological forms which dominate are: adenomatous hyperplasia mix form with 122 (67.41%) patients and follicular adenoma with 55 (22.08%) patients. The thyroid cancer was found in 3.58% (women were 8 or 3.2% and men 2 or 6.9%). The histo-pathological forms were papillary 3 and follicular 7 patients. For 4 patients resulted with thyroid cancer the beginning diagnoses was multinodular non-toxic goiter and for 1 patient it was cold nodule. The average age for the women it was 46.7 years and for men 30.5 years. Conclusions: The incidence of thyroid cancer found in patients with multinodular non-toxic goiter thyroid disease was 2.25% (in literature less than 5%) and 3.4% in patients with cold nodul (in literature less than 5%). The finding of thyroid cancer disease in patients with multinodular non-toxic goiter and cold nodule when it was not suspected clinically show the necessary of FNA (Fine Needle Aspiration) on thyroid gland.

### **ST7. Incidental finding of a cholecysto-biliary fistula during laparoscopic cholecystectomy [FLASH]**

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**Introduction.** The extra-hepatic biliary tree is one of the most frequent sites where anomalies in human anatomy can occur, with numbers that vary between 0.58% and 47.2%. **Case presentation.** We present the case of a 67-year-old woman, admitted to the Emergency Room with severe epigastric and right hypochondrial pain, associated with loss of appetite and altered general state. The patient had a medical history of grade II obesity, grade II hypertension, and myocardial infarction. The clinical examination revealed abdominal tenderness in two quadrants, guarding and a positive Murphy sign. Blood tests revealed leukocytosis, neutrophilia, lymphopenia, direct and total hyperbilirubinemia and hyperglycaemia. The ultrasound examination revealed an enlarged, thin-walled gallbladder and the presence of a gallstone with a diameter of 15 millimetres. Laparoscopic surgery was the procedure of choice. Intraoperatively, the diagnosis of gangrenous cholecystitis was established, followed by the decision of laparoscopic cholecystectomy. During the dissection of the biliary tract, an anatomical variation was observed: the cystic duct drained directly into the right hepatic duct. Distally, a fistula was present between the gallbladder and the right hepatic duct. Right hepatic duct resection was performed, followed by a T-T type anastomosis and external biliary drainage with the tube placed in the right hepatic duct, trans-anastomotic, through a minimal hepatectomy at 0.5 cm above the confluence of those two ducts. The surgical procedure was followed by ERCP with the placement of two stents on each hepatic duct and endoscopic papillotomy with favourable evolution. **Conclusions.** The particularity of this case is represented by the reduced frequency of biliary fistulas which made this case one of the first cases of laparoscopic extra-hepatic biliary tree reconstruction performed in Romania.

### **ST8. Clinico – evolutionary particularities of head injury patients in prehospital [FLASH]**

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**Introduction.** Traumatic brain injury (TBI) is a major cause of death and disability worldwide. The causes of traumatic brain injury vary by age and other demographic characteristics. Mortality after trauma is higher for elderly than younger patients. **Material and methods.** This study has been conducted over 468 patients with TBI, which were evaluated by the National Center of Prehospital Emergency Medicine from Chisinau. The retrospectively collected database includes information on age, sex, mechanism of injury, initial Glasgow Coma Scale score. **Results:** The age of patients varied from 15 to 84 years. The medium average of investigated patients was 49,5 years. This study included 468 cases with 304 (65%) males and 164 (35%) females. Road traffic crashes are the leading cause of TBI, which consist (47.86%).

Accidents at home and aggression also occupies an important place in etiology of head injury (16.88% and 14.1% respectively). Seasonal distribution analysis of traumatic brain injury shows an increased rate of head injury during winter (per season) - 35.89% with the largest spread in February (per month) - 14.74%. The vast majority of patients showed a higher GCS 8 (63.03%). The remaining patients were in coma (36.96%) with a GCS less than 8, GCS 3 – 4 - 10.89%; GCS 5-6 - 10.47%; GCS 7 – 8 - 15.59%. Conclusion: TBI is common and a major public health problem. TBI predominantly affects young male population. Road traffic crashes are the leading cause of TBI.

### **ST9. Surgical treatment in trochanteric fractures: dynamic hip screw versus gamma nail [ORAL]**

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**Introduction:** The aim of the present study is to compare two different osteosynthesis systems: the extramedullar dynamic hip screw (DHS) and intramedullar gamma nail in the fixation of 100 trochanteric fractures of the proximal femur. **Methods:** 63 cases treated in the Clinical Emergency Hospital, Bucharest, between March and September 2017, for trochanteric fractures, were analyzed. Two groups: those operated with DHS and those operated with gamma nail were compared by demographic data, duration of the procedure, need of blood transfusion (due to hemorrhage), in-patient duration and the type of fracture frequency regarding the AO classification, the therapeutic method, the complications. **Results:** DHS group consisted of 8 patients, respectively 12.69% of total (gamma group with 71.42% of total): females 50% (gamma group 82.22%), mean age 72.25 (19, 93) years (gamma group 80 (27, 105) years). The median duration of the procedure of 1.5 hours (shorter than 1 hours in gamma nail grup), 37.5% patients needed blood transfusions (gamma group 22.22%), with a median in-patient duration of 19.125 (6, 40) days (gamma group 12.688 (3, 35) days), with the most frequent AO type of fracture – cominutive 62.5% of patients (gamma group 53.33% of patients). When the surgical procedures were contraindicated, the orthopedic treatment was choose. The most frequent complications were: infections and death. **Conclusions:** The DHS was more invasive than gamma nail (longer duration of the procedure, higher rate of blood transfusion needed and longer in-patient duration), but we should forget that the technique is time limited and depend on the surgeon skills.

### **ST10. Appendicectomie laparoscopique chez les âgés: bénéfices et risques [ORAL]**

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**Objectif:** Les bénéfices de l'appendicectomie sous cœlioscopie sont controversés. L'objectif de cette étude est d'évaluer les avantages et les inconvénients de cette technique pour les âgés. **Matériel et méthodes:** Une étude rétrospective a porté sur 96 patients âgés (personne âgée de 70 ans ou plus) suspects d'appendicite, opérés sous cœlioscopie entre 2013 et 2017. Le diagnostic préopératoire a été corrigé lors de l'exploration cœlioscopique dans 12 % des cas (7 % chez les hommes et 5 % chez les femmes) et le taux de conversion a été de 3,7 %. Il y avait 14 malades avec péritonite généralisée et 21 avec péritonite localisée. Le taux de conversion a été de 7,3 % et la durée opératoire moyenne de 33 minutes. **Résultats:** Il n'y a pas eu de décès postopératoire. Au cours de la première période, la morbidité a été de 2,4 % chez les patients opérés sous cœlioscopie exclusive. Il y avait 6,2 % d'appendices sains à l'examen anatomopathologique. La durée moyenne de séjour a été de 3,6 jours. et Il y a eu 6 complications pariétales mineures. **Conclusion:** Le choix de l'appendicectomie sous cœlioscopie pour les âgés permet de redresser le diagnostic et de simplifier les suites opératoires, et n'a pas d'inconvénients (si ce n'est pas un allongement du temps opératoire), sous réserve que l'intervention soit réalisée par un opérateur entraîné.

**ST11. Effects of vasoactive therapy in patients with sensorineural hypoacusis [ORAL]**

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**Introduction:** Hearing loss is one of the most common health problems which is manifested by a subjective feeling of impaired hearing, the impossibility of listening in noise, intermittent or constant tinnitus. It can be conductive or sensorineural type (SNHL). Sensorineural hearing loss is caused by degeneration of the cochlea, which is responsible for the transduction of sound stimuli into nerve impulse. **Aim:** The aim of this study was to determine the effects of the applied vasoactive and hemokinetic therapy in people with sensorineural hypoacusis who refused embedding hearing aids. **Patients and Methods:** This retrospective study included 51 patients, which were in a three-year period in Clinic of Otorhinolaryngology KC Nis diagnosed with sensorineural hearing loss. Patients were clinically evaluated on the basis of the findings of otoscopy and tonal audiometry. Patients were treated with pentoxifylline, vitamins B1 and B6, cinnarizine (older than 50 years) and betahistine (younger than 50 years), for 28 days. After the treatment, using pure tone audiometry, we monitored the frequency of 125-8000Hz and improvements in decibels. Controls were in 3 to 4 weeks. For analyzing and processing we used the worst finding and the best answer. **Results and discussion:** Applied therapy led to improvements in all frequencies, particularly at high frequencies (2-8kHz) ( $p < 0.001$ ). Subjective symptoms such as tinnitus were absent, or were losing their intensity. Patients had a subjective feeling of better auditory functionality (better communication, better hearing experience of environment). **Conclusion:** In our study, we demonstrated that administration of vasodilators and hemokinetics in the treatment of patients with SNHL has positive effects in all frequencies, especially at high frequencies (2-8kHz).

**ST12. Postoperative delirium in emergency surgery: prevention and multimodal approach – a review of the evidence [FLASH]**

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**Introduction:** A key area for concern and one to which older patients are more vulnerable is post operative delirium. Delirium appears to be an important marker for risk of dementia (or death), even in older people without prior cognitive or functional impairment. **Method:** We performed a search on PubMed database using keywords: geriatrics, elderly patients, gastrointestinal surgery, elective and emergency surgery, postoperative delirium or cognitive dysfunction, anaesthesia and postoperative analgesia. The search yielded 24 relevant articles which were appraised and reviewed. **Results:** Patients with postoperative delirium have been found to be significantly less likely to return to their preoperative level of performance at six months than patients without delirium. Delirium is multi-factorial and several postoperative predictors have been identified. Possible precipitating conditions are uncontrolled pain, hypoxia, pneumonia, infection, electrolyte abnormalities, urinary retention, faecal impaction, medications and hypoglycaemia. Systemic stress and inflammatory response might play an important role in delirium onset. **Conclusions:** Fast-track surgery could reduce these. Postoperative delirium should be treated with multi-component non-pharmacological interventions. Up to a third of delirium is preventable and early attention is needed to identify possible precipitants and adopt approaches in those patients at risk.

**ST13. Long term efficacy of anti-VEGF pharmacotherapy in neovascular age related macular degeneration [ORAL]**

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**Introduction:** To study the long-term efficacy of anti-VEGF therapy in neovascular age related macular degeneration (nvAMD) in a real life clinical setting. **Methods:** Retrospective, non-randomized, interventional case series of patients with nvAMD under anti-VEGF therapy, with a minimal follow-up of 3 years. **Results:** We studied 32 eyes (of 26 patients) with a median age of 77.1 years and median follow-up of 3.2 years. We recorded the best corrected visual acuity (BCVA, Snellen, logMAR) before and during therapy, the number and distribution of injections/visits, as well as the clinical and tomographic details of the neovascular membrane (structural OCT and OCT angiography) before and during treatment. We compared our results to the efficacy data in existing large real life clinical series and analyzed the reasons of long-term



vision loss under treatment. **Conclusions:** Given the poor natural history of nvAMD, anti-VEGF therapy has revolutionized patients' management. Its long-term efficacy – however – depends on the strict application of the therapeutic protocols of the registration trials, and falls short in the everyday clinical practice because of compliance issues, as well as disease parameters that do not respond to anti-VEGF pharmacotherapy (fibrosis, atrophy).

#### **ST14. An aortogastric fistula presenting as massive upper gastrointestinal bleeding: A case report (FLASH)**

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**Introduction:** Aortogastric fistulas are a type of Aortoenteric Fistula (AEF). Few cases of primary and secondary aortogastric fistulas have been reported. Secondary aortoenteric fistulas have been reported as a complication of the Endovascular Aortic Repair (EVAR) with the placement of prosthetic materials. Considering the anatomic relations of the descending thoracic aorta, the formation of an aortic fistula involving the stomach is an extremely rare case. **Material-Methods:** A 77-year-old woman suddenly reported severe mid-thoracic chest and back pain. Several hours later, she was admitted to the hospital. Her medical history included an aneurysm of the descending thoracic aorta, which was treated using the Thoracic Endovascular Repair (TEVAR) method eight months ago. Abdominal CT imaging and the nasogastric tube showed upper gastrointestinal bleeding. The patient suffered two episodes of cardiac arrest and four hours after her admission she died amid haemorrhagic shock. **Results:** The autopsy revealed that an aortogastric fistula was responsible for the massive bleeding in the upper gastrointestinal system. This finding is explained anatomically, as a sliding hiatus hernia was found and a large part of the stomach had entered in the thoracic cavity. The fistula was formed between the part of the aneurysm near the distant stent-graft fixation and the intra-thoracic part of the stomach. **Conclusion:** The early clinical suspicion of aortogastric fistulas on the grounds of thoracic aortic endovascular stent-graft placement is usually hindered because of the rarity of the condition. However, because of their invariably fatal consequences, their prompt diagnosis and treatment is critically important.

#### **ST15. Prolonged postoperative ileus in colorectal surgical patients; causes and possible therapeutic solutions [FLASH]**

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**Introduction:** The causes of prolonged postoperative ileus (PPOI) are still unclear for major abdominal surgery, while the consequences often negatively affect the postoperative outcomes and hospitalization period. This study was performed on surgical patients with colorectal interventions, in order to investigate possible causes and therapeutic solutions for PPOI. **Methods:** The sample of this study was represented by 236 patients admitted and operated over the past five years for colorectal tumors. Symptomatology data, paraclinical investigations, medical and surgical procedures applied have been processed from observation forms. The study included 121 men and 115 women, the average age being approximately seventy-two years. The diagnosis of PPOI was established to patients presenting (at 3 days after laparoscopic interventions, and at 5 days for open surgery) abdominal distension, flatus absence, nausea/ no oral diet, and abdominal radiographic signs. Usual laboratory tests including inflammatory biomarkers (levels of leucocytes, C-reactive protein, etc.) were processed. **Results:** On this sample of 236 patients, the data analyzed showed that 24 subjects (10,17%) developed PPOI. Open abdominal colorectal surgery, smoking history, age, male sex, and chronic pulmonary disease, were found to be independent predictive factors for PPOI. Inflammatory biomarkers were not increased statistically significant to be able to explain/ justify the PPOI. For 24 patients with PPOI the average hospital staying was 21 days, compared to about 10 days of hospitalization for 212 patients without PPI. **Conclusion:** PPOI was associated with severe complications (such as anastomotic leakage, 12,5% vs. 8,02%), and an increased hospitalization period. The main cause of PPOI is now considered surgical manipulation with subsequent inflammatory reaction; however, our study was unable to correlate inflammatory biomarkers with PPOI. Usual prokinetics had minor or no action on PPOI. New investigations should identify causes and establish possible therapeutic solutions, able to diminish/ prevent the occurrence and magnitude of PPOI.

