BFH·A 2020

UNIVERSITY OF ZAGREB
SCHOOL OF MEDICINE

EU2020HR

BETTER FUTURE of HEALTHY AGEING 2020

Theme A

Ageing of Biological Systems

Invited lecture

A1-I

Evolving Needs in Pathology Education

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History of medicine is evidently and strongly connected with the history of human thinking, connection and collaboration with other sciences such physics and chemistry. Pathology as well was and is dependent and involved in technology evolution from its very beginning (Table 1).

TABLE 1

1591	compound microscope
1673	Anton van Leeuwenhoek simple microscopes with single lenses
1848	first microtome (for animal tissues)
1885	Cambridge Rocker microtome
1886	minot microtome
1910	sledge microtomes
mid1800s	paraffin wax for infiltration and support clocks
1893	first use of formalin
	staining hematoxilin and eosin
	silver impregnation

Last century approach is basically still in use for nowadays routine diagnostic, with significant changes in time and quality, but slide preparation for surgical pathology is still artisanal and human dependent. In the sixties of last century, biology introduced the protein purification and the development of antibodies against antigens of cell component, and immunohistochemistry changed the diagnostic perspective, bringing pathology in the real circuit of medical decision about prognosis and therapy. More recently, biology, physics, statistics and chemistry introduced new tools in the approach to human tissues that again obliged to move to different requests from clinicians and a different expertise of pathologists.

In the meanwhile, the pathology laboratories grew in terms of manpower number and expertise of the technical personnel and in terms of machinery, both for sample handling and preparation and for preanalytical, analytical control and finally for Informatics for communication to colleagues and patients.

Medical Education is a national prerogative, but the need for harmonization in Training Programs is an obligation in order to more satisfactorily fulfill the Bologna Declaration about the free movements of Doctors in all EU countries.

Union Européenne des Medecins Specialists (UEMS) produced European Training Requirements (ETR) for each Medical Specialty, and last year the Pathology ETRs were approved during the UEMS General Assembly in London. (https://www.eums.eu/_data/assests/pdf_file/0006111795/UEMS-2019.44-European-TRaining-Requirements-on-Pathology.pdf), where three areas were identified, namely the Residency program and achievements, the trainers and the training center qualifications and facilities. In these ETRs, we stressed that pathology is a specialty in which **time, pre-analytical and technical procedures** are critical, in the everyday routine practice and when during open surgery the modality choice and the rapid on-site evaluation of a frozen section require skills and highest scientific preparation of the dedicated specialist.

Pathology encompasses knowledge and skills of surgical pathology, autopsy pathology and cytopathology and *additional* competences in areas of special interest such as dermatopathology, forensic pathology, neuropathology, paediatric pathology, cardiovascular pathology and paleopathology.

Finally, patient education and public health aspects must be also be considered.

Nowadays, is clear how pathology plays a fundamental role in modern healthcare systems, addressing the comprehensive diagnostic *needs* of all patients, *coordinating and directing* the therapy choices. The pathologist must possess not only the essential scientific knowledge and skills necessary for complete and correct diagnosis, but also the *organizational insights* and capabilities needed to work efficiently in the pathology laboratory/department, cytopathology office, the autoptic and forensic department, additionally joined with molecular biology facility and other *modern technologies* (eg. bioinformatics, biobanking).

Obvious knowledge and data from Hospitals all around the world were confirmed by a rapid survey of
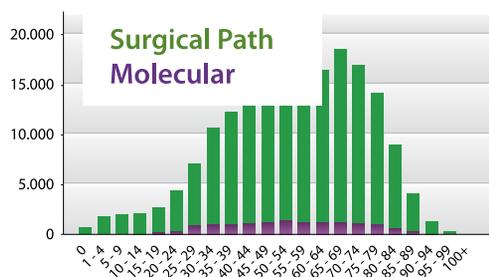
2015–2019 Surgical and Molecular
Pathology (171644)
M 71008   F 100636
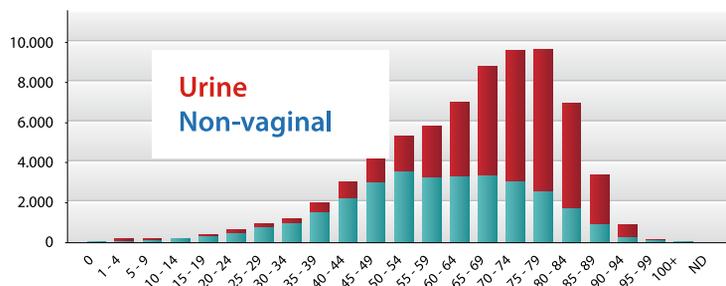
Clinical Cytopathology 2015–19		
Non-vaginal 25025	M 8473 (34%)	F 16552 (66)
Urine Cytology 30918	M 21794 (70,5)	F 9124 (29,5)

the activity of the Department of Medicine, Section of Pathology and Cytopathology of Padova University clearly demonstrating the evident increase of disease in advancing age.

The problem of aging is common for the entire world. The problem of rapid population aging is especially pressing in China, as its population aging rate and aging dependency growth are among the fastest in the world, with the absolute number of the elderly being the largest in the world (about 167 million or 12% of the country population over 65 in 2019, which will grow to as much as 330 million or about 26% by 2050). As the aging health problems increase, so do in-

World Population Prospects 2019:

- Confirms that the world's population continues to grow, albeit at a slowing rate;
- Points to the challenges facing some countries and regions related to rapid population growth driven by high fertility;
- Notes that population size is decreasing in some countries due to sustained low fertility or emigration;
- Underscores the opportunities available to countries where a recent decline in fertility is creating demographic conditions favorable for accelerated economic growth;
- **Highlights the unprecedented ageing of the world's population;**
- **Confirms the ongoing global increase in longevity and the narrowing gap between rich and poor countries, while also pointing to significant disparities in survival that persist across countries and regions;**
- Describes how international migration has become an important determinant of population growth and change in some parts of the world.

crease the capabilities of biomedical science and technology to solve the related problems. For example, 5G technology will allow us to develop from information sharing to internet of things (IOT). Artificial intelligence (AI) will greatly improve our ability to understand and solve complex problems, while the breakthroughs in stem cell technologies and other geroprotective therapies will allow us to redefine healthy aging and to completely treat major diseases.

However, this evidence appears to be sort of neglected in the EU education system, at the contrary for instance to the attention given to the medicine of gender, and, at least in Italy, the few gerontology departments have been closed and patients transferred to general internal medicine wards. Advanced age is not a disease, instead should be regarded as a resource, but if "advanced aged" subjects become patients, their diseases should be reconsidered with the psychological attitudes, social and familiar situation, mental and physical performance status, along with the characteristics of the disease.

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A1-II

Changing Pathology of Ageing Society

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The world is facing an unprecedented situation! There are more older people than children and more people at extreme old age than ever before. As the proportion of older people and the length of life increase throughout the world, key questions arise. Will population ageing be accompanied by a longer period of good health, a sustained sense of well-being, extended periods of social engagement and productivity, or will

it be associated with more illness, disability, and dependency? Ageing will affect health care and social costs.

Global efforts are required to understand and find cures to prevent diseases like Alzheimer and frailty and to extend existing knowledge about the prevention and treatment of heart disease, stroke, diabetes, and cancer.

The improvement in life expectancy is accompanied by the rise in chronic non-communicable diseases such as heart disease, diabetes and cancer. They reflect changes in lifestyle and diet and ageing. The economic and societal costs of non-communicable diseases of this type rise sharply with age.

Ageing is characterised by a progressive degeneration of the tissues that has a negative impact on the structure and function of vital organs. Loss of physiological integrity, a reduced capacity to respond to environmental stimuli with age contribute to increased risk of disease and death. Ageing is among the most important known risk factors for most chronic diseases. In general, it is determined by the interaction between injury and repair and the balance between cell death and cell replacement to maintain organ integrity. If cells die faster than they can be replaced, the remaining cells need to respond to greater demands that can eventually lead to pathological changes and deterioration in cell health. Factors that modify the balance between cell death and replacement have considerable impact on the ageing process.

One common factor underlying the process of ageing is the accumulation of molecular damage and ageing may be considered to result from the accumulation of cellular damage, consequent changes in gene expression and epigenetic factors related to DNA damage, and structural modifications of the DNA such as telomere shortening. Thus, ageing is influenced by the interaction of genetic and environmental factors. Two main theories of ageing are the free radical theory and the replicative senescence theory.

Evidence is accumulating that an optimal amount of radical oxygen species (ROS) are required for ageing. They can trigger proliferative and survival signals in response to physiological and stress signals. With ageing, levels of ROS increase in an attempt to maintain survival until they reach a level where they enhance age-related damage. ROS can also be formed by exogenous processes such as irradiation, environmental pollutants and inflammation, and normal cell metabolism. Free radicals can accelerate replicative senescence via shortening of telomeres, activate inflammatory redox-sensitive transcription factors like nuclear factor-kB (NF-kB) that regulate transcription of genes encoding pro-inflammatory cytokines and induce DNA damage. Chronic inflammation, characterised by higher levels of pro-inflammatory cytokines and the infiltration of inflammatory cells into tissues, is a feature of ageing and most age-related diseases including COPD, cardiovascular disease, osteoporosis, rheumatoid arthritis, cataract and Alzheimer's disease.

The other theory of ageing is the replicative senescence theory based on the fact that with every cell division there is incomplete duplication of the telomeres at the ends of chromosomes containing 1–5 kb of (TTAGGG) repeats that protect DNA against degradation and recombination, thus supporting chromosomal stability. In most somatic cells telomeres shorten with every cell cycle since replicative DNA polymerases lack the capacity to completely replicate the terminal ends of linear DNA molecules, which is a property of the specialised DNA polymerase known as telomerase. Most mammalian somatic cells do not express telomerase which leads to loss of telomere protective sequences at the ends of chromosomes. This is a result of the replication history, but also of a number of factors, such as cumulative oxidative stress and chronic inflammation, acting on progenitor cells. Successive cell divisions result in telomere shortening of chromosomes until cells are no longer capable of dividing. Therefore, the balance between cell death and cell replication is affected and defence, maintenance and repair of the body becomes increasingly impaired. Telomere length is considered as a measure of biological rather than chronological age or as a biomarker of somatic redundancy that is the body's capacity to absorb damage. There is a strong relationship between short telomeres and the risk of mortality.

To conclude, understanding the mechanisms of ageing may provide a novel target for the treatment of this condition.

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Oral presentations

A1-O1

The Joint Programme for Neurodegenerative Diseases (JPND), Towards a Globally Shared Brain Health

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The Joint Programming Initiative was originally created as a Member States-led initiative in Europe. It aims to address "grand challenges" to the EU and global society by coordinating national research programmes to increase the impact and effectiveness of research efforts. Neurodegenerative diseases (ND) and dementia in particular, represent one of the world's most pressing medical and societal challenges and the solutions are likely beyond the scope and resources of any single country. JPND aims to find causes, develop cures and identify better ways of caring for people with neurodegenerative diseases. Although JPND was originally a European initiative, it has since then gone global, with 30 countries participating today. Since its creation, JPND has raised more than €200 million for ND research. The tremendous progress of medicine in the last 50 years has led to a huge increase in total life expectancy for each of us. However, longer life expectancy without disability is greatly dependent upon our brain health: neurodegenerative diseases and dementia affect one third of the aging populations over 85 years of age, mental health disorders including addictions affect 12% of the entire population and neurodevelopmental disorders affect 15% of children. This problem will only get worse as the European and global population inexorably ages. Together with JPND, several large European Commission (EC) initiatives have been established in Europe, to collectively face these huge challenges, namely: NEURON, an ERANET in the other fields of brain health and the Human Brain Project, an EC research flagship. These initiatives have addressed research questions related to determinants of mental health (from depression to addictions and compulsive disorders), neurodegenerative diseases (from Alzheimer's disease and Parkinson's disease to related disorders) and neurodevelopmental disorders (disturbance of the development of the central nervous system). Since last year, all three initiatives have begun discussions in the context of EBRA (European Brain Research Area), to find operational synergies and identify gap. All these three initiatives have now

acquired invaluable experience and trust. Strongly supported by the EC and Member States, the initiatives encompass significant non-European international partners. This has allowed for the development of a unique holistic view of the European Brain Health research. By integrating such cutting-edge research dynamics and initiating an active translational momentum, the way for a powerful innovative force ready to consolidate an ambitious partnership on Brain Health in Horizon Europe is paved.

A1-O2

Healthy Ageing in Men: How to Prevent Andropausal Syndrome?

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The advanced age in men is connected to an array of health disorders that bring significant pressure on public health system. The main androgen in men, testosterone, tends to decrease by 1–2% per year after age of 40. According to the European Male Ageing Study, there is a significant prevalence of low androgens levels (also known as "biochemical hypogonadism") in aging men (40 – 79 years old); it is estimated to be 23.3%. Reduced serum levels of testosterone can occur in both young and aging men. A significant decline in serum testosterone levels affects about 5 million men in USA, including 20%–50% of men over age 60. Other men who also present themselves with biochemical hypogonadism include those with sickle cell disease and spinal cord injury, hypogonadotropic hypogonadism and primary testicular deficiency (primary hypogonadism). However, majority of men with biochemical hypogonadism remain asymptomatic. Those who became symptomatic have broad spectrum of symptoms such as sexual dysfunction, metabolic disorders, overall dissatisfaction, as well as increasing emotional disturbances, moodiness, irritability, nervousness, depression, fatigability, poor concentration, and deteriorating memory. All these symptoms are known as andropausal syndrome. The main source of androgens in men are Leydig cells (>95% of testosterone production). The rest of androgens are coming from the cortex of suprarenal gland. In ageing men, Leydig cells seem to be less responsive to LH. Morevoer, this less responsiveness is often combined with other comorbidities such as metabolic syndrome, prediabetes and

diabetes, adiposity, cardiovascular problems, psychological disturbances (including dementia) and osteoporosis. Early recognition/screening programme of biochemical hypogonadism and andropausal syndrome in particular is critical in prevention of ageing symptoms mentioned above. The screening programme may, among other parameters, include measurements of total testosterone, free testosterone, dehydroepiandrosterone sulfate, and insulin-like growth factor 1. Androgen substitution therapy is one of the strategies how to fight andropausal syndrome.

