



Medical University of Plovdiv



Abstract Book

**SCIENCE and
YOUTH | DAYS of
MEDICAL SCIENCE**

19–21 April | 19 April

2024

Auditorium Complex
MU-Plovdiv

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Програма

Наука и младост

Дни на медицинската наука

2024

Петък, 19 април 2024

11.00 – 12.00	Регистрация	Фоайе ет. 1 Аудиторен комплекс
12.00 – 12.15	Откриване	Зала 2 Аудиторен комплекс
12.15 – 13.00	Пленарна лекция Проф. д-р Виктория Сарафян, дм, дмн Защо наука? Защо в МУ – Пловдив?	Зала 2 Аудиторен комплекс
13.00 – 14.30	Хирургична сесия – 1 част <i> English </i>	Зала 2
13.00 – 13.10	<i>A combination of two localization methods for multifocal, postneoadjuvant, nonpalpable breast cancer.</i> Valentin Ivanov	
13.10 – 13.20	<i>Abdominal actinomycosis complicated with intestinal obstruction, peritoneal abscess, and extensive abdominal fibrosis – a rare case presentation.</i> Anu Thomas Thacheth	
13.20 – 13.30	<i>Acute mesenteric ischemia clinical presentation and management – a review.</i> Anu Thomas Thacheth	
13.30 – 13.40	<i>Morphologic changes in carpal tunnel syndrome.</i> Mihail Tokmakov	
13.40 – 13.50	<i>Abnormal uterine bleeding in perimenopausal women – diagnostic-therapeutic approach – literature review.</i> Harpreet Saul	
13.50 – 14.00	<i>Pediatric orbital tumors: an illustrative case report with a review of differential diagnosis.</i> Nikola Velkov	
14.00 – 14.10	<i>Meningoencephalitis caused by medulloblastoma in adulthood: case report.</i> Vladislav Velchev	
14.10 – 14.20	<i>Advantages and disadvantages of hormonal intrauterine devices – literature review.</i> Magdalena Tarpanliyska	
14.20 – 14.30	Дискусия	

13.00 – 14.30 Сесия „Дни на медицинската наука“ – 1 част Зала 9

- 13.00 – 13.10 Проект КОВ-04/21 – Ръководител проф. д-р Таня Денева, дм**
Презентиращ ас. д-р Десислава Арабаджийска, кат. „Клинична лаборатория“
„Лабораторен мониторинг на прогностични биомаркери при хоспитализирани пациенти с COVID-19“
- 13.10 – 13.20 Проект НО-06/21 – Ръководител проф. д-р Николай Бояджиев, дм**
Презентиращ д-р Веселин Василев, кат. „Физиология“
„Влияние на селективните модулатори на андрогенния рецептор (SARMS) върху физическия работен капацитет на организма и страничните им ефекти при експериментални плъхове“
- 13.20 – 13.30 Проект ДПДП-07/21 – Ръководител проф. д-р Иван Иванов, дм**
Презентиращ ас. Иванка Паскалева, дм, кат. „Педиатрия и медицинска генетика „Проф. д-р Иван Андреев“
„Нисковъглехидратна/кетогенна диета при деца с метаболитен синдром и диабет от 2 тип“
- 13.30 – 13.40 Проект НО-03/22 – Ръководител д-р Никола Боянов, дм**
Презентиращ д-р Никола Боянов, дм, МСТЦ
„Оценка на ефективността и нивото на стрес на участници в симулационна програма за обучение по ендоскопска ретроградна холангиопанкреатография (ERCP)“
- 13.40 – 13.50 Проект ДПДП-01/22 – Ръководител проф. д-р Ангелина Влахова, дм**
Презентиращ ас. д-р Мария Димитрова, кат. „Протетична дентална медицина“
„Сравнително лабораторно и клинично изследване на обемни и оптични изменения на CAD/CAM 3D принтирани и конвенционални топполимеризирани пластмаси, използвани в снемаемото протезиране“
- 13.50 – 14.00 Проект ДПДП-04/22 – Ръководител доц. д-р Елена Порязова, дм**
Презентиращ ас. д-р Даниел Марков, кат. „Обща и клинична патология“
„Експресия на anti HIF1alpha, Ki 67, E-cadherin, β-catenin, SMA в огнища с ендометриоза, при ендометриални и яйчникови карциноми“
- 14.00 – 14.10 Проект ДПДП-06/22 – Ръководител доц. Калин Иванов, дф**
Презентиращ ас. Велислава Тодорова, кат. „Фармакогнозия и фармацевтична химия“
„Фармакоаналитичен контрол на адаптогени от растителен произход – охарактеризиране на екстракт от *Rhaponticum carthamoides*“