### **ST16. Malignant colorectal obstruction in elderly patients; reevaluating the palliative cases and procedures [FLASH]**

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**Introduction:** Obstructive colorectal cancer is a life threatening complication that requires a fast decompression. The good results obtained using SEMS (self-expandable metallic stents) can be enhanced afterwards by chemoradiotherapy (downstaging) and/ or surgical interventions. The aim of this study is to reevaluate the colon cancer distribution/ staging and surgical procedures performed, as a possible premise for extending the current indications of minimal invasive techniques like SEMS, especially in cases with multiple associated commorbidities. **Methods:** This is a retrospective study including 214 elderly patients (91 men and 123 women, mean age about 74 years), admitted with malignant colonic obstruction in the last five years. Evolutive data related to clinical and paraclinical variables, interventions, complications, morbidity and mortality were statistically processed and interpreted. Most patients (97, 19%) were diagnosed

histologically/ after intervention with colorectal adenocarcinoma. Results: Our sample consisted of 63 subjects (29,43%) with right-sided colonic obstruction, and 151 patients (70,56%) with left-sided colonic obstruction. In the first group the right hemicolectomy was performed to 51 patients, ileotransverse anastomosis in 10 patients, and defunctioning loop ileostomy to 2 subjects. In the second group tumor resection was possible to 126 patients (61 with primary anastomosis and 65 with stoma), while palliative procedures were performed to 11 patients (9 colostomies and 2 internal derivations). Nine patients were treated prior to surgery by SEMS, and 5 subjects with SEMS as palliative therapy. Conclusion: Palliative procedures (minimal interventions) were applied to 12 patients with right colon cancer and 16 subjects with left-sided colon cancer. Cumulating these cases, we obtained morbidity and mortality rates statistically lower (12,24% and 8,18%) than for interventions ending with tumor resection (18,21% and 12,22% for right colon, and 24,89% and 20,15% for left colon). Minimal techniques such as SEMS could benefit by extended indications due to better short term outcomes, completing the therapy afterwards with elective surgery and/ or chemoradiotherapy.

### **ST17. The value of intraoperative cholangiography in diagnosis and treatment of iatrogenic lesions of common bile duct [ORAL]**

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Laparoscopic cholecystectomy represents the "gold standard" for calculous biliary disease. Common bile duct lesions represent a major complication of laparoscopic cholecystectomy. The purpose of this study is to present the importance of intraoperative cholangiography in avoiding main bile duct lesions during the cholecistectomy. Methods: A retrospective study has been made on a period of 5 years (2012-2017) in the General Surgery Clinic of the "Elias" Emergency University Hospital, where a total of 2577 cholecystectomy cases were analyzed. Of the total number of cases, 1350 were for acute cholecystitis and the rest 1227 were for chronic cholecystitis, with a prevalence of female patients of up to 1832 cases. Results: A total number of 850 cholangiographies were made. Common bile duct lesions were present in 5 cases: 2 cases of scleroatrophic lithiasic cholecystitis, 2 cases of acute cholecystitis and 1 case of chronic cholecystitis. In all cases the common bile duct lesion was identified during surgery. The lesions were all treated during the same intervention, 3 of the cases laparoscopically and 2 of them requiring conversion to classic surgery. Concerning the mortality, there was only one case, which had multiple comorbidities. Conclusions: Iatrogenic common bile duct lesions represent a rare complication, but which can have important consequences on the patient. Intraoperative cholangiography leads to early identification of the lesions and diminution of the possible lesions during the cholecystectomy, with potential resolution during the same intervention. With the evolution of laparoscopic surgery, this type of lesions can be resolved with minimal invasive procedures.

### **ST18. Preservation of sensory nerves during axillary lymphadenectomy [FLASH]**

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**Introduction:** The complete dissection of axillary lymph nodes is a current practice in managing multiple neoplastic diseases for both staging and therapeutic purposes. The current study corroborates data concerning the anatomy of the intercosto-brachial nerve (ICBN) and the benefits of its preservation during complete axillary lymphadenectomy performed as treatment for an array of neoplasms. : The study group consisted of subjects who underwent axillary lymphadenectomy in our clinic between 2014-2015; the subjects were randomized into two arms, depending on the type of surgery performed, axillary lymphadenectomy with or without preservation of the ICBN. The evaluation consisted in: anatomical variants of the ICBN according to the Cunnick classification, cutaneous sensory deficit, pain, number of lymph nodes removed, operating time, complications arise during and after surgery, local recurrence rate. **Results:** Immediate and long term follow-up of patients have shown a superior tactile sensitivity, reduction or even disappearance of paresthesia and chronic post-surgical pain in the group where ICBN was preserved as opposed to the one where it was not. There were no significant differences in the operating time, number of lymph nodes removed and local recurrence rate in a 2-year interval between the two groups. **Conclusions:** Preserving the ICBN during axillary lymphadenectomy improves the operating technique; it does not affect the oncology result and leads to less pain and sensory disturbances after surgery, with an improvement in the overall quality of life.

### **ST19. Patterns of lymphatic spread in cervical cancer [FLASH]**

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**Introduction:** although screening tests for cervical cancer have been widely implemented, this malignancy remains a serious health problem, an important number of cases being diagnosed in advanced stages of the disease. The most important patterns of spread in these cases remain the lymphatic route, followed by the hematogenous route as well as the dissemination via contiguity. **Methods:** we present a series of 32 patients diagnosed with advanced stage cervical cancer in which pelvic and para-aortic lymph node dissection were performed. **Results:** among these cases 24 patients presented positive pelvic lymph nodes, four of them associating also metastases in the para-aortic lymph nodes. However, in other three cases in which metastases in the para-aortic lymph node stations were reported there was no sign of metastatic cells in the pelvic lymph nodes, demonstrating in this way that serial metastatic pathway (via pelvic lymph nodes in order

to metastasize in the para-aortic lymph nodes) is not mandatory, the pelvic station being skipped by the malignant cells in certain cases. Conclusions: patients with advanced stage cervical cancer might develop para-aortic lymph node metastases in the absence of pelvic lymph node metastases, the para-aortic station being invaded by skipping the pelvic stations.

### **ST20. Liver resection for hepatic metastases from uterine cancer [FLASH]**

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Introduction: the apparition of liver metastases in patients with uterine cancer has been considered for a long period of time as a sign of system relapse; therefore the patient is rather considered as a candidate for palliative oncological treatment rather than for surgical resection. However, in certain cases liver lesions develop as oligometastatic disease, in these cases surgery being performed with curative intent

Method: we present a case series of three patients diagnosed with oligometastatic liver lesions with uterine cancer origin, all cases being submitted to surgery with curative intent Results: all three cases were diagnosed with metachronous liver metastases, the disease free interval ranging between 12 and 19 months. In all cases atypical resections were performed; in the meantime, one of the patients associated a pelvic recurrence which was also resected at the time of performing the liver resection. Postoperatively a single patient developed a biliary fistula which was successfully treated in a conservative manner. At the end of surgery none of the patients presented residual disease. Conclusions: liver resection can be safely associated in patients with oligometastatic disease in order to achieve a good control of this malignancy and to prolong survival

### **ST21. The role of peritoneal resections in advanced stage endometrial cancer [FLASH]**

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Introduction: peritoneal spread remains one of the most important pathways incriminated in the dissemination of endometrial cancer cells. The main mechanisms which explains the apparition of peritoneal carcinomatosis in endometrial cancer is related to the peritoneal fluid movements, leading in this way to the apparition of peritoneal carcinomatosis in the parieto-colic areas as well as in the diaphragmatic area and on the greater omentum. In the meantime the intestinal loops will be protected for a long period of time due to the peristaltic movements. This

mechanism explains best the risk of developing extensive peritoneal carcinomatosis in patients with endometrial cancer. Method: we present a series of eight patients diagnosed with extensive peritoneal carcinomatosis from endometrial cancer. In order to achieve a complete cytoreductive surgery, in all cases peritoneal resections were performed. Results: among the eight patients introduced in the current study pelvic peritoneum was affected in all cases, parietal lesions were seen in six cases and diaphragmatic lesions were seen in one case. In the case who presented diaphragmatic lesions all peritoneal nodules were developed on the left hemi diaphragm, the right space being blocked due to the prior history of duodenal ulcer which conducted to the apparition of an intense process of adhesions at this level. In all but one case cytoreduction to no residual disease was achieved; a single patient presented residual tumors with a maximum diameter of 5 mm at the end of the surgical procedure due to the presence of an extensive mesenteric carcinomatosis. Conclusions: peritoneal resections can be safely associated as part of debulking surgery for advanced stage endometrial cancer.

### **ST22. The importance of Riolan arch in patients with inferior mesenteric artery obstruction [FLASH]**

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Introduction: Riolan arch represents a vascular structure with a particular importance in patients presenting inferior mesenteric artery obstruction. The presence of a functional arch is mandatory in order to provide an adequate blood supply of the left colon as well as of the rectosigmoidian loop. Methods: we exemplify the utility of this arch by presenting the cases of two patients in whom the functionality of the inferior mesenteric artery was affected by chronic compression due to external adenopathic masses and respectively due to the association of a retroperitoneal hematoma. Results: the first two cases were submitted to surgery for advanced stage cervical cancer and were diagnosed with large adenopathic masses compressing the inferior mesenteric artery. In these two cases the artery was ligated at the origin in order to complete the lymph node dissection; however, the presence of a well developed Riolan arch provided an adequate vascularization of the sigmoidian loop. The third case was the one of a patient with previous history of surgically treated cervical cancer who developed a postoperative thrombosis of the inferior limb, so she was submitted to anticoagulant treatment. However, she developed a massive retroperitoneal hematoma due to an accidental fall which compressed the inferior mesenteric artery. In the absence of a functional Riolan arch, she developed a sigmoidian ischemia so she was resubmitted to surgery, a sigmoidectomy being performed. Conclusions: a good functionality of the Riolan arch is mandatory in order to provide an adequate vascularization of the sigmoidian loop whenever the inferior mesenteric artery is no more functional.

### **ST23. Intraoperative decisions in patients with hepatic or splenic artery aneurysms [FLASH]**

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Introduction: visceral artery aneurysms might remain asymptomatic for a long period of time due to the development of a well-functioning collateral circulation. However, in certain cases, they can become symptomatic once complications occur. Methods: we present a case series of three patients diagnosed with hepatic aneurysms (two cases) and splenic artery aneurysms (one case) that were diagnosed due to the apparition of aneurysm related complications Results: cases with hepatic artery aneurysms were investigated for upper digestive bleeding and were diagnosed with a common hepatic artery aneurysm and respectively a right hepatic artery aneurysm. However, due to the long evolution of the disease, a proper collateral circulation was developed in both cases, so the aneurysms were successfully resected without performing any hepatic resection. The vascularization of the liver was provided by accessory hepatic artery in the first case and by the left hepatic artery in the second case. The third case was diagnosed with a large splenic artery aneurysm; due to the large dimension of the aneurysm the patient was submitted to surgery, the lesion being resected en bloc with splenectomy and distal pancreatectomy. Conclusions: visceral arterial aneurysms are usually diagnosed at the time of developing complications. Due to the long evolution of such cases, a good collateral circulation is present at the time of diagnostic, providing the surgeon the possibility of preserving the corresponding viscera; however, the final decision in regard with the extent of the surgical procedure should be taken intraoperatively, after a close inspection of the vascular resources of the collateral pathways.

### **ST24. Multiple digestive resections as part of debulking surgery for ovarian carcinosarcoma [FLASH]**

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Introduction: ovarian sarcomas are recognized as extremely aggressive tumors with poor response to platinum based chemotherapy and worse prognostic when compared to epithelial ovarian carcinoma. Unfortunately most patients are diagnosed in advanced stages of disease when multiple peritoneal lesions are already present. Methods: we present the case of a 54 year old patient who presented for diffuse abdominal pain and distension in association with constipation. The preoperative computed tomography raised the suspicion of peritoneal

carcinomatosis with ovarian origin Results: the patient was submitted to surgery, intraoperatively large tumoral masses involving multiple digestive segments. The frozen section raised the suspicion of a peritoneal sarcomatosis with ovarian origin. The patient was submitted to debulking surgery consisting of total hysterectomy en bloc with bilateral adnexectomy and rectosigmoidectomy, right ileocelectomy and segmental enterectomy. In the meantime, due to the presence of the carcinomatous elements, pelvic and para-aortic lymph node dissection were also associated. The continuity of the digestive tract was reestablished through a side to side entero-enterostomy and a side to end ileotransversostomy while the left colon was exteriorized in terminal colostomy. The postoperative course was uneventful while the histopathological studies confirmed the diagnostic of ovarian carcinosarcoma with peritoneal sarcomatosis. Conclusions: in certain cases multiple digestive resections might be needed in order to maximize the debulking effort in patients with advanced stage ovarian carcinosarcomas.

### **ST25. Influence of the pattern of spread in patients with splenic metastases from ovarian cancer in patients with recurrent disease [FLASH]**

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Introduction: ovarian cancer is characterized by a high capacity of spread via hematogenous, peritoneal and lymphatic route, leading to the apparition of disseminated metastases. However, it seems that a significant difference in terms of survival can be encountered in respect with the pattern of spread. Methods: we present a case series of 14 patients submitted to splenectomy as part of secondary cytoreductive surgery for relapsed epithelial ovarian cancer Results: among these cases 10 patients presented hematogenous metastases, three cases presented peritoneal lesions with limited splenic parenchyma invasion while one case presented lymphatic hilar metastases with capsular invasion. The median overall survival rate was 44 months for patients with peritoneal metastases, 16 months for lesions with hematogenous origin and 17 months for the patient with adenopathic lesions. However, the difference was not statistically significant. Conclusions: among patients with splenic metastases from ovarian cancer cases with peritoneal lesions seem to have a more favorable outcome; however this fact was not statistically significant.