A1-O3

Representative Model of Sporadic Alzheimer's Disease and Its Use for Testing of Novel Therapeutic Strategies

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Ageing has imposed itself as a major risk factor in development of Alzheimer's disease, particularly its sporadic form (sAD) which affects about 13% and 50% of patients aged >65 and >85 years, respectively. sAD is an incurable neurodegenerative disorder characterized by a progressive memory loss. It presents the most common cause of dementia affecting over 45 million people world-wide. Type 2 diabetes mellitus (T2DM) stands out as the most prominent age-related risk factor associated with sAD. Recent data suggests that sAD and T2DM can be considered as "syndrome of accelerated ageing" so elucidation of their common pathophysiology, and their prevention and treatment is of utmost importance for healthier ageing. Brain insulin resistance (BRI) has emerged as a potential link between metabolic and cognitive dysfunction shared by sAD, T2DM and aging, in addition to oxidative stress and neuroinflammation. Thus, approved antidiabetic drugs like glucagon-like peptide-1 (GLP-1) receptor agonists are now being tested as suitable candidates for sAD treatment. Ineffectiveness of the available symptomatic AD therapy and a failure of pharma industry in new AD drug development imposed an urgent need for a successful disease-modifying drug which should be tested in a representative sAD animal model. We have developed a non-transgenic rat sAD model based on the administration of streptozotocin (a compound which following a peripheral administration of high dose induces diabetes mellitus) into the lateral brain ventricles (STZ-icv model). The model develops BIR (but not systemic diabetes) and our research on its further characterization has demonstrated that the model eventually manifests many sAD-like behavioral (cognitive decline), neuropathological (amyloid ß/tau protein accumulation, oxidative stress, neuroinflammation), and cerebral structural (cortical thickness) and metabolic (glucose hypometabolism) characteristics. We use the STZ-icv rat model also as a platform to test novel therapeutic strategies in sAD treatment. Our current research explores stimulation of the endogenous GLP-1 by oral galactose with preliminary results indicating that 2-month daily exposure to oral galactose initiated in the early sAD-like stage improves impaired learning and memory functions in STZ-icv treated rats accompanied by normalization of brain glucose hypometabolism, increments in active plasma GLP-1 levels and increased expression of GLP-1 receptors in the brain. Determination of the therapeutic potential and limitations of this novel nutrient-based therapeutic approach in sAD treatment is in progress. Funded by the Croatian Science Foundation IP-2014-09-4639, IP-2018-01-8938.

Poster presentations

A1-P1

Diagnostic, Prognostic and Predictive Biomarker Testing in Pathology – Needs and Opportunities in Solid Tumour Oncology of the Ageing Society

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Neoplastic disease are, having some exceptions in the field of hemato- and neuropathology, by far more common in older people. The theoretical basis of this is wide, not always will defined by clearly including passing of time as one of the key factors. Simply being around for a longer time period makes us more exposed to intrinsic and extrinsic stressors, meanwhile diminishing our defense mechanisms and capacity. In today's medicine the recently widely opened field of new drugs enabling more directed, „individualized" therapy is currently representing the backbone of a rapidly evolving success in fighting cancer. In most instances these „smart" drugs need „smart" diagnostic tools in order to better define targets for tailored therapeutic approach. Despite the fact that currently most of this happens in the field of genetics, the story begun with hormones – ER i PgR in breast cancer being the first targets of a directed therapy. The next step was also breast cancer – HER-2 (already an amplified gene receptor from the EGFR family). After a relatively silent period (in which we got the c-kit mutated positive GIST as a target of imatinib mesylate) an explosion happened. In the last ten years we are witnessing inclusion of more and more mainly genetically targeted therapy – RAS in metastatic colon cancer and EGFR TKI's leading the group, followed by ALK, ROS and MET in lung cancer, BRAF in melanoma (and lung cancer) and BRCA in triple negative breast and serous ovarian cancer. As of last year the 1p/19q co-deletion is a WHO recognized biomarker in oligodendrogioma. Meanwhile especially in soft tissue and bone tumors a wide array of diagnostic biomarkers is evolving, with so far litle or no therapeutic consequences. Ever sophisticate technologies are today opening widely the field of multigene testing, meanwhile also opening the question of rationalizing diagnostic efforts. Commercial suppliers introducing several strategic, financial and ethical questions often offer this type of testing an open a wide field for discussion.

Should we test everyone? Should we diagnose genetic changes with not known targets? Should we invest more into treating known targets with known drugs or should we try to come to the genetic basis of every malignancy, despite the costs and with doubtful rationale? Can we (financially) treat all our patients with the most high-end therapy? We have many difficult questions to answer but live one of the most exciting periods in modern oncology.

A1-P2

Early Diagnosis of Hidden Hearing Loss as the Prevention of Hearing Impairment in Older Working-age Population

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Introduction. Noise-induced hearing loss (NIHL) is preceded by a cochlear synaptopathy and a consequential hidden hearing loss (HHL) with no shift in hearing threshold. In middle-aged working-age population, HHL or NIHL are exacerbated by the onset of age related-hearing loss. The hearing threshold usually shifts bilaterally at high frequencies after years of exposure to noise intensity levels greater than 87 dB(A) during the 8-hour working day. The objective was to analyse the applicability of existing procedures in the diagnosis of HHL in order to prevent further noise exposure and the following hearing impairment. **Methods.** Literature review was made in PubMed Database using keywords: age-related hearing loss; noise-induced hearing loss; hidden hearing loss. We did our research on studies published in the past 20 years. **Results.** As a direct measure of the cochlear synaptopathy degree, some studies suggest the reduction in the auditory brainstem response wave I amplitude and others an increase in the ratio of summating and action potential. However, wave I amplitude is highly variable in humans, and it is not completely clear how loss of cochlear synapses leads to an increase of summating potential. Loss of synapses was also found in autopsy material of otologically healthy persons, suggesting that this synaptopathy may be independently mediated by aging. On the other hand, prolonged noise exposure at the workplace increases sympathetic activity and causes an increase of the cortisol concentration in the blood. This increase is consistent with

the increase of salivary cortisol and salivary cortisone concentrations easily measured during the workday. **Conclusion.** Auditory and extra-auditory noise effects should be observed simultaneously and measured non-invasively. Except standard audiological test battery, electrophysiological results, such as auditory brainstem response findings should be also taken into account and supplemented by psychometric and hormonal findings. With such diagnosis and with evidence of excessive noise exposure, it is important to find technical solutions or restrict the work in such hazardous working environment and to advise workers on the use of personal protective equipment with regular supervision. Further studies should explain the relative contribution of noise exposure and age, respectively, to the development of cochlear synaptopathy. This kind of approach to the early diagnosis could significantly reduce the risk of developing severe hearing loss in older age and eventually increase the work capacity of noise-exposed workers.

Session A2: Molecular Basis of Ageing

Invited lecture

A2-I

# Lifespan and Health Span in Mice: Mechanisms and Interventions

Dan Ehninger

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Aging is a major risk factor for a large number of adult-onset disorders, including neurodegenerative disorders, cardiovascular diseases and cancers, and is associated with a broad range of functional impairments. Targeting aging processes with suitable pharma- scale analyses of aging-associated molecular, cellular, physiological and histopathological changes constitute an effective approach to identify and dissect possible treatment or prevention effects in animal models.

This presentation will cover data detailing how aging phenotypes, in a range of physiological systems, unfold across the lifespan of mice and humans. Moreover, I will share data examining how key biological processes implicated in aging change over the murine lifespan. Finally, I will discuss the question to what extent lifespan-extending manipulations slow mammalian aging rates and promote overall healthy aging in mammals on the level of organs and tissues. The line of work discussed exemplifies a research approach that is key for providing a foundation for translational opportunities that link the biology of aging to new medicines for the prevention of a broad range of age-related diseases.
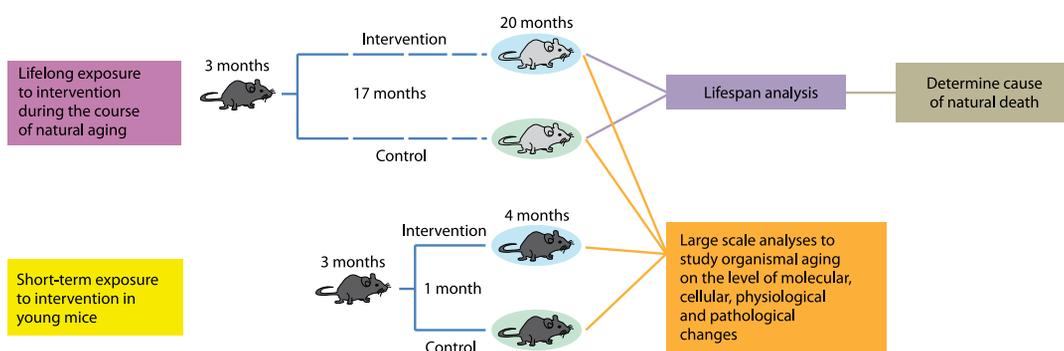
cological or dietary interventions could potentially represent a powerful inroad for the development of preventatives or treatments for aging-associated disorders.

A large number of genes and pathways have been identified that extend lifespan in invertebrates. In some cases, analogous manipulations have been shown to also extend lifespan in mammals. Relatively under-explored, however, is the question to what degree these lifespan-extending manipulations also slow mammalian aging rates and promote overall healthy aging in mammals on the level of organs and tissues. Large-

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Oral presentations

A2-O1

High Capability of Human Prefrontal Cortex Microcircuitry to Maintain Its Structure During Ageing

Zdravko Petanjek, Ana Hladnik, Ivana Bičanić, Domagoj Džaja, Dora Sedmak, Ivan Banovac, Andrea Blažević, Sanja Damopil

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We analyzed changes in dendritic morphology and spine density on associative layer IIIc cortical projecting neurons and large layer V subcortical projecting pyramidal neurons to establish age-related changes within microcircuitries of the human prefrontal cortex (Brodmann area 9). Postmortem human brain tissue of adults was processed using the rapid Golgi method in two age groups: 38 – 64 years (n = 8) and 72 – 91 years, (n = 7). Neuropathological findings were unremarkable in all analyzed brain specimens. From each layer, the basal dendritic arbor and side dendritic branches from 10 – 15 well-impregnated pyramidal neurons per subject were three-dimensionally reconstructed using Neurolucida software. Soma size, total dendritic length, total segment number, individual segment length and spine density were quantitatively analyzed. Regarding layer V neurons, no significant differences were observed between adults and the elderly, either for dendritic morphology or for the spine density. The interindividual differences in the elderly group were however higher than in adults. Regarding associative layer IIIc pyramidal neurons, the mean values of spine density, on both side branches and basal dendrites, were 20–25% lower in the elderly than in adults (p = 0.07). In two aged cases the spine density was around mean level of adult and in the remaining aged subjects values were lower than in all adult subjects. These data show that the dendritic morphology and synaptic connectivity of the major classes of principal neurons in higher order associative areas are largely preserved in aging, while the connectivity of associative cortico-cortical layers is more prone to regression.

A2-O2

Antioxidant Ameliorated Negative Impact of a DNA-Demethylating Agent on Placental Growth and Morphology of Aged Preterm Placentas

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Introduction and Objectives. We showed that a DNA-demethylating agent/ epigenetic drug 5-azacytidine (5azaC) used in treatment of human malignancies is a teratogen that impaired development of both embryos and placentas in treated rat dams, while pretreatment with the antioxidant N–tert– Butyl–α–phenylnitron (PBN) improved development of rat fetuses. We now investigated whether PBN could improve the placental development and aging. **Methods.** On the 12th and 13th days of gestation, Fisher rat dams were pretreated by an i.v. injection of PBN (40 mg/kg) and one hour later by an i.p. injection of 5azaC (5mg/kg) or only with 5azaC. Controls were treated only with PBN or were sham- treated. On the 15th and 20th days of gestation placentas were weighted. Immunohistochemical signals of the Proliferating Cell Nuclear Antigen (PCNA) and markers of oxidative/nitrosative processes (8-oxoDG and nitrotyrosine, respectively) were stereologically quantified by the numerical density (Nv). Apoptotic index was calculated and DNA-methylation was assessed by pyrosequencing. All results were statistically evaluated. **Results.** Pretreatment with PBN ameliorated placental morphology of aged preterm 20-days-old placentas which was disturbed by 5azaC. PBN-pretreatment significantly improved weight of 15- and 20-days old placentas. In aged preterm placentas apoptotic index was significantly lower in samples pretreated with PBN than in only 5azaC treated, and that was associated with a significantly lower Nv of 8-oxoDG and nitrotyrosine. Nv for the cell proliferation marker (PCNA) was significantly lower in all treated with 5zaC than in controls. **Conclusions.** Pretreatment with the antioxidant PBN ameliorated negative impact of the DNA-demethylat-

ing epigenetic drug on the aged, preterm placentas. Because DNA demethylation causing oxidative stress might also be of importance for placental premature aging during human gestation, we propose further investigation of the antioxidant PBN activity.

A2-O3

Glycans as Biomarkers and Functional Effectors of Age and Age-Related Diseases

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The majority of proteins that evolved the after appearance of multicellular life are glycosylated and glycans significantly affect structure and function of these proteins. However, due to structural complexity of glycans and the absence of a direct genetic template, the analysis of protein glycosylation is much more complicated than the analysis of DNA or proteins. Consequently, the knowledge about the importance of individual variation in glycans for both normal physiological processes and diseases is still limited. In the last few years it is becoming increasingly clear that variations in a DNA sequence are only a beginning of the understanding of complex human diseases. Genetic polymorphisms have to be put in the context of complex biology of life and a more elaborate approach that combines different 'omics phenotypes is needed to understand disease mechanisms and perform patient stratification that transcends genomics. Glycomics, as by far the most complex posttranslational modification, has an immense potential in this respect, which is only beginning to be investigated. By generating glycomic data for over 100,000 individuals from some of the best characterized clinical and epidemiological cohorts we enabled glycomics to meet other 'omics. The analysis of this rich gold mind is painting a picture of a very complex genetic and epigenetic regulation of glycosylation that fine tunes protein activity in multiple biological systems and also contributes to ageing at the molecular level. In particular, the evidence is accumulating that in cardiometabolic diseases changes in glycosylation are not only biomarkers, but functional effectors that actively participate in disease development.