14.10 – 14.20 Проект ПМД-01/22 – Ръководител доц. д-р Десислава Бакова, дм

Презентиращ д-р Добромира Шопова, дм, кат. „Протетична дентална медицина“

„Приложение на (био)принтирането в персонализираната медицина – етични, социални и правни аспекти“

14.20 – 14.30 Дискусия

14.30 – 15.00 Кафе пауза

15.00 – 15.30	Пленарна лекция Радмила Филева Бизнес развитие на приложни проекти, насочени към иновации и интелектуална собственост. Инструментариум: насоки за финансиране и реализация	Зала 5 Аудиторен комплекс
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15.30 – 17.00 Хирургична сесия – 2 част Зала 2

15.30 – 15.40 Acute abdomen due to spontaneous rupture of adrenal gland metastasis as initial clinical manifestation of lung cancer – rare case report. **Maritza Chtereov** /English/

15.40 – 15.50 Isolated cystic lymphangiomatosis of the spleen in a patient with diabetes mellitus and hypertension. **Galabin Markov** /English/

15.50 – 16.00 Gallstone ileus: a rare form intestinal obstruction – case study. **Stefan Ivanov** /English/

16.00 – 16.10 Плазмоцитом, имитиращ менингиом – клиничен случай. **Полина Ангелова**

16.10 – 16.20 Приложението на Diffusion Tensor Imaging за оценка на промените в бялото мозъчно вещество при пациенти след чепно-мозъчна травма. **Полина Ангелова**

16.20 – 16.30 Плоскоклетъчен карцином с базалоидна морфология – клинико-патоанатомичен случай. **Гергана Тренова**

16.30 – 16.40 Артроскопско лечение при хрущялни увреди на коляното. **Добромира Дакова**

16.40 – 16.50 Развитие на ингвиналните херниопластики. **Теодора Стойчева**

16.50 – 17.00 Дискусия

17.30 Коктейл

- 15.30 – 15.40** *Проект НО-03/20 – Ръководител д-р Ели Христозова, дм*
Презентиращ д-р Ели Христозова, дм, кат. „Медицинска микробиология и имунология „Проф. д-р Елисей Янев“
„Бърза микробиологична диагностика на генитални инфекции при жени и мъже-сравнителен анализ“
- 15.40 – 15.50** *Проект НО-14/20 – Ръководител проф. д-р Румен Стефанов, дм*
Презентиращ гл. ас. д-р Елеонора Христова-Атанасова, дм, кат. „Социална медицина и обществено здраве“
„Преконцепционна грижа за повече здрави семейства“
- 15.50 – 16.00** *Проект КОВ-02/21 – Ръководител проф. д-р Ангел Учиков, дмн*
Презентиращ гл. ас. Любомир Паунов, дм, кат. „Специална хирургия“
„Пневмоторакс при болни с COVID-19 – клинични и параклинични корелации, усложнения, хирургични подходи за диагностика и лечение“
- 16.00 – 16.10** *Проект НО-03/21 – Ръководител проф. Татяна Владкова, дб*
Презентиращ гл. ас. Илиян Димитров, дб, кат. „Медицинска биохимия“
„Биохимични маркери за оценка на остеointеграцията след поставяне на титанови имплантати“
- 16.10 – 16.20** *Проект НО-13/21 – Ръководител проф. д-р Силвия Цветкова, дм*
Презентиращ гл. ас Любомир Червенков, дм, кат. „Образна диагностика“
„Мултипараметричен МРТ на пациенти с карцином на простатата – нови възможности за стадиране чрез системата PI-RADS 2“
- 16.20 – 16.30** *Проект ДПДП-05/22 – Ръководител проф. д-р Емил Кумчев, дм*
Презентиращ д-р Теодор Кусунов, кат. „Нефрология“
„Серумно ниво на ИНДОСИЛ СУЛФАТ и ПАРА-КРЕЗОЛ при пациенти с ХБЗ IV – V СТ като биохимични маркери за чревна дисбиоза при уремия – клинично значение и възможности за терапевтичен контрол“
- 16.30 – 16.40** *Проект ДПДП-08/22 – Ръководител проф. д-р Мариела Генева-Попова, дм*
Презентиращ гл. ас. Красимир Краев, дм, кат. „Пропедевтика на вътрешните болести „Проф. д-р Антон Митов“
„Изследване на влиянието на фебукостат върху нивото на IL-1, IL-2 и COX-2 при пациенти с подагра“