### **ST26. Medical errors and surgical safety [ORAL]**

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Medical Errors are defined as the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim. Adverse drug events, improper transfusions, surgical injuries, wrong site and side surgeries, falls, burns, pressure ulcers and mistaken patient identities



are among the errors that should be taken into account. Most dangerous places are intensive care units, operating rooms and emergency departments. Medical errors are generally underreported for medico-legal reasons and they have significant tolls not only as human lives but also as financial loss, loss of trust to the health care system and diminished satisfaction by both patients and health professionals. There may be diagnostic and therapeutic errors, errors related with a problem about preventive medicine and related with equipment or other system failure. World Health Organization's Surgical Safety Checklist was implemented to minimize the rate of errors. Written policies, documentation, human factors engineering, information technology is used for the prevention. In addition, surgical time-outs, site signing, instrument and sponge counts and documentation, error reporting systems are implemented. One of the most important issue is the establishment of a safety culture in health institutions. Despite all measures it is not possible to nullify medical errors and this brings our minds the aphorism "To Err is Human".

**ST27. The Romanian Journal of Cardiovascular Surgery: the vascular surgery perspective (2002-2006) [FLASH]**

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The nationally and the internationally overwhelmingly recognized prestigious scientific personality of Professor Doctor Honoris Causa Vasile Candea includes two major achievements in the development of the Cardiac surgery and in the Vascular surgery specialties: Founder and First President, in chronological order of The Romanian society for Cardiovascular Surgery (2002-2006) and Editor-in-Chief and Founding Editor of The Romanian Journal of Cardiovascular Surgery (2002-2011), the entirely written in the English language Official Journal of this society. As a vascular surgeon, I am honoured to be invited to contribute to this unique project of medical scientific press with twelve articles (2002-2006): - four articles, as unique author, dedicated to the Development of the Vascular surgery (three) and to the Arterial aneurismal diseases (one); - four articles, as first author, dedicated to the Development of the Vascular surgery (three) and two the Arterial occlusive diseases (one); -four articles, as co-author, dedicated to the arterial aneurismal diseases (three) and to the Arterial occlusive diseases (one). "Advancing in the Cardiovascular surgery published in the Romanian Scientific Press (2002-2012)"; coordinated by Vasile Candea, Ionel Droc and Francisca Bianca Calinescu, includes four of the these articles: -two of them, as first author, are dedicated to the Development of the Vascular surgery and two of them, as co-author, are dedicated to the Arterial occlusive diseases (one) and to the Arterial aneurismal diseases (one). The Romanian Journal of Cardiovascular Surgery has a important role in the contemporary and in the future development of the Vascular surgery, recently officially recognized in Romania (1999) as a distinct specialty as well as of the Cardiac surgery and of the other specialties implicated in the diagnosis and in the treatment of the patients with cardiovascular diseases.

## **ST28. Laparoscopic approach in abdominal oncologic pathology [FLASH]**

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The improvement of mini-invasive surgical techniques, based on the raise of the surgical ability and the technological support, has allowed the extension of this approach to abdominal oncologic pathology. Laparoscopic approach determinate serious discussions regarding the advantages of laparoscopy: minimal hemorrhage and tissue trauma, rapid recuperation and shorter admission time, the almost complete elimination of the abdominal wall pathology and post operative adhesions and on the other side the onco-laparoscopy disadvantages: unknown oncological radicality, intra-abdominal metastatic dissemination and port site metastases. Laparoscopy allows both oncologic diagnosis and stadialization, and radical or palliative surgical treatment. This 5 years prospective study, beginning in February 2012 until December 2017, include 50 patients with diverse abdominal oncologic pathology – digestive 30 cases and genital 20 cases, all benefitted from laparoscopic approach with diagnostic and therapeutic intention. We performed 11 rectal amputations, 5 segmental sigmoid colectomies, 10 radioablations of hepatic metastases, 14 total hysterectomies with pelvic lymphadenectomy and 6 adnexectomies with omentectomy; the rest of 4 procedures involved diagnostic laparoscopy with peritoneal cytology and biopsy of the liver, omentum or peritoneum. During the study we monitored parameters involved the intra and postoperative complications, the parietal and intra abdominal recurrences, in cases with curative intent, the admission time and the post operative life standard, thus focusing on the main controversial elements of onco-laparoscopy. The clinical experience shows that mini-invasive surgery is a safe approach with similar results in comparison with the open surgery, but with the condition of

## VARIA

### **V1. Reinforcement of the framework for experiential education in healthcare in Serbia [FLASH]**

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Introduction: Republic of Serbia (RS) is making efforts to fulfill requirements for the accession to the European Union (EU). ERASMUS+ project Reinforcement of the Framework for Experiential Education in Healthcare in Serbia (ReFEEHS) objectives refer to assess current practice in health professions education, identify weaknesses, and propose solutions for modernization of health sciences curricula and improvement of professional competencies of health sciences graduates. Methods: Relevant survey questionnaire is designed and used to identify RS students, teaching staff and practitioners/clinical mentors attitudes related to experiential education (EE), interprofessional education (IPE) and teaching competencies development (TCD). The obtained results are used to benchmark actual situation in RS against the current best practices in EU and identify the needs for improvement. Great contribution in strategy building is collaboration and exchange of good practices with consortium partners (universities from 4 EU countries: Bulgaria, Portugal, Hungary and Ireland). Results: Curricula of faculties of medicine, dentistry, pharmacy and nursing at state universities in Belgrade, Kragujevac, Nis and Novi Sad are modified. New IPE courses are accredited and the first generations of students completed them. ReFEEHS guidelines for students and mentors from practice are prepared as well as ReFEEHS standards for practice for medical, dentistry, pharmacy and nursing students. Young teaching staff completed postgraduate teaching competencies courses at University of Dundee and have organized course of TCD for their colleagues. Conclusion: ReFEEHS project fulfill its objectives and contributed to modernization of health sciences curricula at universities in RS: experiential education is updated, interprofessional education is implemented and work on teaching competency is established.

### **V2. Major ozone autohaemotherapy: a therapeutic shock [ORAL]**

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Ozone is a natural but an unstable gaseous molecule which consists of three oxygen atoms. Ozone molecule, as a medical drug, can be administered into the body parts by means of different modalities. Medical ozone generators use photometer which allows to measure precise ozone concentrations (1-100 microgram/ml) in the ozone-oxygen mixture. Ozone therapist must

apply the optimal dose for different therapy modalities also depending on diagnosis. Major Ozone Autohaemotherapy is best known and is the basic application form of ozone-oxygen therapies. In this therapy 50-270 ml venous blood together with an anticoagulant is taken to an ozone resistant bottle and exposed to ozone-oxygen mixture for few minutes, soon after re-infused into the venous circulation. When blood contacts with ozone, it reacts with blood cells and plasma in seconds. This reaction can also be defined as an acute oxidative stress or a “therapeutic shock”. During this reaction many messengers such as hydrogen peroxide, reactive oxygen species (ROS) and lipid oxidation products (LOPs) produced in blood sample and delivered by circulation to whole body. Ozone also reacts with blood cells and oxidizes fatty acid in cell membranes triggering biological pathways in these cells. Moreover, ozone activates antioxidant system which resists the acute oxidative stress. So far available clinical results show that Major Ozone Autohaemotherapy has a promising future in treating vascular ischemic diseases, chronic infected wounds, chronic fatigue syndrome, various types of infections, neurodegenerative diseases, autoimmune diseases, dysmetabolic syndrome and atrophic form of age related macular degeneration.

### **V3. The influence of dietetic value of meals on nutritional status in institutionalized elderly in Nis (Serbia) [FLASH]**

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Introduction: Nutritional well-being is an integral component of the health and quality of life of older individuals. Therefore, malnutrition and poor diet is a significant cause of morbidity and mortality among elderly. The aim of our work was to determine the energy and nutritive value of meals consumed by institutionalized elderly in Nis (Serbia), in respect to a probable risk of malnutrition. Methods: The study had been conducted in the years 2013-2016. Twenty-two samples of the meals were analyzed in the accredited laboratory of the Public Health Institute in Nis according to the ISO 17025 recommendation. A cross-sectional survey in 70 subjects living in a public geriatric home in the city of Nis (Serbia) was done. Body mass index, body fat and arm circumference were assessed as markers of nutritional status. Results: The mean energy value of meals was 2357 kcal (range: 2147 - 2567 kcal) and higher than serbian and ADA guidelines. The average protein intake was 74,5 g (range: 63 -86 g), higher than recommended (46 – 56 g). The average fat intake was high (mean:110g, range: 51 - 169 g) and the average carbohydrate intake was low (mean:230g, range: 195 do 265g). Calcium, magnesium, phosphorus and vitamins A and B1 intake were below recommendations and sodium and vitamin C were higher than recommended. Among subjects 38.3% of were overweight (body mass index >25 -30 kg/m<sup>2</sup>), and 20.1% were obese. Only 5,2% of subject were malnourish. Conclusion: The results of our study indicate that institutionalized elderly in Nis (Serbia), in general, were properly nourished. The energy value of the consumed meals did not pose a risk of developing malnutrition. Planning the nutrition in geriatric institution, with laboratory control of meals, may be an effective strategy in adequate energy intake and prevention of malnutrition.

#### **V4. Le rôle de la médecine intégrative pour vieillir en bonne santé [ORAL]**

Ungureanu VE

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«Les Humains ont peur du temps mais le temps a peur des pyramides» - Proverbe Egyptien. Pourquoi l'être humain a peur du temps? Parce que le temps influence la matière et l'être humain comme entité complexe est directement visé. Comme souligne le Directeur général de L'Organisation Mondiale de la Santé. Dr. Margaret Chan, dans «Le Rapport mondial sur le vieillissement et la santé» élabore en 2015, «Le Vieillissement en bonne santé est le processus de développement et de maintien des capacités fonctionnelles qui permettent aux personnes âgées de jouir d'un état de bien-être». La qualité de notre vie et la façon dont nous évoluons dans la vie dépendent aussi de nous, bien qu'il existe d'autres facteurs qui influencent ces deux aspects.. Vieillir en bonne santé est un défi et un idéal que nous devons accepter et poursuivre. Une courte incursion dans l'histoire des peuples nous permet de découvrir leur mode de vie pour une meilleure santé. Le rôle de la médecine Intégrative est non seulement résoudre les problèmes qui surgissent avec l'avancement en âge, mais aussi de offrir des solutions pour prévenir ces problèmes et pour maintenir une bonne santé. La Médecine intégrative combine la médecine moderne et la médecine alternative pour améliorer l'état de santé de l'être humain du point de vue biologique, psychologique, spirituel et social. En ce sens, aux États-Unis, selon le National Health Interview Survey, en 2012, la médecine complémentaire et intégrative est utilisée par 33,2% des américains. En 2012, l'approche complémentaire et intégrative la plus utilisée mentionnait les produits naturels (compléments alimentaires autres que les vitamines et minéraux). - 17,7% des adultes et 4,9% des enfants de 4 à 17 ans utilisaient des produits naturels. Pourquoi les gens préfèrent cette alternative ? Parce qu'elle met l'accent sur le traitement de la personne dans son ensemble, sa promotion de la santé et du bien-être, sa valorisation de la prévention et son approche souvent plus personnalisée des préoccupations des patients. Dans ce contexte, la médecine intégrative, utilisant différentes techniques comme la musique, la méditation, la médecine ayurvédique, la médecine traditionnelle chinoise, le tai-chi, le su-jok, le yoga, les prières, l'hypnose, les exercices respiratoires, l'alimentation, a une grande importance, non seulement de l'état de notre cœur et du système cardio-vasculaire, mais aussi de toute notre santé. La médecine intégrative comprend des éléments qui stimulent notre énergie pour établir l'harmonie pour notre être tout entier, l'harmonie entre le corps physique, l'équilibre psychologique, son esprit, son esprit et son âme. Découvrir et appliquer les méthodes pour une meilleure santé est un devoir envers nous-mêmes et envers ceux que nous aimons pour avoir une vie heureuse.

#### **V5. The contribution of informal care in healthy ageing in Europe: An interview study along with a literature review [ORAL]**

Tsagkaris C

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According to demographic evidence the elderly population in Europe is to be significantly increased in the forthcoming decades. Healthcare systems which face austerity policies appear unable to deal with this challenge. Consequently, informal care – provided to elderly people on a voluntary basis by individuals who share a family or social relation with them – is anticipated to play a pivotal role in healthy ageing. The purpose of this study is to compare the findings of current research on informal care outcomes with the results of an interview study we conducted on Greek elderly people and their caregivers. Methods: The interview study was conducted on 16 individuals including 9 elderly people and 7 caregivers. The interview was based on ASCOT (adult social care outcomes toolkit) INT4 form. Statistical processing was conducted according to the respective guidelines of the London School of Economics. A narrative part was added to the structured questionnaire. Participants' consent was obtained. Plus, we investigated biomedical databases (Pubmed, Scopus) introducing keywords (ageing, informal care, outcomes, european union) and we extracted data from the SHARE informal care database. Results: The positive impact of informal care on healthy ageing in terms of control over daily life, personal hygiene, nutrition, personal safety, social participation and occupation has been illustrated by several studies. The respective ASCOT scores in the interview study aligned to these trends ranging between 0,8 and 1.00 as far as both the dependent people and the caregivers are concerned. Personal narratives reveal several controversial points. Caregivers appear exhausted and poorly supported by relatives and social infrastructure. Elderly people do not consider the state healthcare services sufficient. Conclusion: Informal care seems to be equally important concerning healthy ageing in Greece in comparison to other European states. The lack of official care services in an urban area of the capital where all the participants live is considered as a deficiency of the Greek healthcare service. Moreover, due to cultural and family mentalities informal caregiving is not equally shared between potential caregivers.