Poster presentations

A2-P1

Senescent Phenotype and Disturbances in Autophagy in ATM-Deficient Neural Precursor Cells

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ATM is a kinase involved in DNA damage response (DDR), regulation of response to oxidative stress, autophagy and mitophagy. Mutations in the ATM gene in humans result in ataxia-telangiectasia disease (A-T) characterized by a variety of symptoms with neurodegeneration and premature ageing among them. In this study, we have focused on the process of senescence in A-T cells. Given that brain is one of the most affected organs in A-T, we turned our attention to neural progenitor cells (NPCs) derived from A-T reprogrammed fibroblasts. We observed that A-T NPCs obtained through neural differentiation of iPSCs in 5% oxygen possessed some features of senescence including increased activity of SA-β-gal and secretion of IL6 and IL8 in comparison to control NPCs. This phenotype of A-T NPC was accompanied by elevated oxidative stress resulting in 4-HNE protein modification. A-T NPCs exhibited symptoms of impaired autophagy and mitophagy with lack of response to chloroquine treatment. Additional sources of oxidative stress like increased oxygen concentration (20%) and H_2O_2 respectively aggravated the phenotype of senescence and additionally disturbed the process of mitophagy. The latter was confirmed by transcriptional analysis of several mitophagy-associated genes. In both cases only A-T NPCs reacted to the treatment. We conclude that oxidative stress may be responsible for the phenotype of senescence and impairment of autophagy in A-T NPCs. Our results point to senescent A-T cells as a potential therapeutic target in this disease.

Invited lecture

A3-I

Idiopathic Rapid Eye Movement Behaviour Disorder

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Idiopathic rapid eye movement (REM) sleep behavior disorder (iRBD) is increasingly recognised as an important precursor disease state of alpha-synucleinopathies. This parasomnia is characterized by a history of recurrent nocturnal dream enactment behaviour, loss of skeletal muscle atonia, and increased phasic muscle activity during REM sleep. Neuroimaging studies of striatal dopamine transporter uptake tracer signalling suggest increasing dopaminergic deficit across the continuum of the alpha-synucleinopathies, with early sleep dysfunction suggestive of early caudate dysfunction. We will discuss the implication of utilising this window of the opportunity in the disease process to intervene, and to potentially abort, further development of neurodegenerative process.

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Oral presentations

A3-O1

Obstructive Sleep Apnoea Assessment in the Elderly

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Obstructive sleep apnea (OSA) is one of the most common sleep related breathing disorders characterized by repetitive episodes of complete (apnea) or partial (hypopnea) cessations of breathing due to obstructions in upper airways followed by significant oxygen desaturations. Chronic intermittent hypoxia combined with frequent arousals during sleep results with dysfunction of autonomic nervous system that promotes development of hypertension, glucose intolerance, cardiovascular and cerebrovascular disorder. Prevalence of OSA tends to increase due to increased prevalence of obesity and ageing of the population. OSA has negative impact on health and quality of life and aggravates ageing and ageing-related diseases and comorbidities. As such, OSA should be adequately screened in order to apply adequate medical care especially in the elderly. Different clinical models have been developed to evaluate patients who are at risk for OSA. Usually we use screening questionnaires such as STOP (Snoring, Tiredness, Observed apnea, and high blood Pressure) and STOP-BANG (STOP + Body mass, Age, Neck circumference, Gender), which are concise and easy-to-use in daily clinical practice. In a large sample of 4136 subjects from the area of Split and Split-Dalmatia County, screened with STOP questionnaire we found that the risk for OSA steadily increases with age. Particularly vulnerable was the group of men aged 41–50 years, in whom the risk of OSA and associated excessive daytime sleepiness was significantly more pronounced compared to female respondents of the same age. In older population (> 60) we found highest risk for OSA, with women becoming at risk for OSA as much as men (55% vs. 51%). When we investigated the validity of OSA screening questionnaires against objective diagnostic polysomnography and polygraphy procedures, the STOP and STOP-BANG questionnaire revealed similarly high sensitivity (0.87), specificity (0.54) and positive predictive value (0.90) in the detection of OSA when applied in a population of

sleep clinics patients in Split Sleep Medicine Center. This indicates that the prevalence in general population is really high, and is strongly associated with ageing. Also, some recent publications indicate that screening for OSA among elderly were prevalence of OSA is as high as 83% requires modifications. Further validation studies of applied questionnaires designed specifically for the elderly population are necessary in order to reduce negative effects on health and avoid unnecessary and costly OSA diagnostic procedures.

A3-O2
I Forgot to Sleep

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Sleep is essential for healthy living and relationship between dementia and insomnia is a complex one. Both conditions are highly prevalent among demented patients and sleep disorders, with insomnia in first place, makes things even more difficult to treat. Contemporary view on insomnia among demented patients and pathways to care will be explained. Non-pharmacological, often neglected methods should be tried out first, with somatic conditions, dose titration and side effects of medication being biggest obstacles in psychopharmacology. Personalized medicine approach regarding stage of dementia, housing conditions, caregiver's possibility and general medical condition should be implemented in treatment.

A3-O3
REM Behaviour Disorder and Neurodegenerative Disorders

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Rapid eye movement (REM) sleep behavior disorder (RBD) is a sleep disorder characterized by enacting one's dreams during the REM sleep, with most of the dreams being violent or aggressive, so that patients often complaint to hurt themselves or bed partner during these episodes. Prevalence of RBD, based on population, is 0.38–2.01 %, but much higher in patients with neurodegenerative disorders, especially synucleinopathies. RBD may herald the emergence of synucleinopathies by decades, such that it may be used as an effective early marker of neurodegenerative disorders, precisely synucleinopathies. Lesion or dysfunction in REM sleep and motor control circuitry in pontomedullary structures cause RBD phenomenology, and degeneration of these structures might explain the presence of RBD years or even decades before the onset of Parkinson's disease (PD), dementia with lewy bodies (DLD) and multiple system atrophy (MSA). RBD occurs in 30–50 % of patients with sporadic PD, preceding the onset of parkinsonism by several years in about 20 % of them. The majority of patients with MSA have RBD, recent meta-analysis reported prevalence of clinically suspected RBD in MSA of 73 %, while polysomnographically confirmed RBD was up to 88 %. RBD is recognized as one of the core features of DLB and may occur either in advance or simultaneously with the onset of DLB. The prevalence of RBD in DLB is up to 76 %. On polysomnography RBD is presented as repeated episodes of vocalization and/or complex motor behaviors during REM sleep which reflects the loss of normally present atonia in REM (i.e. REM sleep without atonia – RSWA). Sometimes when typical behaviors are not seen in polysomnography but are known to exist based on medical hystory, even the presence of RSWA is sufficient to diagnose patients with RBD. In cases of idiopathic RBD, precisely those patients who at the time of diagnosis don't exhibit clinical signs of Parkinson disease, DLB or MSA, the treatment is mainly symptomatic and is based on lowering motor activity in sleep, promoting sleep contiuity and readdressing sleep desynchronization. Clonazepam and melatonin are main substances used in treatment. While there is not known effective neuroprotective substance yet, it is important to recognize these parasomnias as they can precede typical motor and cognitive symptoms of neurodegenerative diseases by many years and as such demmand regular neurological and neuropsychological follow-up.

Poster presentations

A3-P1

Predictors of Sleep Quality in Older Adults in Zagreb

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The changes in sleep-wake process over the lifespan are well established. Epidemiological data show that 50–65% of older adults report impaired sleep quality (SQ). This impairment can rather be attributed to health status and various psychosocial factors than to the aging process per se. The results of our previous study showed the expectedly impaired SQ in nursing home residents, best predicted by self-perceived health and functional ability. The aims of the current study were to examine SQ of older adults living in different arrangements and to examine factors contributing to their SQ. Participants were 334 older adults (73% females) from Zagreb. Half were the NH residents and half OH residents. Their dominant age was 78 years, varying between 69 and 100 years. All were ambulatory, without diagnosis of dementia. Trained interviewers collected data individually, through structured interviews in nursing homes and in gerontology center. Questionnaire comprised of general questions, questions to assess self-perceived health and standardized scales to measure social participation, functional ability, life satisfaction, and SQ. SQ was assessed by the Pittsburgh Sleep Quality Index (PSQI). Our results showed PSQI score greater than 5, indicating poor SQ in 60% of older adults. In NH residents the percentage was higher than in OH residents (71% vs. 50%, p < .001). Selected set of predictors explained small but significant proportion of variance in PSQI score and 7 domains. Predictors explained the highest proportion of variance in the use of sleep medication (22.6%) and subjective SQ (21%). Expectedly, women had poorer total PSQI, longer sleep latency and used more sleep medication than men. Older age significantly predicted only the use of sleep medication, as was expected within this age range. Living in NH predicted worse PSQI, shorter sleep duration, less sleep efficiency, more use of sleep medication and poorer daytime functioning. Greater life satisfaction predicted better total PSQI, higher subjective SQ, longer sleep duration, shorter sleep latency, less sleep disturbances and less use of sleep medication. Poorer self-perceived health predicted poorer PSQI, worse subjective SQ, more sleep disturbances and more use of sleep medication while better functional ability predicted shorter sleep latency and better daytime functioning. Separate predictors' analyses of NH and OH older adults are called for to enable tailoring preventive strategies according to specific needs. Contribution of psychosocial factors in SQ prediction in older age points to the necessity of investment in sleep hygiene education and psychosocial support, especially to NH residents.

A3-P2

Patient-Centred Care Based on Fog Computing Paradigm: A Case of Sleep Apnoea Detection

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Introduction and Objectives. Sleep apnea is medical condition that affects about 4% of the population and may cause various medical complications such as fatigue, hearth problems and elevated blood pressure, diabetes type II, metabolic syndrome and others. Nowadays, there is a huge demand for technology solutions and new care models that will help in understanding patient's needs and characteristics, facilitating treatment adherence and shared-decision making. **Methods.** This paper proposes a system and methodology based on fog computing paradigm to unobtrusively detect sleep apnea and to enable patients with sleep apnea and health care providers to be active participants and collaborate in chronic disease management. The methodology is based on findings that sleep apnea is accompanied by body or leg movement. Therefore, the proposed system uses non-invasive PIR and piezoelectric-based sensors placed under the mattress. Data processing and sleep apnea detection is performed by machine learning algorithms on the edge nodes. Anonymized data are also sent to the cloud for further evaluation and assessment by medical experts and are used for model improvement. **Results.** In order to evaluate the proposed system and methodology, an experiment for continuous monitoring of a single person over a period of 8 hours was conducted. Signals obtained from PIR and bed sensors were segmented and signal features were extracted. Depending on the window length 250 to 270 features in total were

generated, and then reduced to 32 by discarding those with low importance or high data drift sensitivity. Four machine learning algorithms for sleep apnea detection were applied on the obtained feature set and the results were compared. The accuracy of the different classifiers based on different sliding window configurations was analyzed. It was found that, as windows length increases, the accuracy increases too. When using windows of 5 seconds the accuracy was 80%, when the window length was increased to 10 seconds, the accuracy raised to around 90%, and for 20 seconds windows, the accuracy further improved to above 95%. **Conclusions.** The use of novel technology, like unobtrusive sensors and fog computing, can improve the patient-centered care for patients with sleep apnea. The flexibility of the fog architecture enables better placement of computing and network resources. The fact that accuracy is increasing for larger window length is an important discovery. It can be used for design of a system that makes several predictions at the same time. In this proof the concept of the proposed system architecture we have conducted experiment with only 3 patients, which has to be increased.

A3-P3

Teatment of Sleep Disorders in Elderly

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Changes in sleep architecture and duration are a part of a normal ageing. It is crucial not to mistake sleep disorders for physiologic changes in sleep-awake patterns in elderly because untreated sleep disturbances may predict the risk of dementia and they are associated with worse late-life cognition.

Frequent sleep disorders in elderly include: insomnia, obstructive sleep apnoea (OSA), restless legs syndrome (RLS), circadian rhythm sleep disorder with phase advance and REM behaviour disorder (RBD). Treatment of these disorders include different pharmacological measures and non-pharmacological activities which include stimulus control, sleep hygiene education, relaxation therapy, cognitive behavioural therapy, bright light therapy and CPAP for OSA.

Pharmacologic treatment of sleep disorders should be taken with extreme care in older individuals. There is a greater risk of side effect even at lower doses and interactions with concomitant medications. Benzodiazepines and nonbenzodiazepine receptor agonists often used for treating insomnia can lead to tolerance, dependence, rebound insomnia, daytime sedation, motor incoordination, cognitive impairment and increased risk of falls in institutionalized older individual. Because of these adverse effects and superior response seen in cognitive behavioural therapy, use of these drugs should be avoided in older individuals. To avoid similar adverse effects in treating RBD with clonazepam, alternative therapy with melatonin receptor agonist is often used because it is safer and better tolerated. Treating of OSA has some different challenges. Very effective CPAP not only improves sleep quality and daytime sleepiness but adequate use of long-term CPAP therapy improves cardiovascular outcomes. The main problem of CPAP treatment in elderly is that studies show that CPAP adherence decreases as age increases, and it is particularly poor in patients aged >75 years. Individualized treatment and close monitoring could possibly improve compliance.

Sleep disorders are common problem in all age groups, particularly in elderly. If untreated they are associated with cognitive impairment so diagnosis and treatment of sleep disorders are of great importance for healthy ageing.

A3-P4

Obstructive Sleep Apnoea Aggravates Age-Associated Decline in Psychomotor Performance

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Ageing is associated with a decrease in various cognitive and psychomotor abilities as well as problem-solving tasks, probably due to simultaneous structural and functional changes in specific brain regions, precisely in the frontal lobes. In our study assessment of the dynamic properties of the central nervous system has been performed with the computerized psychomotor testing device composed of numerous different tests using chronometric approach. In a large sample of 3420 subjects, we demonstrated that age positively correlated with the reaction times in tests of discrimination of the light signal position, complex psychomotor coordination, and convergent thinking. Thus, our results support the concept of association of reduced cognitive and psychomotor abilities with the advanced age. The prevalence and severity of the obstructive sleep apnea (OSA) increase with advanced age. Moreover, the untreated OSA is associated with various age-related disturbances, including decline in physiologi-

cal and psychological performances. However, does OSA aggravate age-related cognitive and psychomotor decline and to what extent remains to be evaluated. In another study, on a total of 103 patients with moderate and severe OSA, we demonstrated that severe OSA impaired the speed of perception, convergent, and operative thinking, indicated by prolonged reaction times in the perception of visual stimulus, solving simple arithmetic operations, and in tasks requiring psychomotor coordination of the upper and lower limbs. Furthermore, severe OSA decreased the stability toward the end of the test, indicating that OSA patients get considerably slower toward the end of tasks compared to control participants of the same age. Finally, in the test of the complex psychomotor coordination of the computerized psychomotor testing device, OSA patients had significantly more pronounced prolongation of the reaction times in comparison to the control subjects of the same age. In conclusion, both ageing and OSA are associated with the decline in cognitive and psychomotor performance. However, the impairments in complex psychomotor coordination of the limbs are more pronounced in apneic patients supporting the conclusion that OSA aggravates age-related decline in psychomotor performance.