16.40 – 16.50 *Проект ПМД-05/22 – Ръководител проф. д-р Владимир Ставрев, дмн*

Презентиращ ас. д-р Петър Молчовски, кат. „Ортопедия и травматология“

„Прилагане и изследване на концепцията за microlearning (микрообучение) в обучението по „ортопедия и травматология“

16.50 – 17.00 *Проект ПМД-06/22 – Ръководител проф. д-р Анастас Баталов, дм и доц. д-р Росица Димова, дм*

Презентиращ ас. Александар Маринков, кат. „Пропедевтика на вътрешните болести „Проф. д-р Антон Митов“

„Влияние на COVID-19 инфекцията при пациенти с ревматични заболявания и нуждата от отдалечен достъп до медицински грижи по време на пандемията“

17.30 Коктейл

Събота, 20 април 2024

Зала 2

08.30 – 10.00 Медико-биологична сесия – 1 част Зала 2

08.30 – 08.40 Маркери за възпаление и автофагия при пациенти с наивен ревматоиден артрит. **Валентина Михайлова**

08.40 – 08.50 Вирусна пневмония в ранния постоперативен период – аутопсионен случай. **Гергана Тренова**

08.50 – 09.00 Междубелтъчни взаимодействия на мастоцитите при РАС. **Елеонора Ковачева**

09.00 – 09.10 Когнитивен упадък при ранна болест на паркинсон. **Виктор Карадийски**

09.10 – 09.20 Епигенетични и морфологични аспекти на здравословно стареене с функционални храни, обогатени на гама-амино-маслена киселина и полифенолни съединения. **Мария-Франс Китова**

09.20 – 09.30 Проучване на ефектите от нагреваемите тютюневи изделия върху респираторното здраве – преглед на литература. **Аглика Бяндова**

09.30 – 09.40 Деца в предучилищна възраст и функционално изследване на дишането – нова възможност за по-добра диагностика. **Пламена Стоименова**

09.40 – 09.50 Абактериален тромботичен ендокардит – пътят до диагнозата. **Иван Кучмов**

09.50 – 10.00 Анализ на кръвния микробиом при пациенти с белодробна саркоидоза. **Йордан Ходжев**

10.00 – 10.30 Кафе пауза

10.30 – 12.00 Медико-биологична сесия – 2 част /English/ Зала 2

- 10.30 – 10.40** *Lactate as a modern tool of exercise physiology – a review of the literature.* **Nikolay Mandadzhiev**
- 10.40 – 10.50** *Assessment of antimicrobial susceptibility of staphylococcus aureus nasal isolates from preclinical medical students at the Medical university of Plovdiv.* **Aras Budak**
- 10.50 – 11.00** *The possibilities of a non-contrast enhanced abbreviated MRI protocol for breast cancer detection.* **Anna Vasilска**
- 11.00 – 11.10** *Acute myeloid leukemia diagnosed during pregnancy: a case report.* **Stoyan Mitev**
- 11.10 – 11.20** *The seemingly hidden role of right ventricular dysfunction in the pathophysiology of sudden cardiac death among elite athletes.* **Petar Georgiev**
- 11.20 – 11.30** *Hypothalamo-pituitary-gonadal axis imbalance and its role in PCOS pathogenesis.* **Luna Ahmad**
- 11.30 – 11.40** *Case report: cerebral calcification as a result of primary hyperparathyroidism caused by parathyroid adenomas that imitates Fahr's disease.* **Remzi Hyusein**
- 11.40 – 11.50** *Calpains as biomarkers of cardiovascular risk in patients with ischemic heart disease.* **Ademira Borisova**
- 11.50 – 12.00** *Discussion*