## **V6. Nutritive value of iron in fresh fruit of *Vaccinium myrtillus* L. and *Morus* L. [FLASH]**

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Introduction: Iron plays multiple role in the human organism. The process of transporting oxygen from lungs to tissue and erythropoiesis are carried out via chromoproteins such as hemoglobin and myoglobin. Iron, too, is an integral part of numerous enzymes, a, b, c cytochromes, peroxidases, catalases, dehydrogenases and reductases. Recommended daily intake (RDI) of iron for men is 10mg and 15mg for women, but it is considered that daily intake of 0.4 to 1 mg/kg of iron will cause no adverse effects in healthy individuals. In this paper the presence of iron in fresh fruits of *Vaccinium myrtillus* (blueberry) as well as in fresh fruits of *Morus alba* (white mulberry) and *Morus nigra* (black mulberry) was determined. Methods: The samples of exactly determined mass of fresh fruits were basted with 5 cm<sup>3</sup> of HNO<sub>3</sub> and boiled on hot plate magnetic stirrer heater for 1 hour. Afterwards, 5.0 cm<sup>3</sup> of concentrated HNO<sub>3</sub> and 2.0 cm<sup>3</sup> H<sub>2</sub>O<sub>2</sub> were added again and heated for 1 hour. After cooling, the solution was profiltrated through quantitative filter paper into volumetric flask of 25 cm<sup>3</sup>. which was filled up with 2M HNO<sub>3</sub>. Inductively coupled plasma optical emission spectrometry (ICP-OES) was used to

determine the content of iron in the fresh fruit of *Vaccinium myrtillus* L., *M. alba* L. and *M. nigra* L. This method provides rapid and precise analysis of 75 elements of the periodic system. Results: The results shows that quantity of iron in *Vaccinium myrtillus* L. is 1.98 mg per 100 g, in *M. alba* 0.44 mg per 100g, and in *M. nigra* 0.39 mg per 100 g. Conclusion: Quantitative analysis of the content of iron in fresh fruit of *Vaccinium myrtillus* L., *M. alba* L. and *M. nigra* L. by using ICP-OES showed that its content decreases respectively.

## **V7. Causes of lethal iatrogenic injuries [FLASH]**

Bondarev A, Pădure A

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Introduction: Cases of iatrogenic pathology are rare in medical practice and lethal ones, fortunately, represent tragic exception. Nevertheless, these situations do exist and have serious consequences for both patients and physicians. This paper aimed to establish causes of discrepancies between clinical and medico-legal diagnosis in cases of iatrogenic death. Methods: This is retrospective scientific research. Several cases of iatrogenic death in different hospitals were analyzed. All the bodies and medical records of died patients were examined by medico-legal experts at the Centre of Legal Medicine from the Republic of Moldova during last year. Results: Researched cases included two deaths due to iatrogenic pathology represented by anaphylactic shock after lidocaine intramuscular injection. Other cases were iatrogenic injuries – one case of esophagus perforation during intubation in a patient with burns and three cases of subclavian vein puncture with perforation and penetration into pleural cavity, lung injury in patients at different ages and diagnoses. Iatrogenic injuries were associated with severe condition of the patient at the hospitalization. No iatrogenic pathology or injury was diagnosed in the hospital. All patients died in a short time after medical procedures (from 30 minutes up to 16 hours). Conclusion: In some scientific sources iatrogenic pathology is considered as a category of discrepancies between clinical and medico-legal diagnosis, which appears in conditions when the correct diagnosis must be established and represents a medical mistake with decisive role in patient's death. Causes of lethal iatrogenesis could be objective and subjective. Objective ones are usually conditioned by short patient stay in hospital and severe state of patient. Subjective causes include: lack of physical examination; overestimation or underestimation of clinical or laboratory tests' data and other physicians' conclusion.

## **V8. Epidemiology of torture phenomenon in the Republic of Moldova [FLASH]**

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Introduction: Torture is currently considered one of the most serious crimes against human being and it is prohibited by international Human Rights legislation. The Republic of Moldova ratified several international standards on protection of Human Rights including specific UN and

European conventions which protect the right not to be subjected to torture, cruel, inhuman or degrading treatment or punishment. Methods: Statistical analysis of the torture phenomenon epidemiology in the Republic of Moldova was carried out. Data from annual reports of the Centre of Legal Medicine for the period 2004-2017 were studied, systemized and mathematically processed for every district of the Republic of Moldova. Results: 5088 cases of alleged torture and other cruel treatment or punishment were reported during the analyzed period of time. Most frequently torture was recorded in Chisinau (capital) – 36.42%, followed by the north area of the country (24.27%). Despite the fact that torture is a common phenomenon, in the central (19.60%) and southern (15.60%) areas this crime was less reported. Occasionally torture was recorded in the Autonomous Territorial Unit of Gagauzia (4.64%). Conclusion: Although the Republic of Moldova ratified several important instruments of international law on prohibition of torture, unfortunately this phenomenon is still applied by law enforcement. We strongly believe that in a contemporaneous society torture and other cruel treatments are not acceptable. That is why scientific studies aimed to establish its epidemiology and understand the causes are necessary in order to prevent and eradicate it.

### **V9. Perceived stress among medical students at the Faculty of Medicine in Niš [ORAL]**

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Introduction: Numerous studies have reported that a significant percentage of medical students cope with stress. Stress has a negative impact on concentration, memory and learning. It can endanger mental and physical students' health. We aimed to estimate the prevalence and severity of stress and its association with substance use and academic performance. Methods: The research was conducted from January to March 2018, at Faculty of Medicine in Niš. Data were collected using modified Stress questionnaire of the International Stress Management Association UK. The questionnaire was completed by 340 volunteers. Data were analyzed using SPSS version 16.0. Logistic regression analysis and Student's *t*-test were applied. Results: The majority of respondents, 191 (56.18%) are prone to stress, as many as 136 (40,00%) of respondents are stressed, while only 13 (3.82%) are without stress. There is no difference in the representation of stress according to sex. Stress is significantly more common among students of the fourth year of study. The highest number of students without stress is in the fifth year (11.11%), while in the first and fourth year there are no students without stress. More than 29% of students responded positively to questions that indicate learning overload. Lack of self-confidence and feelings of guilt are present in more than 25% of students. Mood oscillations, poor memory and loss of concentration were recorded in over 20% of students. Alcohol, coffee and nicotine are used by 22.53%, students, and sleeping pills and antidepressants by 15.29% of respondents. Conclusion: The majority of medical students is prone to stress or stressed at the Faculty of Medicine in Niš. It is necessary to assess their workload and prevent stress by providing mentoring and professional psychological support.



## **V10. Learning and teaching in medical education [FLASH]**

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Introduction: Learning is an enduring change in behaviour, or the capacity to behave in a given fashion, which results from practice or other forms of experience. So far four learning theories have been introduced: behaviorism, cognitivism, constructivism and social learning. By behaviorists learning represents responses to the positive and negative stimuli. In constructivism teacher should use his knowledge to enable students to connect new concepts with previously learned information. Constructivism equates learning with creating meaning from experience and this method focuses on preparing the student to problem-solve in unsafe and insecure situations. Social learning is a bridge between behaviorist and cognitive learning theories-it encompasses attention, memory, and motivation. The aim of this study was to research existing teaching theories and to make a personal teaching method for the best application to the existing teaching system. This work has been done under the auspices of ReFEEHS (Reinforcement of the Framework for Experiential Education in Healthcare in Serbia, Erasmus project) in introduction of interprofessional education course at Serbian Medical/Health science schools. Discussion: Behaviorism may not primarily teach students how to critically reflect, but shows them that good work will be rewarded. Constructivism calls for elimination of grades and standardized testing, so the students should take a larger role in judging their own progress. The responsibility for the learning outcome is equally distributed between students and the teacher. Individuals addressing practical learning problems cannot afford the luxury of restricting themselves to only one theoretical position, an understanding of every educational theory is of great importance for the good teacher.

Conclusion: When teaching medical students the best way is to carefully analyze their learning methods and combine it with the most appropriate teaching method for their needs. Students do not all learn in the same way, so this approach should be as personalized as possible. The most preferred goal is to achieve future practitioners to critically reflect.

## **V11. Medication review as a tool to optimize prescribing in residential home center for elderly [FLASH]**

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Introduction: aging is often associated with comorbidities and following introduction of numerous drugs in everyday therapy. The potential for negative outcomes and drug related problems regarding multiple medications in older people is well documented. Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) have been developed to identify potential inappropriate prescriptions and potential

prescribing omissions. The aim was to measure the prevalence rates of polypharmacy and potential inappropriate prescriptions in residential home care for older patients using STOPP/START criteria. Secondly, we evaluated the level of medication adherence. Methods: We reviewed therapy of 45 residential home care patients over the 65 in Gerontological centre Nis, Serbia, using the STOPP/START criteria. Also, we determined their level of medication adherence by Morisky 8 scale. All data were statistical processed by SPSS software. Results: Patients with identified STOPP criteria were older and had higher number of drugs. Considering START criteria, there were no differences between patients still; the rate of STOPP criteria per drugs was low ( $0.18 \pm 0.14$ ), as well as the rate of START criteria per drugs ( $0.15 \pm 0.07$ ). The results showed that whether STOPP/START criteria were identified or not, there was high level of medication adherence within investigated population. Conclusion: In spite of the presence of polypharmacy in older patients in residential home centre and number of STOPP criteria, rate of STOPP criteria per drugs was low and level of medication adherence was high. Constant medical supervision may lead to projected health outcomes, but medication review by pharmacist can be reliable tool for optimization and management pharmacotherapy and additional help to physician in everyday practice.

## **V12. The influence of chronic alcohol abuse on aging (FLASH)**

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Introduction: Research suggests that both light and moderate alcohol use has health benefits and it is associated with reduced all-cause mortality. On the other hand, higher levels of alcohol consumption have harmful effects on the body, leading to premature and exaggerated aging. Methods: We performed a literature review on the association between alcohol consumption and aging, based on studies published in medical journals, during the last 10 years. Results: The relationship between alcohol consumption and the aging process is bilateral. On the one hand, the effects of the chronic alcohol abuse on the ageing process include: hypertension, cardiac disorders, various typed of cancer, gastrointestinal diseases, neurocognitive deficits, bone loss, and emotional instability. Alcohol abuse also determines the dehydration the entire body, including the skin, and that will further accelerate the skin aging. On the other hand aging alters the organism's physiological and psychological responses to alcohol. For instance the brain appears to experience an age-related increase in sensitivity to alcohol and a chronic alcohol use leads to global and regional atrophy of the brain. However some research shows that light to moderate drinking may have health benefits, like protecting from coronary heart disease. Also the moderate alcohol consumption influences the mood in a positive way, by its anti-anxiety and anti-stress properties. Conclusion: The relationship between alcohol consumption and aging is bilateral. Chronic alcohol consumption has deleterious effects on almost all the organs and systems of the body. In the same time the aging process alters the organism's physiological and psychological responses to alcohol.

### **V13. Lifestyle at pediatric age: a chance for a healthy adult [FLASH]**

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**Introduction:** Ensuring adequate nutrition in the first 2 years of life is the major element for organogenesis, for the development of the immune system and the nervous system. Decreased growth is associated with low intellectual and cognitive performance, poor immune system. Natural feeding, complementary nutrition (timely introduction of solid foods) according to age, qualitatively and quantitatively in normal socioeconomic conditions will ensure adequate growth and development, and will also reduce the risk of certain pathologies - clinical manifestations allergic type, obesity, gluten intolerance, metabolic disorders with late-onset response. The aim of the study was to identify the risk factors in the first year of life and the development of obesity at children aged between 0-3 years. **Methods:** The lot of study included 32 children aged 6-36 months old diagnosed with nutritional problems. These parameters followed were weight and height at birth, duration of natural feeding, diversification moment, age at onset of the weight gain, family history of obesity, food intake (assessment of protein and caloric intake in diet). Weight, length, weight-for length, and BMI were noted at 6, 12, 18, 24, 30 and 36 months of age. **Results:** In the study group, 62.5% of patients were boys. 7 patients had a family history of obesity and 3 of them had both parents obese. Natural feeding was noted in 31.25% of patients. Early diversification was found in 62.5% of cases. Improper diversification (hypercaloric diet with a lower content in vegetables and fruits) was found in 68.75% of cases. 4 children developed milk protein intolerance. **Conclusion:** Ensuring an early optimal nutritional support is the key element. Given the numerous health risks associated with incorrect nutrition at critical age, the identification of dietary risk factors in early life is very important for prevention. Parent's education is important for a proper nurturing of children in the first 2 years of life in order to prevent pathologies on a long-term.

### **V14. The administration of vitamin D from childhood to adult [ORAL]**

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**Introduction:** The effects and implications of vitamin D in the development and proper functioning of the human body have been well studied, recognizing the importance of this vitamin in the absorption and normal use of calcium and phosphorus and maintaining normal calcium levels in the blood, maintaining bone and muscle health, and tooth structure, normal functioning of the immune system, cell division, obesity. Vitamin D doses are varying depending on body age and needs in the different accelerated growth periods of infancy, puberty and adolescence. **Methods:** Given the major implications of vitamin D deficiency in pathology, the authors present 3 clinical cases that exemplify some of the roles of vitamin D. **Results:** The first case is a 10-month-old infant, diagnosed with malabsorption syndrome, who also has associated vitamin-protein pluri-parental syndrome. The second case is an adolescent with joint and bone

pain, which has been diagnosed with hypovitaminosis D and hypocalcaemia. The third case is a 9-year-old girl, known with obesity and respiratory allergy, in which routine biological evaluation found a major vitamin D deficiency. Conclusion: Knowing the implications of vitamin D in the body and the sensitive periods of growth and development, it is important to make biological determinations of vitamin D levels, in order to do proper prophylaxis and intervene promptly when changes occur. Prophylactic doses of vitamin D will be adjusted depending on the patient's individual characteristics and on the risk factors for the occurrence of different pathologies.