A3-P5

Sleeping 8.5 or More Hours per Day – Is It Too Much? Characteristics of Very Old Persons (85+) According to Sleep Duration

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Institute for Anthropological Research, Zagreb

Introduction and Objectives. The extreme differences in daily sleep duration provoke questions on causality and "normal"/acceptable/recommended ranges. Specifically, it is often not clear whether and when should sleep duration be taken as a warning signal, especially when a person's well-being is under the institutional responsibility, as in retirement homes. This study aims at determining characteristics differing long (8.5+ hours), short (<6.5 hours), and moderate/"normal" (6.5–8.0 hours) sleepers (in a 24h cycle) among the very old persons (85+ yrs.). **Methods.** The rich data collection on 327 very old persons living in retirement homes in Zagreb (HECUBA; CSF IP-01-2018-2497) has been analyzed contrasting three similarly sized groups: long-sleepers (95; 29.1%), short-sleepers (102; 31.2%), and moderate-sleepers (130; 39.8%). **Results.** Long-sleepers spend their leisure

time more frequently with friends/neighbors (p=0.013) and less frequently walking (p=0.037). They more frequently declare that somebody is with them during the night (p=0.020), that they have help in their everyday activities (p=0.028), and they are content with their present life (p=0.041). They less frequently think that loneliness is one of the main problems of the elderly (p=0.033). Long-sleepers less frequently report a chronic disease (p=0.033), and take medications for heart/blood pressure (p=0.037). Short-sleepers more frequently report that they were separated from their families because of their job (p=0.010), they are less frequently content with their past life (p=0.013), and now receive a lower pension (<4,000 HRK) (p=0.046). They more frequently declare that nobody is with them during the evening (p=0.022), and their main current problem is the feeling of uselessness (p=0.037). Short-sleepers more frequently report depression (p=0.029) and a chronic disease (p=0.047). Moderate-sleepers more frequently have higher education (p=0.028), report that because of their education they changed their residence (p=0.046), and now have a higher pension (4,000–10,000 HRK) (p=0.036). They are also more frequently parents (p=0.046). Now they less frequently spend their leisure time with friends/neighbors (p=0.027). Moderate-sleepers less frequently have heart problems (p=0.029) but more frequently have osteoporosis (p=0.015). **Conclusions.** The study showed that in long-lived individuals the sleeping duration is not related to sex and age/longevity or to the psychotropic drug usage, but is predominantly a reflection of the personality, quality of life, and life-long experience. The revealed pattern indicates that the very old persons sleeping less than 6.5 hours are the least content.

A3-P6

Cardiovascular and Metabolic Changes Related to Sleep and Ageing

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Sleep architecture and duration changes throughout the lifespan starting with dramatic changes during the first year of life, continuing to change through the childhood and finally becomes characterized by a reduction in sleep quality and quantity during ageing. Although total sleep time tends to remain constant, older people spend more time in the lighter stages of sleep, sleep latency might increase, REM sleep decline,

and sleep fragmentation occur. The prevalence of sleep disorders also tends to increase with age. As some sleep disturbances among the elderly could be considered as a physiological consequence of ageing, numerous sleep disturbances can be attributed to illnesses and the medications used to treat them. Snoring is the primary cause of sleep disruption for approximately 50% of older population. It is associated with overweight and often becomes worse with age. Loud snoring is particularly serious as it can be a symptom of obstructive sleep apnea (OSA). Sleep is considered to be a modulator of metabolic homeostasis. The impact of sleep duration and sleep-disordered breathing increases the risk for obesity, insulin resistance (IR), type 2 diabetes (T2DM), the metabolic syndrome, and cardiovascular disease risk and mortality. Prevalence of OSA is estimated to be 26% in adults 30–70 years old, and as high as 45% in obese adults. OSA is associated with ageing independently of obesity. The prevalence of OSA among older adults is substantially higher than in younger individuals. OSA is associated with an increased risk for hypertension, possibly via blunting the normal nocturnal blood pressure dipping. The prevalence of OSA in adults with drug-resistant hypertension is as high as 83%. OSA is associated with an increased risk of atherogenic dyslipidemia in adults showing higher total cholesterol and LDL levels, higher triglycerides levels, and lower HDL levels. OSA also increases the risk of cardiovascular and cerebrovascular diseases. The Sleep Heart Health study found that OSA is a significant, independent risk factor for chronic heart disease and heart failure in men aged 40–70 years, and that OSA is increases the risk for ischemic stroke; even in men with very mild OSA. In summary, evidence shows that OSA increases the risk of cardiometabolic morbidities in the context of obesity, hypertension, IR, and T2DM, atherosclerosis, CVD, stroke risk, and CVD-related mortality. Additionally, OSA is associated with ageing. Thus, untreated sleep apnea puts a person at risk for cardiovascular disease and metabolic disturbances, which increases significantly during ageing.

Session A4: Neuroscience and Neurodegenrative Disorders and Ageing

Invited lecture

A4-I

The Impact of Neuroscience Research in Europe for Healthy Ageing

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With a rapidly ageing population, dementia — particularly, Alzheimer's disease (AD) — is a growing public health concern worldwide. In Europe, an estimated 10.9 million people live with dementia, and this number is expected to increase to 18.7 million in 2050. AD is the underlying cause in 70% of people with dementia. AD is a neurodegenerative disease that progresses in stages, beginning with a long silent phase before symptoms appear. The European Brain Council (EBC) is a network of key players in the "Brain Area", with a membership encompassing scientific societies, patient organisations, professional societies and industry partners. Its main mission is to promote brain research with the ultimate goal of improving the lives of the estimated 179 million Europeans living with brain conditions, mental and neurological alike. With the aim to speak with one voice, EBC stands as the platform to foster cooperation between its member organisations and other stakeholders, consistently promoting dialogue between scientists, industry and society. Notably, EBC emphasizes the importance of raising awareness and encouraging education on the brain and the repercussions of neurological and mental health conditions on society as a whole; including diseases like dementia and neurodegeneration, which are strongly influenced by an ageing population, where an increase in healthy ageing is desired. The promotion of healthy ageing will have massive implications not only on health care costs but also on the quality of life for the elderly. In fact, as demonstrated by EBC, in Europe it has been estimated that the total cost of brain diseases on a yearly basis amounts to around 798 billion euro; for dementia only, the cost is 22.000 euro per patient, per year. These are facts and we need to face them: it is therefore obvious that research in the field of ageing and dementia is not only needed but it represents a societal obligation necessary to understanding the causes and developmental pathways of the disease, for its diagnosis, prevention and treatment. In this scenario, and as part of the EBC value of treatment project, the potential impact of a hypothetical Alzheimer's medicine was assessed by researchers from Maastricht University, the Karolinksa Institute, the University

Medical Center Amsterdam and the London School of Economics. A treatment that would delay the rate of disease progression by 50% would have, as a consequence, a smaller proportion of people progressing to advanced stages of the disease. This would result in an increase of quality adjusted life years (QALYs), a measure for both quality and the quantity of life lived, of 1,75 per patient. Overall, a potential treatment is estimated to reduce the total lifetime care costs by 12.406 euro per person, per year. Considering the costs of dementia for the European society and that these costs will increase considerably in the coming years due to the ageing of the European population, one way of curbing this increase and eventually decreasing the costs is via intensified research. It is therefore important to focus our efforts on fundamental as well as in clinical neuroscience research. Only by improving the insight into the basic functioning of the brain and translating this knowledge to the disease state, understanding the causes of the disease process and paving the way for better targeted and improved treatment can the upwards spiral of the costs of brain disorders can be stopped. Furthermore, there is a constant need for strengthening the information flow and accelerating the exchange of experience on the on-going and future projects as well as maintaining continuous dialogue between all the stakeholder groups at the national and European level and initiatives to allow that objectives are aligned, and needs are met.

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Oral presentations

A4-O1

Genes and Mechanisms Modulating Ageing and Neurodegeneration Derived From Studying Down Syndrome

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Down Syndrome (DS) (caused by trisomy 21 (T21)) is an accelerated ageing condition on cellular and organism level. Paradoxically, people with DS have a much lower incidence and mortality from a range of solid tumours. They have an approximately 50–100 fold higher overall incidence of leukaemias in childhood than normal children, including all types of acute myeloid leukaemia (AML) and B-cell acute lymphoblastic leukaemia (ALL). Children with DS are prone to suffer a relapse and have a higher risk of death from therapy-related side effects. Paradoxically though, individuals with DS have a substantially reduced incidence of second malignancies following radiation therapy, even at a juvenile age, despite DS haematopoietic cells in vivo showing a significantly increased "passenger" mutation rate per year of age. We also detected that T21 causes a significantly increased number of DNA double strand breaks (γH2AX foci) in undifferentiated proliferating hiPSCs, post-mitotic neurons derived from hiPSCs, as well as in a transchromosomic mouse model of DS. We also detected that IgG glycans in Down Syndrome individuals show extreme profiles that reflect accelerated aging. Experiments aimed at identifying the chromosome 21 genes whose trisomic overdose is responsible for accelerated ageing and neurodegeneration using iPSC and other cellular models are on-going using iPSCs from partial trisomy 21 cases, as well as CRISPR/Cas9-edited trisomy-correction for specific genes. Using isogenic T21-iPSC-derived cerebral organoids, we also identified a novel mechanism that delays the onset of Alzheimer's disease, despite the triplication of the myloid precursor protein (APP) gene in T21.

A4-O2

The ALZENTIA System: A Sensitive Non-invasive Hidden-Goal Test for Early Cognitive Impairment Screening

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There is a need to identify reliable predictors of mild cognitive impairment (MCI) and dementia due to Alzheimer's disease (AD) in normal elderly people to enable timely intervention. The Mini-Mental State Examination (MMSE) is the best-known and the most often used short screening tool for providing an overall measure of cognitive impairment in clinical, research, and community settings. However, MMSE is not actually a mental status examination designed to detect dementia as it was originally developed to differentiate organic from functional psychiatric patients. The MMSE has low sensitivity in detecting dementia as well as poor specificity, and low negative (NPV), and positive predictive values (PPV), especially in early-stage AD. A recent systematic review also did not find evidence supporting a substantial role of MMSE as a stand-alone single-administration test in the identification of MCI patients who could develop dementia (Cochrane Database Syst Rev. 2015: CD010783). We have developed a new system (ALZENTIA) that helps detect early MCI, mainly caused by AD. This system consists of original software and hardware, and stems from the original efforts by the late Jan Bures and his colleagues to develop a hidden-goal task (HGT) test in which the human subject has to find a target that is not visible; instead, the navigation must be based on a previously memorized target position, in relation to the starting position and/or other navigational landmarks (orientation cues). The average duration of the test is approximately 25 min. per subject. Our preliminary results obtained on 91 healthy controls (HC) and 33 MCI patients have been recently published (J. Neurosci. Methods, 2020; 332: 108547). Receiver operating characteristic (ROC) analysis revealed that two measurements (variables) reached 85% or higher sensitivity and specificity: combined allocentric-egocentric average error of all 8 attempts, and egocentric average error of the first 4 attempts. The high NPVs (over 90% in almost all subtests and at all prevalences) suggested high discriminative capacity and diagnostic potential for the ALZENTIA system as a tool to detect subjects in healthy population who will progress to MCI. Considering the low sensitivity of the MMSE and Montreal Cognitive Assessment (MoCA) tests currently used for

this purpose, we believe that ALZENTIA can significantly improve early identification of MCI patients who will progress to AD. Funded by the Croatian Science Foundation and HAMAG-BICRO.

A4-O3

Genomic Diagnostics in Patients with Neurodegenerative Diseases

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Neurodegenerative diseases are characterized by progressive nervous system dysfunction caused by the death of neurons in the brain and spinal cord. Given the prevalence, clinical hallmarks and associated costs of treatment, neurodegenerative diseases represent a significant and ever increasing public health problem. Despite extensive clinical research and dynamic developments in the field of neurology, especially regarding the development of new disease-modifying drugs and therapeutic procedures, there is still no effective medicine capable of stopping or even slowing neurodegenerative processes. A growing body of research points to the clear role of genetic mechanisms in the development of neurodegenerative diseases such as Alzheimer's and Parkinson's disease or Amyotrophic lateral sclerosis. Insight into the human genome structure provides key information on possible hereditary diseases and genetic rearrangements which can cause common and rare variants of the genotype. Although numerous genes are responsible for the appearance of monogenic forms of neurodegenerative diseases, in most cases, inheritance is genetically complex and occurs through the interaction of multiple genes and the environment. Genomic approaches, such as gene chips or next generation sequencing, provide a better insight into the genetic risk factors that are responsible for neurodegenerative diseases. Next generation sequencing approaches such as whole-genome, exome and panel sequencing have greatly enhanced our ability to detect genetic causes of neurodegenerative diseases. Novel genomic approaches will enable in the future not only the detection of new genetic risk variants, but will also contribute to increased treatment efficiency and reduce the frequency of adverse events to existing and future therapies.

Poster presentations

A4-P1

Challenges in Headache Treatment in Elderly

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Headaches occur less frequently in the elderly than in the younger and middle-aged population, but are nevertheless a challenge for diagnosis and treatment. Any headache that first occurs in the elderly must arouse suspicion of a secondary headache and require diagnostic workup, including a brain imaging. In addition to primary and secondary brain tumors and intracranial haemorrhage, headache in the elderly may also be a consequence of systemic diseases such as arterial hypertension, polymyalgia rheumatica and giant cell arteritis, which also require treatment as soon as possible. Particular problems in older age are the primary headaches that continue since patient's young or middle-age, persistent in frequency and intensity. The treatment of such patients is a problem because of the comorbidities that limit pharmacotherapy, the limitations on the use of specific migraine drugs – triptans, polypragmasy and psychiatric comorbidities. The complexity of treating elderly patients with headache are best described by following case reports from everyday practice: 73 year-old female patient with trigeminal neuralgia, 77 year-old female patient with temporal arteritis, 90 year-old female patient with frequent tension-type headache, and 68 year-old male patient with chronic migraine. If left untreated, headaches significantly reduce the quality of life of elderly patients already burdened with other diseases and conditions and can lead to the occurrence of medication overuse headache.