### **V15. Effect of monoammonium glycyrrhizinate and aminosteroid U-74389 G on DNBS-induced colitis [FLASH]**

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**Introduction:** Dinitrobenzenesulfonic acid-induced colitis allows to investigate the effects of potential drugs and mechanisms underlying damages and inflammatory response. Our aim was to study the protective effect of combination of lazaroid U-74389G with monoammonium glycyrrhizinate (MAG) on 2,4-dinitrobenzenesulfonic acid hydrate (DNBS)-induced colitis in Wistar rats. **Methods:** Animals received U-74389G (at a daily dose 5 mg/kg i.p.) and MAG (at a daily dose 100 mg/kg i.p.) for 6 days, starting 1 day before the induction of colitis with intrarectal administration of 30 mg DNBS in 0.25 ml of 50% ethanol. Body weight of the rats, food intake and consistency of fecal material were recorded as markers of clinical condition. On day 6 colonic tissues were excised and scored for macroscopic and histological damage. Microscopic changes were assessed by light microscopy on hematoxylin/eosin-stained histological slices. **Results:** DNBS decreased significantly bodyweight (from 246.25±7.9 g to 206.25±6.09 g, p=0.04). During the experiment, rats treated with U-74389G and MAG recovered their initial weight. Combined treatment with U-74389G and MAG reduced colonic macroscopic damages (U-74389G plus MAG score was 0.67±0.33, DNBS score was 3.87±0.60; p<0.05). All other assessed macroscopic parameters were significantly improved in animals treated with U-74389G and MAG. The microscopic tests showed that group received the combination had significantly lower score compared with DNBS group. **Conclusion:** These findings indicate that combined treatment with U-74389G and MAG inhibits significantly colonic inflammatory damages in a rat model of inflammatory bowel disease.

### **V16. Ageing and capacity to take informed decisions: a literature analyze of the phenomenon [ORAL]**

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**Introduction:** Informed consent, integral part of the therapeutic relationship, assumes more than just simply putting a signature on the informed consent form. It is a process, during which the patient analyzes, understands and decides voluntarily after receiving the necessary information regarding medical procedure, possible risks and benefits. **Method:** The authors analyzed the literature in order to identify the extent in which the right of elderly patient of being informed regarding the diagnosis and treatment, the right to confidentiality and to take informed decisions regarding the medical procedure and therapy are respected. **Results:** The studies show that medical professionals question the elderly capacity of taking decisions, many times just because of their old age, the doctor-patient relationship returns to the traditional, paternalistic type. Thus, as the person gets older, the smaller the number of patients which receive complete information regarding: diagnosis, treatment, informed consent form, and the agreement to inform the family members or friends. On the contrary, it is much higher the number of cases in which the doctor asks first (or only) the family to take medical decisions on behalf of the elderly patient. **Conclusion:** Studies results underline the importance of being respected the autonomy of the patient, extending the request for informed consent to the family members requiring a careful objective analyze of the mental capacity of the elderly to understand the information and to take informed decisions. Subjective assessments such as old age should be avoided as well.

### **V17. Elder abuse: an alarm towards prevention [ORAL]**

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**Introduction:** Elder abuse is a serious form of violence, with more than half of the offenders being family members. As the world's older population is in a continuous growth, the number of abused elder persons increases correspondingly. Therefore, this phenomenon requires the implementation of programs meant to help the victims. **Methods:** We made a research in the literature in order to identify the magnitude and the various types of elder abuse, the risk factors, consequences over the victims and methods to prevent and combat this form of violence. **Results:** WHO estimates that 15.7% of the people over 60 years are subjected to abuse, with a higher rate in women. In reality the number may be even higher, as many of the victims do not report the abuse, estimating that for 1 reported victim 23 remain unreported. Elder abuse comprises many forms: physical abuse (0.2–4.9%), psychological abuse (0.7–6.3%), financial abuse (1.0–9.2%), neglect (0.2–5.5%), sexual abuse (0.04–0.82%) and violation of rights. Regarding risk factors, people significantly disabled, in poor physical health, with depression and low income or socioeconomic status present the highest risk to be the victims of abuse. The most severe consequence of the elder abuse is the victims' premature death. The victims may also suffer from pain, sleep disturbances, different types of injuries, as well as stress and depression. **Methods to combat and prevent elder abuse** include awareness campaigns, residential care policies to define and improve standards of care, development of evidence-based interventions to prevent elder abuse, providing services to victims of elder abuse and collaboration between criminal justice, health and social services. **Conclusion:** Elder abuse is an alarming issue, and more complex the problem is, more difficult being to prevent it. Nevertheless, collaboration between public services (justice, health, social) might significantly increase the rate of success.

### **V18. Attenuation of amiodarone-induced pneumotoxicity by Mn (III tetrakis (4-benzoic acid) porphyrin [FLASH]**

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**Introduction:** Catalytic antioxidant metalloporphyrins have been proved to have protective role in inflammatory conditions, inhibiting inflammatory gene expression in response to reduced generation of reactive oxygen species such as superoxide, peroxide, peroxy nitrite and lipid peroxy radicals. We examined the effect of manganese(III)tetrakis(4-benzoic acid)porphyrin (MnTBAP) on amiodarone (AD)-induced pulmonary toxicity in the rat model. **Methods:** The study was carried out on 48 male Wistar rats, divided into four groups: (1)–controls; (2)– treated intratracheally (i.t.) with AD; (3)–treated with AD and MnTBAP; (4)–treated with MnTBAP. AD was administered i.t. on days 0 and 2 (6.25 mg/kg). MnTBAP was injected intraperitoneally at a dose 10 mg/kg on day 0, 1 and 2. Cytologic and biochemical (activity of lactate dehydrogenase (LDH), acid phosphatase (AcPh), alkaline phosphatase (AlPh) assays of bronchoalveolar lavage fluid (BALF) was performed on day 3. Pulmonary fibrosis was assessed by measuring hydroxyproline (HP) content in lung homogenate (LH) on day 28 after AD administration. **Results:** AD treatment resulted in significantly increased protein content; total cell count; polymorphonuclear cells; activity of LDH, AcPh and AlPh; and content of HP. The treatment with AD and MnTBAP decreased the markers of pulmonary inflammation and cytotoxicity in BALF compared to AD group. The content of HP in AD+MnTBAP (2.25±0.16 mcg/ml LH) group was decreased compared to AD alone (3.34±0.15mcg/ml LH) on day 28 (p<0.05). **Conclusion:** MnTBAP reduced early AD-induced inflammatory injury and can protect animals from AD-induced pulmonary fibrosis.

### **V19. Unresectable malignant liver disease: treatment with percutaneous radiofrequency ablation [FLASH]**

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**Purpose:** To evaluate the efficacy of radiofrequency ablation (RFA) in malignant liver disease (hepatocellular carcinoma and liver metastases), which are considered to be unresectable because of their distribution, their number, and/or the presence of liver dysfunction. **Methods:** In the period from 2005-2017, 84 patients were treated using RFA during a total of 111 sessions and treating 123 lesions of various size, number and localization. The median diameter of tumor was 3.1 cm (range 1.7-6.9 cm). The method of RFA was applied percutaneously under computed tomography (CT) (57 patients) or ultrasonographic (USG) navigation (27 patients). The choice of the electrode type was based on lesion size and location. A pulsed RF energy was applied for

15–20 min (depending on the size of the lesion and the vessel next to it) to evaluate the lesion's immediate response and identify any potential complications, dualphase dynamic contrast-enhanced CT was performed. After ablation patients were hospitalized for 24-h monitoring. Results: No serious complications after RFA treatment occurred. Complete tumor necrosis was achieved in 85.7% and tumor recurred in 12 patients (14.3%) with lesions larger than 5cm. Distant intrahepatic recurrence was diagnosed in another 15 (17.8%). Distant metastases were found in 24 (28.6%) patients. 12 of these 24 patients had also distant intrahepatic recurrence of disease. One year survival rates were 82%. Conclusions: RFA is appreciated as a minimally invasive method of treatment for liver malignancies that reduces morbidity and mortality.

### **V20. Super selective segmental renal artery embolization as treatment in massive renal hemorrhage [FLASH]**

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Objective: Renal haemorrhage is a major life-threatening condition that can be caused by trauma, operation, biopsy, as well as sudden spontaneous rupture of renal tumours or aneurysms. We report our experience with super selective segmental renal artery catheterization and embolization as therapeutic options for such cases. Method: The last 3 years, 11 patients with severe renal haemorrhage were admitted for evaluation and possible further treatment. 4 of them had a history of previous biopsy, 1 patient had a recent percutaneous nephrostomy, 4 patients presented with renal mass ruptures (2 patients renal cell carcinoma, 2 patient angiomyolipoma), 1 patient hemorrhagic cysts, and 1 patient was hospitalized after a car accident. They all presented with clinical signs of hemodynamic instability. Angiographic investigation of the kidneys preceded further intervention in all cases. All of the 11 patients underwent super selective embolization of the specific bleeding vessel with the use of microspheres and/or onyx. Results: All patients treated by super selective segmental renal artery embolization had a successful outcome, including a steady renal function and a stable clinical course. No complications occurred. Conclusion: Super selective segmental renal artery catheterization and embolization is a safe and efficient method for the treatment of patients with severe renal haemorrhage, preserving healthy renal parenchyma and renal function.

### **V21. Image guided percutaneous cholecystostomy in critically ill patients hospitalized in intensive care unit [FLASH]**

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Purpose: to evaluate the efficacy of image directional percutaneous cholecystostomy in cases of lithiasic or acalculous cholecystitis in critical condition patients, hospitalized in intensive care unit. Material and method: 24 patients hospitalized in the intensive care unit have been managed with percutaneous cholecystostomy, because of possible lithiasic or acalculous cholecystitis. The

indication for this procedure emerged according to the clinical signs- fever of no other origin- and the ultrasound findings that revealed possible inflammation of gall bladder - dilatation, double wall, pericholecystic fluid, debris and possible gallstones. In 14 patients the procedure took place at the ICU under ultrasound guidance. The rest 10 patients could remove to fluoroscopy department and the procedure accomplished under fluoroscopy. After the fixation of gall bladder to the abdominal wall with the proper hooks, a drainage tube was placed intraluminal between the hooks, for the drainage of bile. Results: percutaneous drainage of gall bladder with total removal of its content, was successful in all the patients and no complications occurred. Clinical improvement appeared in 18 of 24 patients. After full recovery 9 of 24 patients underwent surgical cholecystectomy. Conclusion: percutaneous cholecystostomy remains an important method for the management of patients with clinical suspicion of cholecystitis and who also have contraindication for surgery. Especially for patients hospitalized in intensive care unit, percutaneous cholecystostomy is preferred instead of open cholecystectomy, as it provides lower morbidity with equal success and equal direct outcome for the patients.

## **V22. The importance of supplementing with essential fatty acids: from intrauterine to adult life [ORAL]**

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Introduction: Fatty acid are important in terms of their impact on human health. Studies had shown that fatty acids improves plasma TG levels and influence the levels of other lipids and lipoproteins including HDL-C and LDL-C. By modifying lipid profiles, fatty acid may have protective effect against cardiovascular events associated with obesity. There is also evidence that increased intakes of these fatty acids can reduce body fat in humans. Methods: The study cohort consists of 61 overweight and obese adolescents with dyslipidemia evaluated in Saint Mary Children's Hospital Iasi. Anthropometric examination (weight, height, waist circumference, body mass index), liver aminotransferase levels, glucose and lipid profile were assessed. Obesity and overweight were defined according to CDC recommendations. Children with dyslipidemia received poly-unsaturated fatty acid supplementation. Results: From the study group 42.6 % of patients had borderline values of cholesterol and 18 % had high cholesterol, 5 % had high LDL-cholesterol and 11.5% had borderline values of LDL-cholesterol. 29.5 % of patients had hypertriglyceridemia and 6 patients had mixed dyslipidemia. From the study group 9 patients had hepatic steatosis. After 3 month of fatty acid supplementation triglyceride levels reduced by at least 10% compared with baseline, but levels of total and low-density lipoprotein cholesterol levels did not change significantly. Also, the ultrasonographic aspects of steatosis improved in all children. Conclusion: Daily supplementation with fatty acid improves triglyceride levels and lowers the degree of steatosis in obese adolescents.



### **V23. Relations between valuables profiles and valuables typology in medical professionals (wis/svp) (FLASH)**

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Introduction: In our country the studies among the medical personnel are sporadic. One of the targets of the executed complex search (Research project at Medical University – Pleven) is to determine the specific nature of work-connected value orientation. Methods: In this material are commented the results of WIS/SVP Method –An appraisal scale of professional values with 72 doctors, nurses and obstetricians all at UMHAT –city of Pleven. In the method were specified five groups of value profiles: MATER, SELFO, OTHER, INDEP and CHALL and six value types: creative, calm, ambitious, tough, autonomous and social. For surveying the dependencies was used statistic program StatGraf. Results: Positive significant dependencies are stated between materialistic orientation and orientation to challenges ( $r=.396$ ,  $p=0.000$ ) and with the value profile “ambitious” ( $r=.750$ ,  $p=0.000$ ). The ambitious value type has a negative statistic connection with the creative type profile” ( $r=-.501$ ,  $p=0.000$ ) and a positive connection with calm value type ( $r=.358$ ,  $p=0.000$ ). Tough value type shows features that differ from these of the creative type ( $r=-.302$ ,  $p=0.01$ ). Persons orientated to their selves ( $r=-.451$ ,  $p=0.000$ ) do not fall to this group as well. The calm value type is orientated to the others ( $r=.369$ ,  $p=0.001$ ), to the materialistic ( $r=.299$ ,  $p=0.01$ ); it correlates positively with the markers of ambitious one ( $r=.358$ ,  $p=0.000$ ) and it correlates negatively with the markers of autonomous ( $r=-.461$ ,  $p=0.0001$ ) and the social value type ( $r=-.424$ ,  $p=0.0003$ ). Tough (strong) type has as a specific feature “orientation to challenges” ( $r=.548$ ,  $p=0.000$ ), it is in negative statistic relation with “orientation to oneself” ( $r=-.451$ ,  $p=0.0001$ ) and with the features modeling the creative value type ( $r=-.302$ ,  $p=0.01$ ). Conclusion: The research demonstrates interrelations between the value types and orientation types in the sphere of professional activity. Among the respondents the representatives of calm type, then follow the persons of creative and ambitious type. The group of tough value type has contradictive typology. The results of the commented indices of this method are not significantly influenced by the demographic data; this confirms a already completed personal typology.

### **V24. Treatment of occupationally related damages of intervertebral discs in the lumbar region [FLASH]**

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**Introduction.** Intervertebral discs are a form of mobile bonding, which is due to their specific structure. The clinical picture of injuries includes pain, vertebral and radicular syndromes. The aim of the study is to investigate lumbar disc damages in patients with occupational risk and to propose a treatment algorithm. **Material and methods.** The subject of the study is 35 cases of damage to intervertebral discs in the lumbar region in patients with occupational risk. Clinical, instrumental and statistical methods of investigation are used. **Results.** In 82% of patients, improvement of pain and sensory lower leg syndromes was identified. 80% of people improved the gait and performance of day - to - day activities. The volume of movements in the lumbar region and the hip joints increased. **Conclusions.** Complex medical and physical treatment is effective in patients with professional disc pathology in the lumbar region. The proposed algorithm for treatment is effective, accessible and easy to implement in hospital care units.

## **V25. Genetic awareness of breast cancer [FLASH]**

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**Introduction:** Breast cancer is the most common cause of cancer deaths in women. It has been estimated that in the United States at the age of 70 , one in ten women will develop breast cancer. **Method:** It has been reviewed the Greek and international bibliography and specific articles referring to the genetic awareness of breast cancer, which have been published in the databases Pub Med and Science Direct , during 2002-2017. **Results:** The pathogenesis of breast cancer is complicated and depends on physiological, environmental and genetic factors. Clinical signs that create suspicion of familiar cancer are the disease of two close relatives, multiple or bilateral cancers in the same individual, early appearance and accumulation of tumors. The human genes BRCA1 (Breast cancer Type 1 susceptibility gene) and BRCA2 (Breast cancer Type 2 susceptibility gene) belong to the class of tumor suppressor genes, genes whose normal function prevents tumor genesis. These genes control the growth and division of cells, that control breast milk pores. Mutations in these genes have been associated with hereditary breast or ovarian cancer. The risk of developing breast cancer in the female population increases if a deficiency mutation is inherited in the BRCA1 and BRCA2 genes. Mutations in these genes are responsible for just 5-10% of breast cancer cases. But they are not all high-risk mutations, some are harmless. Considering the male population, the carriers of pathogenic mutations in the BRCA1 and BRCA2 genes have an 8% risk of developing breast cancer, compared to 0,1% of the general population. There is an increase in risk by 80 times. **Conclusions:** The appearance of such high-risk mutations in the male and female population does not mean that cancer will definitely develop. If, in the end, cancer is developed, it cannot be attributed solely to these mutations.

## **V26. General classes of cancer genes [FLASH]**

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Introduction: Cancer occurs through a series of body changes in DNA, resulting in cellular multiplication. The field of study of these mutations, as well as the consequences, is known as Cancer Genetics. Method: It has been reviewed the Greek and international bibliography and specific articles referring to the general classes of cancerous genes, which have been published in the databases Pub Med and Science Direct, during 2002-2017. Results: Changes in the DNA sequence due to physical transformations, and then to cellular multiplication, may result from some random replication errors, from carcinogenic exposure (e.g. radiation) or from incorrect DNA repair procedures. Almost all cancers originate from only one cell. This clonal origin is an element of the distinction between neoplasia and hyperplasia. For the transfer of the normal to the wholly malignant phenotype, many cumulative mutagenic events are required. The stages of progression of a physical mutation, with accumulation of conversions in different genes, results in the progressive transition of the epithelium into adenoma and then into carcinoma. The flow of cancer is as follows: 1. Normal epithelium, 2. Early adenoma, 3. Intermediate adenoma, 4. Subsequent adenoma, 5. Carcinoma and 6. Metastasis. The first major class of cancerous genes is included in genes. Genes that directly affect cell growth with either oncogenes or tumor suppressors. These genes by their ability to control cell division have an effect on tumor growth. In cancerous cells, oncogenes introduce mutations and lead to increased activity of gene products. The second major class of cancerous genes is the administrators, where they do not directly affect cellular growth. Administrators influence the ability of the cell to maintain the integrity of its genome. Deficient cells in these genes have a high percentage of mutations in all genes, including oncogenes and tumor suppressor genes. Conclusions. The mutation phenotype was first reported by Loeb, by explaining how multiple mutational events are essential for carcinogenesis.

## **V27. A multidisciplinary approach in identifying a missing person based on craniofacial skeleton: a case report [FLASH]**

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Forensic expertise performed on skeletal fragments has a crucial role in identifying the person. The purpose of this presentation is to establish the importance of the multidisciplinary approach based on the collaboration between forensic doctor, forensic artist, criminal investigators and prosecution authority, in identification of a missing persons, even if we are talking about just a

skeletonised skull. We will present the case of a human craniofacial skeleton, forensic examined at Bihor County Forensic Service. The skull was found at the edge of a forest in Bihor County; no other human bone fragments have been identified in the surrounding area. We proceed cranioscopic examination and craniometric measurements for the determination of race, gender and age. The electronic teller, the anthropometric compass of Martin type and the millimeter ribbon were used. Digital photos were taken. Biological samples were also sampled for possible genetic testing. Our conclusions lead us to a human skull, of a 45-55 years old, male, without post-traumatic lesions. A forensic artist performed the robot portrait of the missing person, applying the bidimensional facial reconstruction technique. He took in consideration photos of the human skull and the results of the anthropometric measurements. Corroborating the results of forensic expertise, the robot portrait and the data obtained from criminal investigators, we managed to obtain a biological profile of the missing person.

### **V28. Fatal ground- level falls in the region of Attica, Greece, 2011-2015 (FLASH)**

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**Introduction:** Falls have emerged as one of the major causes of unintentional fatal injury in several developed countries. As aging is accompanied by deterioration on various systems and abilities of the human body and affects gait and stability, older people are known to be a particularly vulnerable age group to fatal ground- level falls. **Methods:** We identified 36 cases of fatal accidental ground-level falls, which occurred in the region of Attica and were assigned to our Department during the years 2011-2015. The epidemiological characteristics of the subjects, the circumstances of the accidents and the characteristics of the injuries were recorded. **Results:** In 20 of the cases the victims were men (55.6%), while in 16 (44.4%) women. Victims' ages ranged between 45 and 96 years old with the vast majority (31 cases -86.1%) being >65 years old. Half of the cases of the fatal ground- level falls (18 cases) took place inside or near the victims' residence, 9 occurred in public places (for example on the street), 1 in the victim's workplace and in 5 cases the place of the fall was unknown. Seventeen of the fallers died within 24h of the accident while the rest were hospitalized for up to 45 days before their death. The cause of death was mainly craniocerebral trauma (12 cases) or endocranial haemorrhage (13 cases) alone or in some cases (4 cases) accompanied with neck trauma. Notably, 5 people died due to post-traumatic complications (pneumonia, myocardial infarct or multiple organ failure), which occurred during their hospitalization. **Conclusion:** People over 65 years old seem to be more often victims of fatal accidental ground- level falls occurring mostly inside or near their residence. Head and neck are the main body regions seriously injured after a ground- level fall.

### **V29. Foci of Hard Ticks (Ixodidae) in areas with increased outdoor activity near to the town of Pleven, Bulgaria [FLASH]**

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**Introduction:** Ticks were the first arthropods established as vectors of pathogens and currently they are recognized, along with mosquitoes, as the main arthropod vectors of disease agents to humans and domestic animals globally. **Aim:** To identify areas with high population density of ticks and the risk to public health. **Material and methods:** During the period 2016-2018 were collected hard ticks through drag-flag method from areas around Pleven with increased outdoor activities. Species, stage of development and sex were determined of all specimens. Among the collected ticks, *Ixodes ricinus* specimens were examined by darkfield microscopy for the presence of *Borrelia* spp. The density of the tick population in the different areas was determined. **Results:** For the period 2016 – 2018 during the months of February to June were collected a total of 759 questing hard ticks. The highest number was *Ixodes ricinus* (n = 575). Three hundred and fifty-four of them were examined by darkfield microscopy. Presence of *Borrelia* spp. was found in 114. The analysis of the data allowed the identification of 5 areas around the city of Pleven with a high frequency of *Ixodes ricinus* ticks. The degree of infection with *Borrelia* spp. ranges between 15.5% and 41.9%. **Conclusion:** Pleven region, with its geographical localization and climate, is an appropriate area for tick abundance. Our results show that during their outdoor activities, people are exposed to tick bites and there is a potential risk for Lyme borreliosis infection.

### **V30. Blastocystosis in the Pleven region [FLASH]**

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**Introduction.** Although it was discovered more than a century ago (1911, Alexieff), *Blastocystis* spp. is still a microorganism with a pathogenic potential not fully understood, and whose place in the classification of species is unclear. This parasite is characterized by a morphological diversity pronounced and is found in vacuolar, granular, ameboid and cystic forms. Routine light microscopy investigations most often reveal vacuolar forms of *Blastocystis* spp., sized 4 to 150 µm. We aimed to study the incidence of blastocystosis in different categories and age groups of the population of Pleven region in the period 2015 through 2017. **Materials:** Medical records of 21766 subjects, from who fresh stool samples collected. The samples were investigated by light microscopy, in native preparation stained with Lugol solution. The investigations were made at the laboratory of parasitology at the second outpatient clinic in Pleven. The subjects investigated were referred for prophylactic checkups or because of clinical findings. **Results:** Of the 21766 subjects investigated just once, *Blastocystis* spp. was found in 486 (2,23 %). Of all the 21766 subjects, 19245 (88,42%) were checked for the purposes of prophylaxis, and 2521 (11,58%) sought medical advice because of complaints. The prevalence of blastocystosis among those prophylactically investigated was 1,69 %., and among those with clinical findings the it was 6,39

% Conclusion: The investigations carried out on a large group of subjects, including both children and adults, showed a prevalence of *Blastocystis* spp. of 2,23 %. These findings indicate that both healthy subjects and such with clinical symptoms are carriers of the pathogen.

### **V31. Comparison of retinol concentrations in colostrum samples: influence of maternal age, dietary habits and lifestyle [FLASH]**

Denić M, Sunarić S, Kocić G

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Introduction: Nowadays, there is a great interest in research on the composition of human milk obtained from nursing mothers over 35 years compared to younger mothers. As retinol plays a crucial role in protecting newborns from oxidative stress and infections and is required for normal differentiation of epithelial tissues and the visual process, the purpose of our study was to determine the retinol concentrations in colostrums samples and assess its potential relationship with maternal age, dietary habits and lifestyle. Methods: Colostrum samples were collected from healthy mothers who delivered healthy term babies. All participants were divided in two groups: A (aged  $\geq 35$ , n=22) and B (aged  $< 35$ , n=21). Maternal dietary patterns and lifestyle (smoking and alcohol drinking) habits were obtained through questionnaire. Total lipids concentration was measured by gravimetric method and retinol concentration was determined by HPLC. Results: In group A, considerably higher levels of retinol and lipids ( $0.960 \pm 0.128$   $\mu\text{g/mL}$ ;  $3.376 \pm 0.309\%$ ) were found compared to group B ( $0.728 \pm 0.124$   $\mu\text{g/mL}$ ;  $2.425 \pm 0.311\%$ ) ( $p < 0.05$ ). In general, strong positive correlations between retinol and fat concentrations ( $r = 0.668$ ), retinol concentrations and maternal age ( $r = 0.646$ ) and fat concentrations and maternal age ( $r = 0.821$ ) were observed. Comparing retinol levels and maternal dietary habits, we found moderate positive correlation for group A ( $r = 0.424$ ) and weak positive correlation for group B ( $r = 0.321$ ). Contrary, comparing retinol levels and maternal smoking and alcohol drinking habits, very weak negative correlations were obtained for both groups (A:  $r = -0.159$ ,  $r = -0.035$ ; B:  $r = -0.023$ ,  $r = -0.092$ ). Conclusion: Mean retinol concentration in colostrums obtained from mothers with advanced maternal age is elevated compared to younger mothers. Primarily, these differences might be greatly related to higher total lipids content, as well as, in lesser extent with maternal dietary habits. Additionally, this finding is not significantly affected by maternal smoking and alcohol drinking habits. Acknowledgements: This research was funded by the Ministry of Education, Science and Technological Development of Serbia (Project No. TR 31060) and Faculty of Medicine, University of Niš (Internal scientific project No. 2; 11-14629-4/2).

### **V32. Retinol and $\beta$ -carotene content in some enriched and flavoured milk products popular among younger population [FLASH]**

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Introduction: Vitamin A (retinol) is essential fat-soluble vitamin that is necessary for normal development, growth, immune function and eyesight. Retinol is found in milk and dairy

products, whereas  $\beta$ -carotene (pro-vitamin A) is present in foods of plant and animal origin and can be converted into retinol in the human body. Adequate intake of vitamin A through diet is particularly important for children and younger populations in the period of growth and development in order to prevent the deficiency of this vitamin. The objective of our study was to evaluate retinol and  $\beta$ -carotene content in some enriched and flavoured milk products popular among younger population. Methods: Enriched milks, chocolate milks and milkshakes were collected from local shops and prepared for analysis right after opening. After samples saponification and extraction, retinol and  $\beta$ -carotene content were determined by HPLC. Results: Retinol and  $\beta$ -carotene contents in analyzed samples were in the range of 68.9-87.5  $\mu\text{g}/100\text{mL}$  and 3.6-5.5  $\mu\text{g}/100\text{mL}$  for enriched milks, 11.6-26.1  $\mu\text{g}/100\text{mL}$  and 0.42-1.13  $\mu\text{g}/100\text{mL}$  for chocolate milks and 17.4-20.8  $\mu\text{g}/100\text{mL}$  and 0.86-0.94  $\mu\text{g}/100\text{mL}$  for milkshakes, respectively. Conclusion: Enriched milk samples could easily supply RDA values for vitamin A for children and younger population, primarily, because of optimal fortification of this type of products with retinol and  $\beta$ -carotene, as well as, because of higher fat content (2.8%-3.2%). Lower levels of retinol and  $\beta$ -carotene in chocolate milks and milkshake samples might be related with significantly minor milk fats (0.5%-1.0%) so these products could not completely provide required amounts of vitamin A. Acknowledgements: This research was funded by the Ministry of Education, Science and Technological Development of Serbia (Project No. TR 31060) and Faculty of Medicine, University of Niš (Internal scientific project No. 2; 11-14629-4/2).