A4-P2

Hallmarks of Corticogenesis After Ischemic Stroke in Mice

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Introduction and objectives. Stroke represents the most common acute neurological condition leading to permanent disability, and as such a significant burden of disease in a modern aging society. Animal models of ischemic stroke mirror the postischemic changes at the molecular and cellular level, enabling the study of recovery mechanisms, that are presumably based on revoking the process of corticogenesis. The goal of this study was to identify the role of prominent markers of corticogenesis, SatB2 and Ctip2, in postischemic recovery. **Methods.** Transient middle cerebral artery occlusion (tMCAo) was performed on male adult C57Bl6 mice (n = 5) and the lesion was followed up using 7T BioSpec MRI system, as well as observing neurological deficit (NS) in the analysis of behaviour (Day 3, 7). Control group underwent the sham surgery. From Day 3 to 7 both groups received 5 dosages of 5-bromo-2'-deoxyuridine (BrdU) in order to mark the newly proliferating cells. On the day 7 mice were anaesthetized, perfused by saline and 4% paraformaldehyde (PFA) to preserve the brain anatomy for immunofluorescence (IF) using antibodies specific for SatB2, Ctip2, NeuN, cCASP3, GFAP and BrdU. Slides were imaged using the confocal microscope (Olympus, CIBR) and positive cells were counted for each marker in the ipsilateral (IL) and contralateral (CL) cortex, hippocampus and striatum. Results were correlated to the lesion size determined by the MRI and cresyl-violet slides, and to the neurological score. **Results**. The lesion was the largest on the Day 3 after tMCAo, and this was in positive correlation with the ND. IF signal of SatB2 and Ctip2 was significantly different between the IL and CL hemispheres of the tMCAo mice, and in comparison to the sham operated group. Also, the amount of cells co-expressing both markers increased after tMCAo, as well as the number of BrdU positive cells. GFAP has shown an astrocytic reaction, while the total number of neurons (NeuN) was impaired in IL hemisphere after tMCAO. **Conclusions.** Subacute stage of ischemic stroke in mice includes increased proliferation of cells, as well as the changes in the neuronal cortical profiling (SatB2, Ctip2) that resemble immature patters during corticogenesis. Modulation of those events could not only prevent the postischemic epileptogenic conversion, but also enhance the speed and quality of rehabilitation in affected patients.

A4-P3

Effects of Age on Retinal Macrophage Responses to Acute Elevation of Intraocular Pressure

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Introduction and objectives. There is accumulating evidence that aging shifts the central nervous system milieu towards a proinflammatory state, with increased reactivity of microglia in the aging eye and brain having been implicated in the development of age-related neurodegenerative conditions. Indeed, alterations to microglial morphology and function have been recognized as a part of normal aging. Here, we sought to assess the effects of age on the retinal microglial and macrophage response to acute intraocular pressure (IOP) elevation and further, determine whether the age of bone marrow would alter the macrophage response to injury in bone marrow chimeric mice. **Methods.** For the first part of this study, C57BL/6J mice of 3 and 12 months of age underwent IOP elevation. Briefly, the anterior chamber was cannulated and intraocular pressure elevated to 50 mmHg for 30 minutes. Control eyes were cannulated and pressure was maintained at physiological IOP (12 mm Hg). In the second part of this study, bone marrow from young (8 week old) or middle-aged (12 month old) mice was used to reconstitute the bone marrow of whole-body irradiated 12 month old mice. Bone marrow chimeric mice underwent cannulation and IOP elevation 8 weeks after bone marrow transplantation. For both studies, eyes were collected for analysis 1 week after IOP elevation. Immunofluorescence staining was performed on retinal wholemounts to assess changes to the density of retinal macrophages, microglial process length and activation of glial cells. **Results.** Retinal macrophage reactivity and microglial morphological changes were enhanced in older mice when compared to younger mice in response to injury. When IOP elevation was performed after whole-body irradiation and bone marrow rescue, we noted a reduction in subretinal macrophage accumulation and attenuation of glial reactivity compared to non-irradiated mice that had also undergone IOP elevation. This effect was evident in both groups of chimeric mice that had received either young or middle-aged bone marrow. **Conclusions.** Our data suggest irradiation itself may alter the macrophage and glial response to retinal injury rather than the age of bone marrow.

A4-P4

Cognitive Training: New Therapeutic Approach to the Patients with Mild Cognitive Impairment

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Cognitive training (CT) has attained attention as a non-pharmacological approach to maintain cognition in older adults. CT involves guided drill-and-practice on standardized tasks designed to load on specific cognitive processes, typically without explicit teaching of memory or problem-solving strategies. CT can target multiple domains and usually adapts task difficulty to individual performance. Recent randomized control trials and meta-analyses of experimental studies indicate positive effects of CT on the cognitive function of healthy older adults but also patients that demonstrate impaired cognitive functions due to several reasons. Furthermore, a large-scale randomized control trial with older adults, independent at entry, indicated that CT delayed their cognitive and functional decline over a five-year follow-up. This supports CT as a potentially efficient method to postpone cognitive decline in persons with mild cognitive impairment (MCI) and CT as therapeutic option able to prevent or delay cognitive or functional decline. Training in elderly with MCI had greater effect in the younger old and more cognitively preserved individuals. In MCI, CT is efficacious on global cognition, memory, working memory, and attention and helps improve psychosocial functioning, including depressive symptoms. Effect of CT was corroborated by a moderate effect size on common clinical measures of global cognition (mainly the Mini-Mental State Examination). Moderate effect sizes on memory is encouraging, as amnestic MCI profiles are at higher risk for dementia conversion. Participants in CT groups improved significantly over the intervention period but there are still insufficient data to determine whether training gains can be maintained over the long-term without further training. Cognitive interventions can contribute toward promoting health and independence among patients with MCI. Further investigations in large samples with long follow up pe-

riod are now warranted to verify the role of cognitive interventions as reliable tool to prevent cognitive functions and wellbeing.

A4-P5

Role of Vibrational Spectroscopy in the Early Detection of Glaucoma

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Introduction and objectives. Glaucoma is a disease of the optic nerve that causes retinal ganglion cell (RGC) decay and retinal nerve fiber layer (RNFL) thinning, resulting in the visual field damage. It is one of the major causes of irreversible blindness in the world and is therefore a major public health problem since. Also, it is estimated that 80 million people will suffer from glaucoma by 2020. The most common type of glaucoma is primary open-angle glaucoma (POAG), and, despite numerous studies, the exact pathomechanism of its occurrence has not yet been determined. Numerous risk factors for the onset and progression of glaucoma have been identified, the most important being the height of intraocular pressure (IOP), the degree of damage at the time of diagnosis and the life expectancy of the patient. Currently, the only treatment option to slow the progression of the disease is to lower IOP. The goal is to detect glaucoma as early as possible to ensure the best possible quality of life and prevent blindness. Since there are currently no glaucoma-specific biomarkers yet identified and no glaucoma screening method available, we decided to analyze molecular structure of aqueous humor using FTIR spectroscopy which offers a unique opportunity to investigate the composition of unknown substances on a molecular basis. **Methods.** The study included 80 age matched subjects from the Reference Center for Glaucoma, UHC "Sestre milosrdnice", divided into two groups 1) 40 glaucoma patients and 2) a control group comprising 40 patients with cataracts. For the purpose of molecular analysis, all aqueous humor samples were collected at the start of the glaucoma or cataract surgery. FTIR spectra of the samples dried on transparent silicon windows were obtained in a transmission mode, followed by principal component analysis (PCA) modeling of the recorded spectra. **Results.** FTIR spectra with vibrational modes specific to glaucoma and cataract were examined. In the chemomet-

ric analysis of the spectroscopic data, all 40 (100%) of the cataract eyes were correctly diagnosed as the cataract group and all 40 (100%) glaucoma eyes were diagnosed as the glaucoma group, demonstrating a distinct correlation between studied eye diseases and their FTIR spectra. **Conclusions.** FTIR spectroscopy combined with the chemometrics has proven to be a promising method for molecular analysis of the aqueous humor as the differentiation between eyes with cataract and glaucoma has been achieved. Separation of the two groups of FTIR spectra in the created PCA statistical model also indicates that this method may have a promising role in the discovery of glaucoma biomarkers.

A4-P6

BDNF, IL-6, PPARγ Gene and BDNF Protein Polymorphisms in Patients with Glaucoma

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Introduction and objectives. Glaucoma is a slowly progressive, chronic optic neuropathy that is characterized by retinal ganglion cell (RGC) death with subsequent loss of optic nerve axons and decrements in visual function. It is one of the major causes of irreversible blindness in the world and is a major public health problem. It is estimated that 80 million people will suffer from glaucoma by 2020. Several types of glaucoma are known, and the most frequent is primary open-angle glaucoma (POAG). Despite numerous studies, the exact pathomechanism of its occurrence has not yet been determined. Current treatment for glaucoma is directed toward lowering the IOP, but this approach only limits disease progression. The goal is to detect glaucoma as early as possible to ensure the best possible quality of life and prevent blindness. The molecular events responsible for glaucoma are currently poorly understood, complicating the design of therapies based on the underlying disease mechanisms. Since glaucoma is accompanied by profound biochemical changes, proteomic profiling or specific biomarker detection in the aqueous humor may be a way to follow glaucoma progression and potentially to monitor treatment efficacy. The aim of this study is to

analyze the concentration of BDNF in aqueous humor and serum and to identify polymorphisms of the BDNF, IL-6 and PPARγ genes. **Methods.** The study included 145 age matched subjects from the Reference Center for Glaucoma, UHC "Sestre milosrdnice", divided into two groups 1) 83 glaucoma patients and 2) a control group comprising 62 patients with cataracts. For the purpose of molecular analysis, all aqueous humor samples were collected at the start of glaucoma or cataract surgery. BDNF concentration was measured in aqueous humor and serum by ELISA method and BDNF polymorphism (Val66Met, VM), IL-6 (-174, GC) and PPARγ (Pro12Ala, CG) by PCR-RFLP. **Results.** BDNF concentration in serum and aqueous humor: glaucoma /cataract 13.0/13.9 ng/mL and 4.5/3.0 pg/mL. Polymorphism gene distribution (%): BDNF VV 61.4/58.1, VM 36.1/35.5, MM 2.4/6.5; IL-6 GG 38.9/41.9, GC 45.8/41.9, CC 13.3/16.1; PPARγ CC 75.9/74.2, CG 21.7/24.2, GG 2.4/1.6. **Conclusions.** Preliminary polymorphism results indicate possible polygenic markers of BDNF MM, IL-6 CC, and PPARγ GG and differences in aqueous humor BDNF concentration between examinee with glaucoma and cataract. Given the difference in the concentration of BDNF in aqueous humor between two groups, the potential for new treatment modalities opens. More research on a larger number of samples is needed to better understand the role of gene and polygenic markers in glaucoma.

chological, emotional and financial exhaustion. Family caregivers sometimes find it difficult to find a balance between work and family life, so they need help and support of the community which often doesn't understand the needs of patients and their families. A big issue is the late diagnosis of dementia, since the early symptoms of the disease are difficult to recognize. The project contributes to preventing the early institutionalization of patients, enables a better work-life balance for family members caring for patients, and increases the number of professionals working with patients. The Call Center will also support the whole community. The target groups of the project are people with Alzheimer's and other dementias, their families, the professionals who work with them as well as the general public.

A4-P7

Lend a Hand Project

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Međimurje County

The project „Lend a hand" solves the issue of social exclusion of people with Alzheimer's dementia and other forms of dementia in the Međimurje County, Krapina-Zagorje County, Požega-Slavonia County, Osijek-Baranja County and Koprivnica-Križevci County by improving the quality of life of the patients and their families. The purpose of the project is to include 30 Alheimer affected persons into the community, therefore preventing their premature institutionalization. This will enable family members to reconcile between family and business life. This will be achieved during the 18 months the expert team will work daily with the patients. The general public will become more aware of Alzheimer's dementia and other forms of dementia through the Alzheimer cafe opening in 5 counties. Dementia, as a progressive and incurable illness, quickly leads to loss of independence and thus directly affects the families of patients, leading to physical, psy-

Invited lecture

A5-I

Good Clinical Practices for the Improvement of the Age-Related Diseases

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The rise in the prevalence of multimorbidity (the co-occurrence of two or more chronic medical conditions in an individual person) in ageing societies is one of the greatest challenges now faced by health services internationally. Despite this, most medical research, guidelines, and contractual agreements (such as pay-for-performance initiatives) are focused on the management of single disease states. In these patients, individually treating each condition inevitably leads to the use of multiple medications (polypharmacy), the risks and benefits of which are largely unproven and often unpredictable.

It is important to note that polypharmacy is not inappropriate per se, and it is often beneficial. For example, effective secondary prevention of myocardial infarction requires the use of at least four different classes of drugs (antiplatelets, statins, angiotensin-converting enzyme inhibitors, and beta-blockers However, polypharmacy becomes inappropriate when the risks of multiple medications begin to outweigh their potential benefits for an individual patient. The risk of harm is generally higher in older people with multimorbidity than in younger patients due to their reduced ability to clear drugs (e.g., due to renal and/or hepatic impairment) and increased vulnerability to drugs' adverse effects (due to general frailty and drug–drug and drug–disease interactions) and medication burden . However, the increased risk of harm is not always offset by increased benefits, and for many preventive medicines, such benefits may never be realized due to a shortened life expectancy.

There is mounting evidence that polypharmacy is a public health threat and a major source of unnecessary harm, greater use of health services, hospitalization, reduced quality of life, and substantial financial cost to health-care systems. In 2012, the US Institute for Healthcare Informatics estimated that inappropriate polypharmacy contributes to 4% of the avoidable costs of health care, equating to an expenditure of $18 bil-lion worldwide, and one recommendation was to support pharmacist collaboration with physicians for medication reviews. Up to 11% of unplanned hospital admissions in the UK are attributable to mostly avoidable harm from medicines, and of these, over 70% are in elderly patients on multiple medicines. There are, therefore, significant opportunities to reduce this burden by timely and effective interventions. If this was extrapolated across the EU, this would result in 8.6M admissions . Similarly, it has been found that medicine related visits accounted for 12.5% of attendances, the main causes being adverse drug reactions (ADR) and non-adherence to medicines (33% and 19% respectively). The EU SIMPATHY project, evaluated all the guidance documents that were available across the EU. The literature review identified that there are guidance documents available relating to the management of polypharmacy in only 3 of the 28 EU countries only the guidance documents from Scotland, Netherlands and Germany score the maximum on the AGREE II-GRS criteria for quality. The third edition of *Polypharmacy Guidance, Realistic Prescribing*, published in 2018, aims to provide guidance on preventing inappropriate polypharmacy at every stage of the patient journey. It contains a clear structure for both the initiation of new treatments and the review of existing treatments, and has been updated to place a greater emphasis on "what matters to the patient?" The 7 steps were informed by existing literature and initially agreed upon and subsequently refined (based on feedback from practicing clinicians and patients) by a guideline development group comprising a mix of pharmacists and primary (general practitioners) and secondary care physicians with backgrounds in clinical practice and academia.