### **V33. Comparative studies of different chitosan types for medical applications [FLASH]**

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Introduction: Nowadays, one of the food supplement used in dietary regimen is the chitosan, known as a functional, biocompatible and biodegradable biopolymer. Chitosan has good lipid adsorbent properties as well as a good solubility in diluted acidic solutions due to the presence of amino groups in the glucopyranose ring. Due to the absorption capacity of lipids, especially of circulating cholesterol, it is necessary to study chitosan as a useful therapeutic element in the hypocholesterolemia therapy with antiatherogenic effects and prevention of cardiovascular hazard. At the same time, the effect of blood cholesterol decreasing could be used in hepatic steatosis. Methods: Two samples of chitosan extracted from local marine sources were investigated and compared with those of three commercial food supplements based on chitosan existing on Romanian market, chosen as references. Analyses were carried out according to ASTM F 2103-11, concerning their chemical structure (FTIR analyses), solubility in diluted acetic acid, fat binding capacity and insoluble impurities. Different types of fats were tested in order to establish the most effective fat type adsorbed by chitosan. Results: The obtained results revealed that although chitosan origin is different, it does not affect its solubility and fat binding capacity and from point of view of the chemical structure, the studied samples are similar. Conclusion: New chitosan extracted from local marine sources could be used as a potential

material in biomedical applications. More detailed medical studies will be performed in order to establish chitosan effectiveness in dietary regimen.

### **V34. Damage of the intervertebral discs in the lumbar spine when working under occupational risk [FLASH]**

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**Introduction.** The aim of the study is to examine the damage of intervertebral discs in the lumbar spine at work in occupational risk and to propose measures for the prevention of occupational diseases. **Material and methods.** The subject of the study is 35 cases of disc pathology in patients hospitalized in the Department of Occupational diseases, University Hospital – Pleven, in the period 2013 – 2017. Clinical, laboratory, functional and imaging diagnostic methods have been used. **Results.** All persons surveyed have more than 5 years experience in professional risk. Over 80% of persons work in a forced posture. More than 60 % of patients perform system work requiring lifting or carrying heavy loads. **Conclusions.** Damage of the intervertebral discs in the lumbar spine is an actual health problem for people working in a number of professions. Preventive measures are needed to protect the health and employability of workers in occupational risk.

### **V35. Aggressiveness in children: an alarming reality [ORAL]**

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**Motto:** Who did not feel it, he cannot believe what violent passions he or she is doing in the heart of the child, like a snake nestled in the breast; quoted from Joan Lluís Vives. Aggressiveness is an attribute present in the animal world on all its evolutionary scales, ethnologists have affirmed; they draw attention to the fact that, in the case of the human being, beyond its usefulness for the success of an action, aggression has evolved from the innate reaction to adaptation to destructive and violent behavior towards persons, objects or to oneself. Aggressiveness in children is a very important problem that we often encounter in our society. This behavior, beginning at very young ages, 2, 3 years, can have very serious consequences leading to unhealthy aging. Parents often do not know how to manage this situation even reaching out by accepting this behavior of their children. However, there are parents who are intuitive about future issues and are looking



for specialized help, often reaching to a psychologist. But the problem of aggression in children may have other causes, of a medical nature. A series of biochemical investigations they led me to see that aggressiveness is caused by a high level of heavy metals – lead in their blood and a high level of testosterone. The desired outcome is to achieve a treatment that will improve or even stop aggressiveness in children. It can be stopped with a good collaboration between parents, teachers, doctors and psychologists. The healing of society must begin with the healing of children. They have to grow healthy.

### **V36. Ultrasonic influence on biofilm-forming bacteria isolated in patients with diabetic foot syndrome**

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**Introduction.** It has been estimated that a high percent of infections, in generally are caused by biofilms. Knowing this fact, in the present study was investigated the effect of ultrasound on biofilm-forming gram-positive *Staphylococcus aureus* and gram-negative *Escherichia coli* to clinical strains isolated from patients with diabetic foot syndrome (DFS). So the present study revealed that short-term exposure to ultrasound did not significantly affect the virulence factor, as well as the cultural and morphological properties of the *Staphylococcus aureus* isolated from patients with (DFS). Also morphological analysis is useful for the purpose of our study. **Methods.** Aim of the study is to show the effect of ultrasound on biofilm-forming gram-positive *Staphylococcus aureus* and gram-negative *Escherichia coli* to clinical strains isolated from patients with diabetic foot syndrome. Ultrasonic action on hospital strains of microorganisms was carried out by the apparatus UZT 1.03. Biofilms were evaluated by the optical density with a StatFax-2100 photometer. Microscopic method has been also used. **Results.** A number of *Staphylococcus aureus* strains and *Escherichia coli* strains with biofilm forming activity, were selected for analysis. Short-term exposure to ultrasound, respectively seconds, did not significantly affect the growth of *Staphylococcus aureus*. The density of biofilm after a few minutes ultrasound exposure significantly decreased in comparison with the initial indicator ( $P < 0,001$ ). Microscopic examination showed that a few minutes ultrasound exposure causes significant changes; the cells increased in size and the density of the cell matrix visually decreased. Relatively similar results were observed also for *Escherichia coli*. **Conclusion.** Short-term exposure to ultrasound did not significantly affect the virulence factor as a biofilm-forming ability, as well as the cultural and morphological properties of the *Staphylococcus aureus* and *Escherichia coli* isolated from patient with DFS. Ultrasonic exposure for a few minutes had a killing effect, however, the morphological, tinctorial properties and biofilm activity were changed earlier with a few minutes exposure.

### **V37. Attachement style, existential loneliness and depression among resident physicians in public hospitals of Athens [ORAL]**

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The Attachment Theory, as formulated by Bowlby, suggests that the quality of the attachment formed at the beginning of life, between the child and the caregiver, has a direct association with mental health and general functioning when the child passes into adulthood. Several mental health professionals, such as psychologists and psychiatrists, have long recognized the usefulness of Attachment Theory, as it relates to the provision of care to their patients and the psychotherapeutic interventions they apply. Physicians are often under stressful and pressing conditions, such as increased responsibility for others, life or death decisions, overtime shifts, long-lasting education (Maslach & Jackson, 1982). Their emotional exhaustion, due to their burdens, has been found to be associated with the patient's satisfaction of the services that the physician has to offer (Anagnostopoulos, Liolios, Persefonis, Sluter, Kafetsios & Niakas, 2012). Already from the first year of their specialty, resident physicians feel the pressure of their future profession and this triggers anxiety, loneliness and depression. Most researches related to physicians' loneliness concern their social and emotional dimension (Hoferek & Sarnowski, 1981. Wolf, Scurria & Webster, 1998). No findings, so far, about existential loneliness by this population, a gap that we hope, our research will cover. The aim of this research is to investigate whether the likelihood of depression is predicted / interpreted by being a physician, other demographic factors (gender, marital status, origin), social factors (work and social network), interperonal/psychological factors, such as anxiety and avoidance, according to Attachment Theory and other psychological factors, such as loneliness, preference for solitude and coping strategies of loneliness. Another purpose of the research is to investigate whether the psychological factors of Existential Loneliness and Attachment Style (ATS) will play a particularly powerful role in predicting / interpreting the likelihood of depression among doctors rather than among non-doctors. The sample consisted of 287 participants, 140 of them were resident physicians and 147 came from no medical professions. Physicians' specialties that were surveyed: Pathology, Surgery, Neurology/Psychiatry, Maternal-Child. The results of this work have shown that Existential Loneliness for both populations, doctors and non-doctors, is a predictive factor of Depression. In addition, gender has been found to be crucial for non-doctors, since women tend to declare more depression than men, which is not found among physicians. In addition, physicians are using strategies to cope with their loneliness, while on the other hand factors such as social network and working conditions have not been found to be associated with Depression. Both the origin and being in a relationship act as protective factors associated with reduced levels of Depression. Surgeons and psychiatrists / neurologists experience higher depression. No relations found, between year of specialty and Loneliness and Depression. In conclusion, the main contribution of this research is the development of intervention practices, such as "Counselling Offices" in Medical Schools, in order to manage painful feelings, of Loneliness and Depression by resident physicians.

### **V38. Chemical composition and antioxidant activity of some Romanian apple varieties [FLASH]**

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Introduction: *Malus sylvestris* L. (common apple) has a wide range of varieties and it is well known for its complex chemical composition. Fresh apples are an important source of vitamins (ascorbic acid, carotenoids, vitamins B), phenolcarboxylic acids (caffeic, chlorogenic, syringic, sinapic acids), triterpenes, flavones (rutin), tannins, calcones (phloridzine) and mineral elements. Apples are well known for their antioxidant, hypoglycemic, hypocholesterolemic, antibacterial, anti-inflammatory, cardioprotective and anticancer effects. The aim of this study was the phytochemical screening and in vitro antioxidant activity of different apple varieties grown in Romania. Material and methods: As material we have used "Florina" (F), "Ionatan" (I), "Redix" (R), "Golden Delicious" (GD), "Idared" (ID) and "Enterprise" (E) apple varieties, which were harvested in fall of 2016 from Boteni, Arges county, Romania. Assays were conducted on both fresh juices and peels. Phytochemical screening was performed using qualitative (specific chemical reactions) and quantitative (spectrophotometric evaluation of total phenolic content) assays. The juices antioxidant capacity was determined based on ferric reducing power method and expressed as ascorbic acid equivalents (mg vitamin C/100 mL fresh juice). Results. Both fresh juices and peels are a source of phenols (flavones, tannins, proanthocyanidins), polysaccharides and sterolic/triterpenic compounds. The total phenolic content (expressed as mg tannic acid/100 mL fresh juice) decreased as follows: R (0.234) > GD (0.201) > E (0.196) > I (0.188) > F (0.185) > ID (0.151). Regarding peels the highest total phenolic content was found for E (1.318 mg tannic acid/100 g peels), whilst F (0.793 mg tannic acid/100 g peels) had the lowest one. The fresh juices antioxidant capacity decreased as follows: GD > E > R > ID > I > F. Conclusion. Analyzed apples are a source of bioactive compounds with antioxidant activity. Future pharmacological research is needed in order to establish the exact mechanism of action.

### **V39. Analysis of the level of Interleukin-4 in children with allergic rhinitis [FLASH]**

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Introduction: Allergic rhinitis is a widespread worldwide disease. The prevalence of the disease in different countries varies between 10-25 % of the population. In Kazakhstan, allergic rhinitis is differently spread. In the South- East of the Republic the sickness rate reaches 25 % of the population, in the North of the country – 5-10 %. In Almaty, about 100,000 patients suffer from allergy. Methods: The present study of the peculiarities of the level of interleukin 4 in children with allergic rhinitis was carried out when analyzing the indices in children who were on treatment with allergic rhinitis. Results: A total of 56 children were examined, of which 62%

were boys. The level of interleukin 4 was determined on the basis of the Immunological Laboratory of Karaganda State Medical University by means of an enzyme-linked immunosorbent assay for the concentration of interleukin 4 in human biological fluids and culture media using the Interleukin 4-ELISA-BEST reagent kit. It was revealed that the main tendency of interleukin 4 level was to increase, depending on severity and age. The statistical methods of processing were used to carry out the data analysis, applying in the medical data analysis. The calculation was made on the basis use of computer applications Microsoft Excel 7.0 and SPSS 12.0. Conclusion. Studies of interleukin 4 in biological fluids with allergic rhinitis can be used as the least traumatic method.

#### **V40. How does ultraviolet occupational exposition affect eyesight? [FLASH]**

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Introduction: Ultraviolet radiation (UVR), present in sunlight, constitutes about 10% of the total light output of the Sun. It is also produced by electric arcs and specialized lights, such as mercury-vapor lamps, tanning lamps, and black lights. Long-wavelength UVR can cause chemical reactions and causes many substances to glow or fluoresce. Consequently, chemical and biological effects of UV light are greater than simple heating effects, and many practical applications of UVR derive from its interactions with organic molecules. Long- and short-term exposure to UVR can harm the eyes, affect vision, and compromise overall eye health. Methods: The aim was to explore occupational eye damage from UVR while analyzing data from work environment studies. Case control study comprised 76 people with professions of varying degrees of UVR exposure: welders, smelters, medical technologists, graphic designers, manufacturers of electronic circuit boards, lifeguards, farmers and builders. Comprehensive eye examinations were given to workers with professional experience of 5-10 years. Results: over half of examined workers presented with eye diseases and conditions caused or aggravated by exposure to UVR. Macular Degeneration was found, caused by damage to the retina over time and is the leading cause of age-related blindness as well as Cataracts (clouding of the eye lens), Pterygium (pink, non-cancerous growth that forms on the layer of conjunctiva over the white of eye); Photokeratitis (corneal sunburn) or "snow blindness" (from high short-term exposure to UV-B rays). Conclusions: With increased levels of UVR radiation, it is important to take the necessary precautions to protect eyes: for example monitoring eye health of workers exposed to UVR, maintaining good vision and keeping track of solar radiation protection needs as well as new advances in eye protection.

#### **V41. Medical-technological aspects of ageing as reflected of industrial property documents [ORAL]**

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**Introduction:** The aim of this paper is to correlate important Medical-Technological aspects of ageing with the “innovation boom” of the last decades and to attempt to “quantify” the relationship of earth’s increasing populations, to the degree of the advancement achieved, for the components of successfully ageing. **Methods:** The “inter-disciplinary innovation trail” has been followed, as reflected on crucial Statistical-data and numerous Industrial Property Documents (IP-Docs/Patents), related to relevant aspects of Ageing. **Results:** The UNO key-trends in population ageing and the living arrangements of older persons has been the starting point of this Project. Some important Medical aspects of ageing appear on Data for 67 Countries indicating that older persons have become more likely in recent decades to live independently (~37% in 2010 compared to ~24% in 1990). Co-residence with children has become less common (~53% in 2010 compared to ~65% in 1990). As the average age of populations continues to rise, Governments should implement policies to address the needs and interests of older persons, including those related to housing, employment, health care, social protection, and other forms of intergenerational solidarity. On the other hand, an heuristic method has been developed and adopted in the present Paper, in order to estimate the Clinical needs of the Ageing population and to control whether the orientation of the Medical, Pharmaceutical and Biomedical Technology R&D activity, in the field of Ageing, ensures the necessary innovative spirit, in order to maximize the preventive and therapeutic influence on the increasingly ageing Population. **Conclusion:** The numbers of Patent-applications, related to the treatment of 25 selected Chronic Diseases, appearing frequently in the Ageing Population, constitute a reliable measure of both, effective medication and treatment of the patients, as well as, motivation of the said R&D activities of the corresponding Health-care Industries.