Agreeing specific objectives with the patient in terms of both therapeutic objectives and current life priorities (step 1) sets the context within which all further decisions are made, namely on which medicines are essential (step 2) or unnecessary (step 3), whether therapeutic objectives that matter to the patient are achieved (step 4), which medicines are too risky or cause unacceptable adverse effects (step 5), which medicines are not cost effective (step 6), and whether the patient is willing and able to manage their medicines in a way that avoids harm and maximises benefit (step 7).

While guideline development is a necessary first step, improving patient outcomes relies on their effective implementation. The challenge of safely using multiple medicines for patients with multiple morbidities is beginning to gain international attention. In

7 STEPS TO APPROPRIATE POLYPHARMACY

April 2017, at the European launch of the SIMPATHY publication *Polypharmacy Management by 2030: A Patient Safety Challenge* (15), the Scottish Cabinet Secretary for Health called on the other 27 EU counties to take action on addressing polypharmacy, and this was also supported by WHO. This work has identified six key recommendations to implement programs to improve medication safety, of which polypharmacy is an essential element: (*a*) Use a systems approach that has multidisciplinary clinical and policy leadership; (*b*) nurture a culture that encourages and prioritizes the safety and quality of prescribing; (*c*) ensure that patients are integral to the decisions made about their medicines and are empowered and supported to do so; (*d*) use data to drive change and measure outcomes; (*e*) adopt an evidence-based approach with a bias toward action; and (*f*) utilize, develop, and share tools to support implementation. The WHO Third Global Patient Safety Challenge (12), *Medication Without Harm*, has included the appropriate management of polypharmacy as a key flagship area to address across health care systems.

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Oral presentations

A5-O1

Early Intervention Optimizes Long-Term Treatment Results in Patients with Inflammatory Rheumatic Diseases

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Rheumatic diseases are a prevalent group of entities with a significant impact on quality of life and morbidity in the population. Progress in rheumatology over the last 20 years has led to a significant increase in overall life and work prognosis. Rheumatoid arthritis (RA) decreases life expectancy by 10 years. Inadequately treated patients with active RA develop irreversible functional impairment in over 50%. Introduction of new drugs – biological and targeted synthetic agents – has changed treatment outcomes tremendously. In addition to the evolvement of therapy, new diagnostic algorhythms have enabled early diagnosis. Adequate timing of contemporary treatment that is available in Croatia has led to prevention of disability, decline in sick leave, prolongation of time actively spent at work, as well as increased survival. Over 800 patients have been treated with targeted therapies at our institution – 650 are currently under treatment. Continuous and focused education of family physicians over the past 10 years enabled us to optimize screening of incident patients. The latter serves as a prerequisite for better treatment outcomes. Systemic lupus erythematosus (SLE) is a typical systemic inflammatory rheumatic disease. Five-year survival in the 1950s was 50%, in contrast to 95% at the beginning of this century. Data from the literature suggested a bimodal mortality pattern. Results of a study performed in Croatia demonstrated a 5-year survival of 90%. However, the study did not confirm a bimodal pattern: this may be explained by a decline in early mortality owing to early diagnosis and therapy, as well as by a lack of complications of aggressive therapy. This study demonstrated problems in the collection of public health data for patients with SLE. Insufficiency of the current criteria for SLE has resulted in a project within an international working group and, subsequently, proposal and publication of new criteria for the diagnosis of SLE (our Division was included as the Referral Center for SLE of the Croatian Ministry of Health). Progress has been noted in the diagnosis and treatment of common rheumatic diseases of the elderly such as polymyalgia rheumatica and giant cell arteritis. Our experience in the use of contemporary therapeutics showed good results and better treatment tolerance. Finally, further steps have been noted in the treatment of osteoarthritis, commonly perceived as the most important rheumatic disease in the elderly. Improvement of surgical techniques and higher quality endoprostheses have increased treatment outcomes. Steps forward in the area of osteoarthritis pharmacotherapy have also been observed.

A5-O2

Pharmacogenomics – a Promising Tool for Elderly Patients on Polytherapy

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Introduction and objectives. Polypharmacy is prevalent in elderly patients and is associated with drug-drug interactions, adverse drug reactions (ADRs), more frequent hospital admissions and higher healthcare costs. A pharmacogenomic approach enables personalized medication regimens based on individual genetic variations predominantly of ADME genes, involved in the pharmacokinetics of medicinal products. The majority of current pharmacogenomic decision support tools provide assessment only of single drug-gene interactions without taking into account complex drug-drug and drug-drug-gene interactions which are prevalent in polypharmacy and can result in ADRs or insufficient drug efficacy. Genotyping of metabolic enzymes of phase I (CYPs, DPD), phase II (TPMT, UGTs, NAT2), ABC, SLC transporters, and drug targets, represents a valuable tool for analysing the causal relationship between drug intake and dose related ADRs. The availability of genomic testing has grown, but its clinical application is still insufficient. The objective was to develop comprehensive pharmacogenomic decision support for medication risk assessment in elderly polymedicated patients. **Methods.** To study the

possible genetic associations with ADRs, School of Medicine University of Zagreb, University Hospital Centre Zagreb, and Croatian Agency for Medicinal Products & Medical Devices (HALMED) have piloted a project to collect DNA and phenotype data of ADR cases using international standardized phenotypic criteria. Patients with ADRs (N=860) and controls were genotyped for pharmacogenes. Univariate and multivariate prediction of ADRs were carried by means of binary logistic regression in order to identify novel associations or validate findings in cohorts of patients with well-defined phenotypes. **Results.** We developed a comprehensive knowledge repository of actionable pharmacogenes. HALMED developed a method for informing physicians or pharmacists and their patients about a possible pharmacogenetic involvement in the ADR pathogenesis. An anonymized copy of the test results has been used for the interpretation of possible signals. Several publications from this project have been published, depending on the medication in question (warfarin, statins, clopidogrel, methotrexate, AEDs, psychotropic drugs). **Conclusion**. Pharmacogenomic knowledge repository is an excellent starting point for pharmacogenomic testing implementation in clinical practice and pharmacogenetic counselling after a reported ADR. By using a pharmacogenomics approach, individualized strategies in medication can improve drug safety and efficacy in the elderly patient population.

A5-O3

International Networking and Clinical Practice in Neurodegenerative Diseases

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Aging is a well-known risk factor for neurodegenerative disease. As world population is continuously aging, both incidence and prevalence of neurodegenerative diseases are rising.

The term neurodegeneration means that there is an irreversible loss of neurons. Available treatments can only modify and slow down the natural course of the disease, but not stop disease progression. Therefore, it is not surprising that the field of research and interest in these diseases is continuously growing. Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterised by progressive loss of motor neurons leading to death in 3–5 years from symptom onset. Since there is still no cure, treatment is based on a multidisciplinary approach in palliative care to improve the quality of life. To improve care and make expensive clinical research more available to our patients, Centre for Neuromuscular diseases and Clinical Electromyoneurography, Clinical hospital centre Zagreb became a member of ENCALS (European network to cure ALS) in 2017.

After joining the network, our Centre continued to provide up-to-date medical care, treatment and support for patients with ALS as well as actively seeking ways to contribute to the pool of knowledge about motor neuron disease. This is reflected in activities undertaken over the last two years – clinically based registry of ALS patients was created as well as blood and CSF bank. Registry provided up to date epidemiological data about Centre's patient population. We included new members into our multidisciplinary team with genomics and sleep disorders specialists. Following this team expansion first genetic testing results for Centre's patients with familial ALS are available. All of this enabled us to join TRICALS research initiative to find cure for ALS. Centre has also started validation and standardisation of the Croatian ECAS (Edinburgh Cognitive and Behavioural ALS screen) in collaboration with Prof. Abrahams' team from University of Edinburgh. Following this, same is intended with DAS (Dimensional Apathy Scale). Currently our Centre is exploring the quality of life of patients with ALS (first results pending). Considering all of the above it appears there has been a change in Centre's activity with increased productivity and improved structure, and change in team's attitude from mechanistic to optimistic which is sometimes even more difficult to achieve.

In this report we want to illustrate the practical importance of clinical and scientific network and its positive impact in everyday quality of clinical work in the demanding field of neurodegenerative diseases, especially ALS.

Poster presentations

A5-P1

Common Clinical Challenges When Prescribing Dermatologic Therapy in Geriatric Patients

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One hundred years ago, only 2% of the U.S. population was over 65 years old. By 1980, this percentage was 11%, and by the year 2030, it will be 20%. With this tremendous increase in the proportion of elderly in the global population, geriatric medicine has become of great interest and importance. Data shows that around 40% of Americans between the ages of 65 and 74 years have had a skin disease significant enough to warrant treatment by a physician. Given the high incidence of significant dermatologic disorders in the elderly, it is clear that all health providers need to familiarize themselves with the diagnosis, prevention, and treatment of skin diseases seen in this population. The mainstay of therapeutic approach in the elderly should be proper skincare and treatment due to the preventable nature of most of the age-related skin diseases or treatable nature of another skin disease with their age-related specificities. Particular attention needs to be directed towards geriatric dermato-pharmacology as an ageing population has brought many therapeutic challenges that we need to recognize and overcome. Safely prescribing in the field of geriatric dermatology is a complicated task since there is an increased risk of drug interactions that may be caused by various factors including the prescribing factor, patient-related factors or difficulties within the healthcare system such as poor or insufficient communication between the patients and medical professionals. Dermatologists and other specialists should be aware that prescribing medicines to their mature patients is a dynamic process that involves many patient-doctor-health-care providers' oriented steps, which may influence the therapeutic result. Also, they need to be aware of the age-related changes in the pharmacokinetics of common dermatologic drugs, their various interactions potentially occurring in the elderly, and the principles, and evidence-based strategies for their prevention, detection and management to improve adherence to therapy in order to ensure the best and the safest treatment of dermatoses occurring in the seniors. By implementing these gerontopharmacologic principles and strategies, and a team-based, holistic, personalized, and multi-disciplinary professional dynamic approach we can achieve the desired therapeutic outcome and improved quality of life for this fragile group of patients.

A5-P2

Voice Disorders and Voice Therapy in Elderly

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Introduction and Objectives. Voice disorders in the elderly are usually the result of physiological changes in the larynx that result in poor voice quality, vocal fatigue, and vocal strain. However, part of the diagnosed voice disorders in this population is not due to aging. The aim of this paper is to present a clinical snapshot of such voice disorders – specifically the ones that accompany organic changes in the vocal cords – as well as to demonstrate the results of their rehabilitation. **Methods.** The study involved 23 women and 7 men aged 60 to 89 years with paralysis of the vocal cords caused by thyroidectomy (12), gastroesophageal reflux (LPR) (9), post-operative vagal glomus tumor (2), Reinke's edema (6) and vocal cord polyp (1). Their self-assessment of voice-related quality of life and their acoustic voice characteristics (jitter, shimmer, and harmonic-to-noise ratio) were compared before and after rehabilitation. **Results.** After rehabilitation, the acoustic parameters improved significantly, indicating that, regardless of patient age or the impact of functional dysphonia in the elderly population, a good rehabilitation procedure can evoke objectively measurable positive voice changes. Self-assessment revealed that poorer voice quality affects quality of life among these patients as well, even though they are no longer professionally involved or maximally socially active. **Conclusion.** The results of this study clearly demonstrate the need for the involvement of elderly persons in voice rehabilitation and the benefits of exploring various rehabilitation options in daily clinical work to raise or preserve their quality of life.

A5-P3
The Person-Centred Medical Interview for Elderly Patients

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As in other medical branches, person-centered medical interview is an essential and very important tool when caring for the elderly. The medical interview is an integral part of the comprehensive geriatric assessment and diagnostic. The interview must include a complete range of biological, psychological, social and spiritual components. In communication with the elderly and the elderly patients, a special emphasis should be placed on certain challenges that highlight our communication skills, knowledge and personal views. It is essential to understand that older people will have to a much greater extent some functional difficulties that we need to be able to recognize and accommodate in the interview. One of the challenges in communication is certainly the issue how to convey various bad news to patients with serious diseases. When communicating with this type of patients, it is also important to recognize some of the specific emotional responses of old people to the disease. Finally, when we are talking about medical interview, it is of immense importance to organize the consultations with a whole family when we have an elderly patient with an illness. For medical practitioners, it is essential the knowledge how to conduct the interview which will have a high motivational effect on the patient and their health. The interview should be led in such a way to promote healthy aging – to point out the good parts and to encourage healthy life habits – while at the same time explaining to the patient that they can still live a quality life regardless the numerous illnesses. The geriatric assessment is interdisciplinary, requiring a high level of quality communication within the medical team. The patient and their family must be also a member of this team and equal participants in the communication process. Recognizing the importance of the above, we are pleased to have promoted and gradually introduced into the curriculum of the School of medicine University of Zagreb over the past ten years, the new modules dedicated to the communication with the elderly. In the teaching, we have included patients, too, through so called "model patient as a teacher". This experiential learning method has proven to be excellent and has had the most impact on changing knowledge and attitudes among students and healthcare professionals. We believe that promoting healthy aging is a continuous process in which the improvement of communication is essential element.