#### **V42. Merging precision medicine and biology of aging in aging-related diseases [ORAL]**

Tsoukalas D

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During the last decades the medical community has achieved important breakthroughs and has significantly diminished the number of deaths from acute illness. However, age-related diseases are responsible for 2/3 of deaths worldwide and significantly deteriorate the quality of life. They often cause disability that affect the ability to work, require long-term treatment and constant follow-up of the patient leading to rapidly increasing costs of health care and economic burden. Non-communicable diseases are the most common cause of death in older ages. According to the World Health Organization 80% of non-communicable deaths are caused by modifiable epigenetic factors and can be prevented. Precision medicine has emerged as a medical model that integrates data from genes, microbiome, lifestyle habits and environmental factors to formulate a personal biological profile. Health professionals can provide personalized care plan to improve quality of life, irrespective of condition. Among others, metabolomics is a powerful tool of precision medicine and provides a detailed overview of the phenotype. That is the outcome of genetic expression in the regulation of environment, represented by metabolites. Quantification of metabolites can identify underlying conditions even before symptoms appear and help health professionals monitor the response to treatment. A complementary approach to track aging and the onset of aging-related diseases are analysis of telomeres, the protective caps

of chromosomes. Telomeres shorten every time cell divide and the pace of telomere attrition is a robust marker of aging and aging-related diseases. Life-expectancy has increased two-fold the last century, stressing the need to develop personalized strategies to tackle conditions related to aging.

#### **V43. Maintaining good health in later years is associated with the frequency of health checks [FLASH]**

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Background: General population preventive examinations are designed to reduce morbidity, disability and prolong life. The implementation of population-based preventive health checks has declined over the past decades. Healthcare organization and low participation may partly explain why population-based general health checks have been ineffective in preventing disease at the population level. The aging population structure in 2017 for Lovech region, Bulgaria, is confirmed by a demographic substitute = 0.63. The age group over 65 is 26.65% of the population. Enforcing healthy aging is an important challenge for health authorities; therefore the Regulation №8/2016 (on preventive medical examinations) was introduced. Methods: According to Regulation №8/2016, anyone over 18 years should have routine checkups and blood sugar testing at a frequency appropriate for their age. The regulation includes medical examinations and tests for the group of the population over 65. The objective of this study was to examine residents of Lovech over 65. Two measures were applied: questionnaire for risk assessment for disease development and routine checkups with complete blood count, lipid profile. Results: In analysis only adjusting for age and sex, a higher proportion of those over 65 participated in the health check. Results presented here support the importance of traits such as early diagnosis of any pathology, as well as a positive attitude and lifestyle to aid health and activity in later years. Consolidation for regular prophylactic examinations reduced severity of illnesses and their consequences. Higher level of neighborhood social capital was associated with higher probability of participating in the health check phase of population-based lifestyle intervention. Conclusion: Activating social relations in the community may be an avenue for boosting participation rates in population-based health checks. There is a clear belief that prophylactic care is expensive but social, economic and moral effect of its successful implementation has not yet been accurately calculated.

#### **V44. Orthodontic treatment compliance and abandonment in a Romanian North-Western population group [ORAL]**

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**Introduction:** Patient compliance is an important factor in the outcome of orthodontic treatment. The term of compliance in orthodontics refers to good oral hygiene, appliances maintenance for proper functioning and punctuality in keeping appointments. In spite of orthodontist efforts to answer the patients' requests and the variety of therapeutic methods that require more or less compliance, orthodontic treatment is frequently given up. The aim of this study was to evaluate the orthodontic treatment compliance and abandonment in a Romanian population group in relation with age, environment of origin, family economic background, parental educational attainment, the main compliance they presented with, motivation for treatment, type of appliance and regular dental check-up before treatment. **Methods:** A retrospective study from 2009-2014 was conducted on 573 patients records from Orthodontic Department of University of Medicine and Pharmacy, Cluj-Napoca, Romania. A clinical compliance was used to assess the level of compliance (high-compliance-control group, low compliance and abandonment group). **Results:** Most of the patients who completed orthodontic treatment were above age of 12 while most of whom abandoned orthodontic treatment were under 9 ( $p<0.001$ ). Most of the patients who abandoned treatment were from rural areas ( $p<0.001$ ). Compliance was significantly influenced by the economic background, regular check-ups before treatment, patient motivation, any type of appliance, parents' educational level and increased along with the number of patients who wanted to improve their appearance ( $p<0.001$  for all comparisons). Low compliance and abandonment group had mainly external motivation ( $p=0.3$ ). **Conclusion:** Orthodontic treatment compliance and abandonment are strongly related to age, environment of origin, family economic background, parental educational attainment, the main compliance the patient presented with, motivation for treatment, type of appliance and regular dental check-up before treatment. The physician should pay attention to techniques for improving compliance and to educate the patients about the importance of compliance.

#### **V45. Policy and practice on health promotion and disease prevention in Bulgaria – [FLASH]**

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**Introduction:** Healthcare system is one of the social systems in which the Bulgarian Government is committed to carry out key reforms aimed at a sustainable improvement of the Bulgarian publichealth indicators. An active policy in the field of promoting health and preventing diseases was pointed as a key to this objective. The aim of the study is to analyze the expenditure foractions of the policy "Promotion, Prevention and Control of Public Health" in Bulgaria for the period 2010-2017 and to evaluate its actual place among priorities of the national health policy. **Methods:** Documents reviewand financial statements analysis for the expenditure frombasic funding sources as National Health Insurance Fund (NHIF) and the budget of the Health Ministry for the period 2010-2017 was made. **Results:** During the period under studythe expenditure for the Policy on Promotion, Prevention and Control of Public Health have been reduced from 4.84% to 3.88% of the total costs of health care. At the same time expenditure for capitation and hospital care is increasing. The funds expended by the Ministry of Health under this policy are constantly decreasing from 64.43% at the beginning to 49.07% at the end of the period. The costs laid out by the NHIF in terms of promotion anddisease prevention have been

increased from 35.57% to 50.93%. However NHIF pays only to health insured persons. In case of a large number of persons without a health insurance, as the current situation is, prophylactic programs prove to be ineffective. Moreover, less than a half of insured people visit regular checkups because a lack of information and other reasons. Conclusion: Bulgarian Government declares willingness for health promotion action. To be more effective health promotion practice should be improved by better allocation of expenditures and improvement of people's responsibility for health.

#### **V46. Trends in life expectancy and healthy life expectancy at age 65 years: Balkan countries comparison (2006-2016) [FLASH]**

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Introduction: Life expectancy (LE) is informative demographic indicators for public health assessment. A LE is an average number of years that a person is expected to live if current age specific mortality rates continue to apply. Health-adjusted life expectancy (HALE) is an average number of years that a person can expect to live in "full" health. HALE is the reliable indicator for Global Burden of Diseases (GBD). Thanks to large-scale GBD studies the global scientific community and health policy makers today have access to strong evidence on global health trends. This report aims to analyze the trends in life expectancy and healthy life expectancy at age 65 years among Balkan countries over the period 2006-2016. Methods: The information from European Health Information Gateway was performed. Content analysis of published data on GBD studies has been applied to monitor the changes in observed indicators. The data and trends are presented in multiple tables and graphs. Results. At a region level LE and HALE at age 65 years continue to show improvements. Regionally, individuals could expect to live substantially longer lives in 2016 than they could in 2006. In 2016, LE for females and males was as follow: Albania (19.59; 16.11), Bulgaria (17.60; 14.28), Cyprus (20.17; 17.44), MKD (16.26; 13.67), Greece (20.98; 18.34), Romania (18.11; 14.78), Serbia (17.87; 14.95) and Turkey (21.09; 17.32). In 2016, HALE at age 65 years was as follow: Albania (14.70; 12.07), Bulgaria (13.07; 10.50), Cyprus (15.38; 13.39), MKD (12.08; 10.13), Greece (16.07; 14.12), Romania (13.40; 10.79), Serbia (13.12; 10.92) and Turkey (15.03; 12.82). Conclusion: The increasing of LE and HALE should be placed in the focus of future researches in order to implementing adequate public health policies to continue this process of improvement of public health in Balkan countries.

#### **V47. The effects of probiotics on microbiota of elderly population [ORAL]**

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The term microbiota refers to a vast number of microbes that inhabit the human body and coexist with the host. More specifically, the gut microbiota and their metabolites, have a crucial role in human health and disease. However, the microbial composition of the gastrointestinal tract changes through life stages and especially in the elderly, it has been observed a decrease in the diversity of microbiota and beneficial bacteria, such as Bifidobacteria and Firmicutes. These age-related changes in the composition and activity of the intestinal microbiota seem to be responsible for a greater vulnerability to inflammatory and chronic diseases such as bowel disease, autoimmune diseases and colon cancer. Therefore, maintaining the microbial homeostasis may have a significant health impact on the elderly population. One way for attaining the intestinal balance could be probiotic intervention. Probiotics, derived from a Greek word meaning "for life", are defined as live, non-pathogenic microorganisms which, when administered in adequate quantity, confer health benefits on host's health. In order to exert their benefits on the host, they should not only be capable of surviving through their passage in the gastrointestinal tract but should also be able to proliferate in the gut. Probiotics are usually bacterial components of the gastrointestinal microflora, including lactobacilli and bifidobacteria, that they result in the production of lactate and short chain fatty acids such as acetate and butyrate during their metabolism. There are numerous studies supporting that specific probiotic strains exert beneficial effects on elderly population. It has been demonstrated that probiotic supplementation increases and maintains in high levels the beneficial microbes, including lactobacilli, bifidobacteria, and enterococci, which may counter the age-related changes in microbiota and therefore, reduce the risk of infections. Moreover, it has been shown that probiotics confer an increased mineral absorption, particularly that of calcium and magnesium. More intriguing is the fact that apart from the use of probiotics in the area of gastro-intestinal disorders, probiotics may have beneficial impact on extra-intestinal disorders, such as obesity, atopic dermatitis, and respiratory tract infections. Furthermore, administration of probiotics has been demonstrated to confer immunomodulatory effects in the elderly population, including increase of natural killer cells and phagocytic activity. Although side effects have been sporadically reported, probiotics seems to have a promising role in either shortening the duration or preventing of infections and can be considered safe in general.

#### **V48. Anonymous: the innominate human artery and its COCA variation [FLASH]**

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Brachiocephalic artery (Greek: βραχιονοκεφαλική αρτηρία, brachio-βραχίονας-arm, cephalic-κεφαλική-head), a vessel with a precise name is vaguely referred as the "innominate artery", that is an "anonymous" artery. The English adapted the term of the 17th century from the late Latin word "innominatus" derived by the Greek word "anonymous" (Greek: ανώνυμος, with no name), which was firstly used in the writings of the early sixth-century philosopher Anicius Manlius Severinus Boethius (477-524 AD). Boethius spoke fluently Greek, composing thus this term and introducing it into Latin terminology. English physician and zoologist George Rolleston (1829-

1881) in his masterpiece "Forms of Animal Life" in 1870 was probably the first to introduce the term in angiology by noting: "The aorta in birds divides after a very short course into three great trunks, by giving off two subequal innominate arteries". Irish born physician Robert Bentley Todd (1809-1860), in the work "The Cyclopaedia of Anatomy and Physiology" in 1836-1839, wrote an entry for the "brachio-cephalic artery", years before Rolleston's reference. Mosby's Medical Dictionary notes that the term "innominate" is sometimes used for body parts that have descriptive names rather than precise ones. This explanation means that when a name only describes an anatomical vascular trajectory or a simple function of a vessel, the term "innominate" should be adopted. Due to the fact that "brachio-cephalic artery" as nomination describes the very essence of the artery, that is the blood supply to the right arm, the head and the neck in human body, we may propose the Hellenic term "anonymous artery" (Greek: ανώνυμος αρτηρία) as officially introduced since the rebirth of the modern Greek Anatomic School in 1843. Anonymous artery as a definition still is used among the modern anatomists, especially among many Greek and Italian physicians. The aortic arch may present a plethora of anatomical variations, which may cause a cluster of complications in interventional procedures in surgery and angiography. We present a rare case of a common origin of both the common carotids arteries from the brachiocephalic trunk (anonymous artery), with the left common carotid artery emerging from the initial portion of it, forming a small common trunk. We propose for this variation the following nomination "COCA-Anonymous" (Common Origin Carotid Arteries).

#### **V49. Anatomic variations of the left internal spermatic vein and their clinical implications [FLASH]**

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Anatomic variations of the left internal spermatic vein represent a common finding in current urological surgery. Reflux in incompetent internal spermatic veins is the main etiology of varicocele formation. In addition, endoscopic urologic procedures use the left internal spermatic vein as a landmark for orientation, especially in endoscopic nephrectomies. For the aforementioned reasons, familiarity with left internal spermatic vein variants is of paramount importance for the treating physician. Traditionally, Type I left internal spermatic vein show a single incompetent vein; Type II left internal spermatic vein demonstrate reflux to a single vein with tributaries from lumbar or iliac veins, Type III, show duplication or trifurcation of the left internal spermatic vein; Type IV, show reflux through renal hilar or perirenal veins; and Type V, demonstrate a left internal spermatic vein draining in a duplicated renal vein. In our presentation, we will review common and uncommon anatomic variations of the left internal spermatic vein, which are more frequently demonstrated by retrograde venography and more often recognized in the urology literature.

### **V50. Anatomic variations of the extrahepatic bile ducts [FLASH]**

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The aim of this study is the literature review of extrahepatic bile ducts' anatomical variants and their related abnormalities. The knowledge of the anatomy is essential for the comprehension of the pathological entities in the area. A review of the international literature (Pub med, Scopus) and a study of recent research articles and papers, was carried out. The anatomical area of the extrahepatic bile ducts exhibits plethora of anatomic variants. The awareness of the type and incidence of each variant and its clinical significance is crucial during a surgical procedure, since inadequate knowledge of the regional anatomy can cause severe surgical complications. The detailed study and comprehension of anatomic variants of extrahepatic bile ducts is a prerequisite in order to avoid the intraoperative biliary tract complications but it is also necessary for the targeted treatment of any sequelae.