A5-P4
Stroke and Mechanical Thrombectomy in Elderly

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Introduction. The worldwide elderly population is rapidly growing, so absolute number of strokes is expected to significantly increase over the course of the next century. Therefore, the benefit of endovascular treatment (EVT) of stroke in the elderly becomes more relevant. Mechanical thrombectomy is an established treatment for acute ischemic stroke (AIS) due to a large vessel occlusion (LVO) involving the anterior cerebral circulation in all patients within 6 h and in some selected patients with advanced imaging findings up to 24 h from stroke onset. However, in most recent meta-analysis (HERMES), the older patients did worse than the younger patients regardless of treatment modality, and increasing age was a strong predictor of poor outcome. This single center analysis aimed to compare the outcomes of elderly patients with younger patients after EVT for AIS. **Methods.** We performed single center retrospective analysis of 60 patients (30 of them over 80 years and 30 under 80 years) who received EVT for anterior circulation in AIS. We aimed to determine 90-day good functional outcomes (modified Rankin Scale mRS 0–2) in patients ≥80 vs. <80 years, compare incidence of symptomatic intracranial hemorrhage (SICH), mortality and successful reperfusion rate (on TICI 0–2 scale) between groups. **Results.** Thirty two percent of our elderly cohort achieved good 90-day mRS outcome compared to 40% of younger patients. Successful reperfusion rate and SICH were similar (73% and 12% in younger group vs 76 % and 10% in elderly group). Morality was slightly higher in elderly group (22 % vs 17 %) which was most likely contributed to higher prestroke comorbidity. **Conclusion.** Our results support some of previous findings that although older patients may have worse outcomes overall, there is no heterogeneity of EVT effect seen by age. Mechanical thrombectomy is just as effective in elderly patients as it is in younger ones.

A5-P5

Different Faces of the Same Problem: Lipid-Lowering Therapy in the Elderly

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Introduction and Objectives. At least 85 million patients in Europe suffer from cardiovascular diseases which are the cause of 3,9 million deaths per year. Most of them are elderly people over 65 years old, who have an indication for lipid-lowering drug therapy. However, there is a question whether benefits of this treatment arises its harms considering frequent co-morbidities in elderly population. **Methods.** Four types of patients that we meet daily in medical practice will be outlined. Their cardiovascular risk according to SCORE (Systematic Coronary Risk Estimation), patient assessment, blood pressure (BP), laboratory values: TC, HDL, LDL, eGFR and life expectancy, will be calculated. Given the calculated parameters and combined with an individual approach, decision of using lipid therapy will be made. **Results.** The first patient, female, 65 years old, BP 140/80 mmHg, TC 5.9 mmol/L, HDL 1.4 mmol/L, LDL 3.5 mmol/L, eGFR 89 mL/min/1.73m², non-smoker. 10-year CV risk: 4%. This patient belongs to the moderate risk group (SCORE ≥1% and <5%) and her LDL values are 3.5 mmol/L with no indication for initiation of therapy (IIa/A). The second patient, male, 65 years old, BP 140/80 mmHg, TC 4.9 mmol/L, HDL 0.9 mmol/L, LDL 3.1 mmol/L, eGFR 65 mL/min/1.73m², non-smoker. 10-year CV risk: 9%. This patient is in the high-risk group (SCORE ≥5% and <10%) and his LDL is 3.1 mmol/L, which means that therapy is recommended (I/A). The third patient, female, 80 years old, BP 150/90 mmHg, TC 6.9 mmol/L, HDL 0.7 mmol/L, LDL 4.5 mmol/L, eGFR 55 mL/min/1.73m², smoker with documented ASCVD. This patient due to ASCVD belongs to the very high risk group and therapy is recommended (LDL goal <1.4mmol/L) (I/A). The fourth patient, male, 80 years old, BP 150/90 mmHg, TC 7.8 mmol/L, HDL 1.1 mmol/L, LDL 5.1 mmol/L, eGFR <30 mL/min/1.73m², smoker with documented dementia and heart failure. Due to severe CKD (eGFR <30 mL/min/1.73m²), this patient belongs to the very high risk group, LDL is 5.1 mmol/L, which requires the gradual introduction of therapy at lower doses (I/C). Life expectancy is 3.3 years. **Conclusions.** According to the guidelines, particular attention should be paid to life expectancy and in some patients ap-proach should be individual. In these cases, it is quite clear that it makes sense to introduce the therapy to the second and third patient, since their life expectancy is long enough for the therapy to reach its maximum effect, which takes 2–3 years. However, if the last case is looked at, the efficacy of the therapy depends on life expectancy and the dose should be modificated depending on renal function and other comorbidities.

A5-P6

Therapeutic Options of Non-melanoma Skin Cancer in Elderly

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Non-melanoma skin cancer (NMSC) is the most common human cancer, with increasing incidence in the last decades. Cumulative sun exposure has the main role in the development of NMSC, so a higher prevalence of NMSC in the elderly is expected. A median age at diagnosis is 71 years. Of all NMSC, approximately 80% include basal cell carcinoma (BCC) and 20% squamous cell carcinoma (SCC). Other skin tumors account for about 1% of NMSC. In the elderly, therapy for NMSC can be surgical and nonsurgical. Surgical treatment of NMSC is the most effective treatment that provides high cure rate of over 90% for both SCC and BCC, and over 95% for BCC. Despite the high cure rates achieved with surgery, this treatment modality is associated with the risk of morbidities such as infections, which may be fatal in this age group. Other therapeutic modalities depend on tumor localization, histological type, and biologic behavior, as well as patient comorbidities, age, and life expectancy. Nonsurgical treatments include cryotherapy, local therapies (imiquimod, 5-fluorouracil, ingenol-mebutate, and diclofenac), photodynamic therapy, radiotherapy, and hedgehog inhibitors. Some of these treatments can be combined with curettage and electrodesiccation for better outcomes. Every treatment modality has advantages and disadvantages that must be carefully considered individually. Because the facial area is the most common localization of NMSC, treatment modalities with better cosmetic outcome are preferred. Many times, despite good clinical condition, a surgery is refused by the patient because of their age. Patient life expectancy, functional and socioeconomic status, and quality of life should be taken in consideration when choosing the most suitable treatment modality

for this non-fatal disease. Surgical excision after the procedure requires outpatient visits, which can be inconvenient because older patients are dependent on others because of the transport and a home care. On the other hand, nonsurgical treatments also require outpatient visits because of the novel applications which are sometimes unfamiliar to the patients. After choosing the best therapeutic option for a patient, it is crucial that the patient's quality of life is preserved in this sensitive age.

A5-P7
Characteristics of Multiple Sclerosis in Elderly Patients

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Introduction. Multiple sclerosis (MS) is an autoimmune chronic demyelinating disease of the central nervous system that usually starts between 20 and 40 years. Rarely, in about less than 10% , it starts after age 50. Currently, approximately a quarter of people with MS are mature adults over 65 years old. **Methods.** We have analyzed demographic characteristics of patients aged ≥65 years, clinical data including type of MS, age of disease onset, duration, Expanded Disability Status Scale (EDSS) and type of treatment. **Results.** Among 133 patients, 12 (9.02%) were ≥65 years old, 9 (75%) was female and 3 (25%) male. The youngest patient was 66 and the oldest 86 years old. The average age was 73.6 years. The average age of disease onset was 40.4 years, ranging between 25 and 63 years. Th average disease duration was 33.2 years, range between 8 and 48 years. The most common type of disease was secondary progressive MS, present in 8 patients (66.7%), 2 (16.7%) patients had relapsing remitting MS and 2 (16.7%) primary progressive MS. The average EDSS was 4.5, range between 1 and 9. Most patients, 91.7%, received only symptomatic treatment, 1 patient took immunomodulatory drug. **Conclusion.** This small pilot study on characteristics of MS in elderly patients proved data found in the literature. As in the young age, female patients dominate. Longer disease duration means more frequent transition to secondary progressive MS and higher EDSS, while in the late onset of MS, after age of 50, primary progressive MS is more common. Immunomodulatory drugs, according to Croatian Health Organisation, until 2018 were reserved for patients younger than 55 years. Most patients in our study were treated only by symptomatic treatment, which could explain higher EDSS and progressive type of disease.

A5-P8
Outcomes and Patient Satisfaction in Women Undergoing Three Different Operating Techniques for Pelvic Organ Prolapse – a Pilot Study

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Introduction and Objectives. There are different methods for surgical management of pelvic organ prolapse. Surgical treatment includes vaginal native tissue repair, vaginal augmentation with mesh, and laparoscopic approach. The aim of this pilot study was to compare outcomes and patient satisfaction between three different operating techniques in a single hospital centre. **Methods.** A retrospective cohort study included total of 60 women who underwent surgery for apical and anterior prolapse. They were divided into three equal groups according to operating technique: vaginal native tissue repair (N=20), vaginal augmentation with mesh (N=20) and laparoscopic lateral suspension with mesh (N=20). Data collected included baseline patients characteristic (age, BMI, menopausal status, prior surgery), intra and perioperative variables (operative time, hospital stay, haemorrhage, wound infection, urinary complications) and six month follow up outcomes (recurrent prolapse, dyspareunia, de novo urinary incontinence or urgency, patient satisfaction calculated on scale 1–10). **Results.** Baseline characteristics of women included were similar. The mean operating time was significantly longer in the laparoscopic lateral suspension group (95 min) when compared with other two groups (p < 0.01). Nevertheless, hospital stay was shorter in aforementioned group (p<0.001). Further perioperative complications were rare and comparable between the groups. During the six-month follow-up period, no prolapse recurrence and mesh erosion were observed in any group. De novo stress urinary incontinence and urgency were infrequently observed and comparable between the groups. Overall satisfaction was higher in laparoscopic lateral suspension group (p<0.05). **Conclusion.** No difference is found in complication rates and short-term outcomes between three different surgical techniques for apical and anterior prolapse. Nevertheless,

shorter hospital stay as well as higher overall satisfaction confirms laparoscopic lateral suspension as a promising endoscopic prolapse surgery technique. Future prospective studies with larger sample sizes demonstrating the long-term outcomes are warranted to confirm these conclusions.

Osteoarthritis – Leading Cause of Disability in the Elderly

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Introduction and objectives. Osteoarthritis (OA) is a slowly progressive musculoskeletal disorder associated with increased age and is characterized by joint pain and tenderness, limitation of motion, joint deformity and instability. It has long been considered a noninflammatory process, but new insights suggest a role of proinflammatory mediators and proteases therefore enabling development of new treatment targets. **Methods.** Pathological findings in articular cartilage, bone, synovium and soft tissues of patients with OA are similar and vary in the degree of damage, suggesting a uniform response to various insults. Multiple risk factors for developing OA have been identified, including age, obesity, joint injury, genetics, gender, as well as anatomical factors. The pathogenesis of osteoarthritis involves various cytokines, chemokines and proteases and resembles that of a chronic nonhealing wound. There is growing evidence implying activation of the innate immune system as a result of tissue damage. Epigenetic changes contribute to development of OA as well and are being actively investigated. **Results.** Available treatment modalities consist of pain management but no treatment has been proven to alter the structural progression of the disease. Agents inhibiting catabolic processes and those stimulating anabolic processes, as well as drugs that modify inflammatory pathways and bone remodelling are being investigated and are reffered to as disease-modifying OA drugs (DMOADs) or structure-modifying OA drugs (SMOADs). Investigational drugs targeting pain have focused on inhibiting nerve growth factor. **Conclusion.** Osteoarthritis is the most common form of arthritis. Since it affects mainly the elderly and is associated with substantial disability and reduced quality of life, it represents a great burden for the aging population. Novel insights into pathophysiology of the disease promise new treatment modalities, as opposed to current treatment targeting symptomatic relief.

Therapeutic Movement Therapy (TMT) and the Healthy Lifestyles (HLS) Education in the Day Hospital (DH) – Reflections and Suggestions

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Therapeutic movement therapy (TMT) and the healthy life styles (HLS) education in the Day Hospital have been successful part of the program of the Day Hospital for the patients who suffer from depression, anxiety, grief , psychosomatic and stress related disorders, treated within this program. Patients who are treated are both sex, ages between 18–65, majority in the middle ages, with somatic diagnosis as comorbidity. Taking care of body helps to improve wellbeing. In this poster we will present patients´ reflections and suggestions about this part of the program.

Assessing Fitness to Work Among Older Workers: Literature Review

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Introduction and Objectives. Decreases in physical and mental functional ability due to aging can impair work capacity, productivity and fitness for work among older workers. There is no precise, generally recognized age at which someone is considered as an older worker. Some studies have focused on workers older than 55, while other studies examined those 45 years or older. It is vital to make appropriate fitness to work assessment of older workers duo to serious increase of aged working population. Objective of our study is to summarise current situation in assessing fitness to work of older workers from data available in recent literature. **Methods.** Literature review has been made in PubMed database regarding following key words: ageing worker; fitness to work; functional capacity; work ability. We focused our search for time period of past 20 years. **Results.** We found only five publications that satisfied are inclusion criteria. All studies agreed that tong-term health issues increase with age. At the same

time, mental and physical fitness are closely related and should be assessed together. Conclusion of fitness to work assessment is predisposed by the interface among functional capacity, health, the type of work, and options for work accommodation or change. In general, studies report that older workers exhibit lesser turnover, more commitment to the workplace, and have more positive work values. Absenteeism is less prevalent in relation to younger workers, although it is longer when it is caused by the injury or chronic illness. With respect to clinical and/or laboratory measurements, some authors have recommended the use of a 'work ability index' for specific occupations as a practical means of selecting the appropriate worker for the job. Such index has been made at Finnish Institute of Occupational Health as an instrument used in occupational health care and research to assess work ability of workers during health examinations and workplace surveys. **Conclusions.** Appropriate understanding of the work nature and workplace settings are essential for any fitness to work assessment among older workers. The assessment should include physical, mental and social capacity, as well as assessment of any disability. Occupational physicians have an important role in making longer working lifetimes as possible with productive and healthy older workers.

A5-P12

Is Ischemic Heart Disease as Huge Problem as We Think, or Is It Much Bigger?

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Ischemic heart disease (IHD) is a major cause of morbidity and mortality among elderly, as the age represents the strongest risk factor for development of the atherosclerotic changes along the arterial tree. Beside age, older patients are more exposed to many other known cardiovascular risk factors, especially arterial hypertension, diabetes mellitus, dyslipidemia, renal dysfunction, smoking etc. Many different studies have demonstrated a higher prevalence of advanced coronary artery disease (CAD) in elderly, like severe calcifications, obstructive lesions of coronary arteries, commonly affected left main coronary artery, multivessel disease etc. From epidemiological point of view, according to famous trials NHANES, FHS, CHS, men older than 80 years of age are more affected with CAD than women, who present more likely with chronic coronary syndrome. Older patients often have atypical clinical presentation, and according to MESA and CHS trials one part of them have subclinical disease assessed by carotid intimal media thickness or coronary artery calcium. On the other hand, GRACE trial showed that elderly present more frequently with non–ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA). Only 33% of elderly are revascularised after ACS, while according to CRUSADE trial approximately 40%. Prognosis of such patients is unfavourable due to higher incidence of mortality, which reaches up to 50% at 3 years follow up. In EuroHeart survey in hospital mortality for ACS for people older than 85 years of age is approximately 17%. ACS in elderly is more complicated with various conditions such as cardiogenic shock, heart failure, papillary muscle rupture, malignant ventricular tachyarrhytmias, heart blocks, etc. Eventually, older people are more prone to develope second type of myocardial infarction, most frequently due to anemia, respiratory failure, infections. To date, the major problem represents small number of older patients recruited in ACS trials. Large registries like GRACE, NRMI and CRUSADE involve just under 30 % of STEMI and approximately 40% of NSTEMI patients. Stated facts leave for the task on future trials to involve more elderly in their investigations, therefore patophysiology, presentation and treatment can be better understood.

A5-P13

Depression and Quality of Life in Patients with Epilepsy – Single Centre Experience

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Introduction and objectives. Epilepsy is often associated with comorbid psychiatric illnesses and the most frequent of these, in around 40% of patients, is major depressive disorder. Compared to general population epidemiological studies show a consistent increased prevalence of depression in epilepsy. The main

aim of this study was to evaluate the relationship between epilepsy, antiepileptic drugs (AEDs) and depression. We also wanted to evaluate possible association between depressive symptoms in patients with epilepsy with the quality of life (QoL). **Methods.** This was a prospective cross-sectional study carried out at the tertiary teaching hospital (University Hospital Centre Zagreb, Croatia) with Ethics committee approval. Questionnaires evaluating depressive symptoms and QoL were administered to consecutive patients treated in the Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy. Depressive symptoms were evaluated using Hamilton Rating Scale for Depression (HAM- D17). Quality of life was assessed using Quality of life in epilepsy-31 inventory (QOLIE-31). Statistical analysis was done using statistical software IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp, using t-test, one way ANOVA, post hoc Scheffe test, Bonferroni, Tukey test, and Pearson correlation coefficient. **Results.** 108 patients (63% women, 37% men; mean age 39.54 ± 15.91 years) with epilepsy were included. 14.8% of patients had focal, 35.2% generalised and 40.7% both types of epilepsy. Majority of patients (65.74%) were on two and more AEDs and quarter was on monotherapy (25%); 42% were on newer, 19% on older and 39% on both AEDs. Mean total score on HAM- D17 was 9.94 ± 8.18 (men – mean total score 10.16 ± 8.85, women – mean total score 9.81 ±7.84). There were no significant differences on HAM- D17 regarding gender and age. We didn't find statistically significant differences regarding AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM- D17, nor between the type of epilepsy and results on HAM – D17. We found strong negative correlation between the higher QoL and HAM – D17 (p=0.000). **Conclusions.** Results of this study evaluating depressive symptoms in patients with epilepsy demonstrate that our patients mainly experience mild depressive symptoms, with no significant differences on HAM- D17 regarding gender and age. Patients with epilepsy with less pronounced depressive symptoms were found to have higher QoL. We did not find statistically significant differences regarding the type of epilepsy and results on HAM – D17, nor between the AEDs (older vs. newer AEDs, or both types AEDs) and results on HAM- D17.

A5-P14

Immunosenescence and Stroke

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Aging is a complex phenomenon leading to numerous changes in the physiological systems of the body. Age-related diseases are closely related to age-induced immune dysfunction, by which reductions in the efficiency and specificity of the immune system are termed „immunosenescence". Immunosenescence predispose aged individuals to development of cerebrovascular risk factors.In neuro intensive care units several neuro-related diseases including stroke are related to immunosenescence and neuroinflammation in the elderly. Profound systemic immunodepression occurs as early as 12 hours after ischemic stroke and may persist for several weeks. T lymphocytes are central to the development of a sustained inflammatory response. There is evidence that they accumulate in the post-ischemic brain within a few hours of reperfusion. Infectious complications, predominantly chest and urinary tract infections, occur in many stroke patients within the first days of the stroke. The development of an infection soon after the stroke is associated with worse outcome. The immune system is also a key player in central nervous system repair and maintenance that undergoes a profound remodeling process over the lifetime and has a major impact on individual's poststroke neurorehabilitaion, survival and outcome. Several advanced countries with superaged societies face the new challenge of improving the long-term prognosis of stroke patients. A better understanding of the multiple biological phenomena leading to diseases via the immunosenescence associated with inflammmaging provides a powerful target for interventions to increase the healthspan of elderly subjects.

A5-P15

Preparing Life for Healthy Longevity

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Psychiatry, more than any other field of medicine, needs to view a person as a whole, recognizing and accepting every patient's individuality. A personalized approach is very important when working with patients of older age for multiple reasons: these patients

come to us with a lifetime of trauma, they not only have medical but also social issues, they are isolated and less functional, aside from psychological disorders, they also have somatic comorbidities and are generally more sensitive to pharmacotherapy. They are a particularly vulnerable group of patients in every way. This is why with these patients psychopharmaceuticals are prescribed very cautiously and various support therapy techniques are used, which includes stimulating patients towards a meaningful life. The importance of seeking meaning in life and positive attitudes towards life has been talked about since ancient times; Aristotle speaks of eudaimonia and resilience is a popular term today. For the past ten years research has been conducted on the impact that finding meaning in life has on a person's overall health and in reducing the risk of certain diseases, including dementia, stroke and heart attack, by increasing cognitive reserve and reducing the infection response. Frankl, the founder of logotherapy, states that a person's basic need is to search for purpose and that he/she is willing to suffer if that suffering has a purpose, that purpose in life (and in the moment) is individual and must be sought out daily on an individual level. Logotherapy, as a method of psychotherapy, encourages patients to look for strengths within them and then direct themselves towards meaningful action, which is the most satisfying when directed at others. An individual approach is emphasized; together with the patient, his/her strengths, talents and aspirations from youth are sought out and encouraged, focusing on identifying positive moments. By designing daily activities, especially those that restore the patient's sense of being needed by others, that they should not give up because of those around them (family members), a brighter perspective is created, symptoms of anxiety and depression are eliminated and dementia is slowed through cognitive skills training. This approach achieves the preventative and curative effect that is necessary in order to increase the quality of life of the elderly and to increase lifespan.

A5-P16

Current Approaches to the Prevention and Treatment of Age-Related Macular Degeneration

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Macular degeneration, also known as age-related macular degeneration (AMD or ARMD), is a degenerative ailment affecting the macula. It is defined by the presence of distinct clinical findings, including drusen and retinal pigment epithelium (RPE) changes, in the absence of another malady. Later stages of the disease are correlated with impairment of vision. AMD is multifactorial in aetiology where age and heredity have a central place in the disease occurrence. The recent epidemiological studies have shown that there are about 0.4% of people between 50 and 60 , 0.7% of people between 60 to 70, 2.3% of those 70 to 80, and nearly 12% of people over 80 years old diagnosed with AMD. Furthermore, smoking and obesity are associated with a higher prevalence of the disease. Modern classification divides AMD into two main types: non-exudative (dry, non-neovascular) holding around 90% of diagnosed disease and exudative (wet, neovascular) associated with more prompt progression of sight loss. The disease is diagnosed by funduscopic examination where the presence of multiple drusen is frequent for early AMD. The drusen may appear confluent in intermediate AMD with significant pigment variations and pigment accumulation. Furthermore, the retinal pigment epithelium (RPE) often appears atrophic, with easier visualization of the underlying choroid vascular plexus. On the other hand, advanced exudative AMD appears with choroidal neovascularization, RPE elevation or haemorrhage. Further procedures such as fluorescein angiography, Amsler grid evaluation, ocular coherence tomography (OCT) of the retina and ocular coherence tomography angiography (OCTA) of the retina confirm the diagnosis of AMD. Disease management can be divided into prophylaxis and active treatment. The first focus on the prevention of the non-exudative AMD, whereas the active approach is more common for the exudative AMD. Preventive efforts include exercising, eating well, and not smoking. No remedy or treatment returns already lost vision. In the exudative form, anti-VEGF medication injected into the eye or less ordinarily laser coagulation or photodynamic therapy may decrease the disease progression. Antioxidants and minerals do not appear to be useful for prevention. However, dietary supplements may slow the progression of the disease itself. The

most recent disease control approach include subretinal stem cell transplantation and intravitreal injection of ciliary neurotrophic factor, steroid inserts and neuroprotective drugs, including brimonidine.

A5-P17

Why Care About Nutrition and Eating Habits in Early Life? Impact on Healthy Ageing

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Introduction and objectives. The rapid increase of non-communicable diseases (NCDs) is a major global health concern. The increase has happened too fast thus suggests that epigenetic phenomena may play a pivotal role. The most critical period in life is during the first 1000 days (from conception until 2 years) that offers a critical window of opportunity to shape both short and long-term health, while nutrition plays a crucial role. An imbalanced intake of nutrients can have profound effects on the child development, including risk of NCDs in later life. Meeting the specific nutritional needs in this period can positively influence health outcome throughout life and therefore represents the first step towards healthy aging. Feeding difficulties (FDs) are among the most common pediatric problems. Incidence is higher in children with psychomotor developmental disorders and chronic illnesses. According to some authors, 25–30% of parents report specific feeding problems, and 1–2% have serious problems classified as early feeding disorders (EFDs). This difficulty significantly increase the risk of malnutrition and can adversely affect healthy aging. The aim of this research was to analyze the characteristics of children with FDs in our department and applied therapeutic interventions. **Methods.** Medical chart retrospective analysis of children who attended department due to FDs in the past two-year. **Results.** During the analyzed period, a total of 174 children with nutrition-related disorders were treated (FDs and eating disorders). Fifty-seven, average age 16.31±9.2 months, had FDs. Only 6/47 had a severe form (EFDs), while rest had mild form of FDs. Most prevalent was selective form of FDs, and infantile anorexia the rarest. On average, the difficulties lasted for 7.29±5.32 month before treatment. Organic diseases were excluded (GERD, food allergy, celiac disease). 40/57 children presented with failure to thrive and 35/57 had signs of malnutrition. Regarding risk factors, 24/57 children had psychomotor development difficulties and 13/57

had perinatal complications. Therapeutic interventions implied parental reassurance, education on feeding patterns and nutritional supplementations. Only children with EFDs were included in further multidisciplinary treatment. **Conclusions.** Feeding difficulties are common in pediatric practice, but are not seen as a potentially serious problem that can have long-term health effects. When recognized early, the intervention is simple and significantly reduces the risk of malnutrition and the negative impact on healthy aging. Thus, timely recognition and intervention are an important goal, for families and health professionals.

A5-P18

Clinical Practices for Improvement of Psoriasis in Elderly

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Psoriasis is a systemic inflammatory disease of multifactorial etiology, in which an increased release of proinflammatory cytokines and activation of the immune system cause damage to various tissues and organs. It is a chronic disease affecting 2–3% of the population, characterized by inflammation and scaling of the skin, but not limited to it. Mild psoriasis is generally treated with topical therapy, while phototherapy, oral systemic medications or biologic therapy are treatment options for moderate to severe disease. Taking into account the chronic course of this disease and the continuing rise in life expectancy, the prevalence of psoriasis among the elderly will further increase, which makes management of psoriasis in the elderly an important health care problem.

Management of psoriasis in elderly patients may be challenging since they are often excluded from clinical trials, and the data regarding efficacy and safety in this population is lacking. Consequently, some dermatologists recommend only topical therapy and avoid prescribing systemic therapy, which may lead to inadequate treatment response in this population. Individualized treatment to each elderly patient should be provided due to possible drug-induced or aggravated psoriasis, higher prevalence of comorbidities, polypharmacy, adverse effects, self-care capability and quality of life.

Topical therapy is probably the safest option for treating elderly patients with psoriasis, although topical corticosteroids should be used with caution due to

the physiologic changes in older skin and a higher risk of cutaneous side effects. The physical limitations and dependence on caregivers should also be taken into account, as compliance may be reduced due to difficulty in applying topical agents. Due to a higher prevalence of hypertension and decreased renal and hepatic function in the elderly, special caution should be taken when prescribing conventional systemic therapy – methotrexate, cyclosporine, and acitretin. Biologic therapy is more often initiated in younger than in elderly patients, although it may be a safer option than conventional systemic therapy in the elderly due to its high efficacy, a lower rate of adverse events, and lower frequency of hospital visits. Still, regular follow-up is necessary because of the increased risk of infections and malignancies.

Since psoriasis is becoming increasingly widespread in the elderly, it is surprising that studies regarding treatment efficacy and safety in the geriatric population are scarce. Further clinical research on treatment modalities in the elderly are needed, in order to improve management outcomes in this population.

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Education of Physicians to Provide Healthcare to Elderly in Croatia

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Introduction and objectives. The aging population rises the need for adequate education of specialist focused on medical care for elderly. Physicians should be trained to adopt the expertise in certain areas to changing biological functioning and communicational and social challenges of elderly patient. Objective of this study is to present the most recent educational program for physicians providing health care for elderly in Croatia. **Methods.** Medical Faculty in Zagreb introduced the postgraduate program tailored to adopt the most recent recommendation of UEMS to the current best practices in all areas of medical care for elderly in Croatia. The program is structured for graduated medical doctors. **Results.** Training for health care of elderly is presents in almost of all specialty training programs and postgraduate education in Croatia, most notably in specialty training program in geriatric medicine. The five-year specialty training program in geriatric medicine includes internal common trunk during 22 months and specific part of specialty training program in geriatric medicine during 33 months. During the internal common trunk residents in geriatric medicine have the same program as all other residents included in specialty training programs with internal common trunk. During specific part of specialty training program in geriatric medicine residents spend three months at internal medicine departments and acquire the competencies necessary for the providing health care for elderly, two months in training for interventional diagnostic and therapeutic procedures for elderly, five months are reserved for neurogeriatric topics, five and half months for psychogeriatric topics, two and half months for palliative care, two months for rehabilitation, one and half months for orthopedics ant traumatology, one and half months for endocrinology, one and half months for oncology and radiotherapy, one month for infectology and fifteen days for nutrition in elderly . Specialty training program in geriatric medicine includes five months for education in gerontology and public health. During specialty training in geriatric medicine residents spend two months in family medicine because family physicians are basic physicians in primary health care in Croatia. Specialty training program in geriatric medicine in Croatia includes three months' theoretical postgraduate education in geriatric medicine as obligatory part of education of this kind of medical expert. **Conclusion.** Education in Croatia enable physicians for providing health care for elderly, mostly during specialty training in geriatric medicine.