12.00 – 12.45 Пленарна лекция Зала 2

Prof. Blasé Billack, PhD

To Teach or to Do Research – That is the Question

12.45 – 13.30 Пленарна лекция Зала 2

Дончо Минков

AI в полза на научните изследвания и публикации

13.30 – 14.30 Обедна почивка

14.30 – 15.30 Терапевтична сесия – 1 част /English/ Зала 2

- 14.30 – 14.40** *Drug approach in post-covid high-grade ventricular arrhythmias – a case report.* **Spas Kitov**
- 14.40 – 14.50** *Contained rupture of the thoracic aorta mimicking mediastinal malignancy: a case report.* **Dayvid Ouloo**
- 14.50 – 15.00** *The impact of asbestos on workers' health – a clinical case.* **Hussin Musannar**
- 15.00 – 15.10** *Administration of botulinum toxin for a patient with Raynaud's syndrome: a case report.* **Plamen Penchev**
- 15.10 – 15.20** *Left ventricular noncompaction cardiomyopathy in combination with atrial septal aneurism and defect – better or worse?* **Vaishnav Krishna**
- 15.20 – 15.30** *Discussion*

15.40 – 16.40 Терапевтична сесия – 2 част

Зала 2

15.40 – 15.50 Treatment strategy in a random heart failure patient – it is always a challenge! **Jahnavi Sharma**

15.50 – 16.00 A clinical case of isolated right-sided infective endocarditis. **Joana Duarte Simoes**

16.00 – 16.10 Concomitant JAK-2 and BCR-ABL1 expression in a patient with chronic myeloid leukemia. Clinical evolution and cardiac impact. **Evgenia Marinova**

16.10 – 16.20 Trait mindfulness and the experience of stuttering. **Megan Arney**

16.20 – 16.30 Еднострранна парализа на н. abducens като изолирана проява на церебрална синовенозна тромбоза. **Ерай Каймакам**

16.30 – 16.40 Дискусия

Събота, 20 април 2024

Зала 3

08.30 – 09.40 Сесия „Фармация и фармакотерапия“ – 1 част Зала 3

08.30 – 08.40 Назални нанокомпозитни микросфери за насочена лекарствена доставка в мозъка. **Радка Буюклиева**

08.40 – 08.50 Хидрогел с липозоми, натоварени с тетрациклин, за лечение на бактериални инфекции на кожата. **Селин Сербезова**

08.50 – 09.00 Зелен синтез наnanoчастичи с магнитни свойства – получаване и характеризиране. **Владислав Велчев**

09.00 – 09.10 Таблетки за смучене с мукоадхезивни липозоми, натоварени сベンзидамин. **Ванеса Денева**

09.10 – 09.20 Химически модифицирани системи за имобилизиране на лекарствени вещества (обзор). **Даниел Аргилашки**

09.20 – 09.30 Разработване и охарактеризиране на липозоми натоварени с идебенон, за таргетна доставка в дебелото черво. **Йоана Чукова**

09.30 – 09.40 Дискусия

10.00 – 10.30 Кафе пауза

10.30 – 11.30 Сесия „Фармация и фармакотерапия“ – 2 част Зала 3

10.30 – 10.40 Лечение на рак сベンзамиди: постигнат прогрес и бъдещи перспективи. **Кристиян Величков**

10.40 – 10.50 BETX определяне на парацетамол, диклофенак натрий и омепразол в таблетки. **Данислава Запрянова**

10.50 – 11.00 Български лечебни растения, използвани за лечение на захарен диабет. **Атанас Ламбрев**

11.00 – 11.10 Изследване на риска и безопасността при употребата на растителни лекарствени продукти при бременни и кърмещи жени. **Десислава Андонова**

11.10 – 11.20 Специфични процедури за ранен достъп до нови лекарствени продукти в ЕС: ретроспективен анализ за периода 2015 – 2023 г. **Аделена Боянова**

11.20 – 11.30 Дискусия

12.00 – 12.45 Пленарна лекция Зала 2

Prof. Blasé Billack, PhD
To Teach or to Do Research – That is the Question

12.45 – 13.30 Пленарна лекция Зала 2

Дончо Минков
AI в полза на научните изследвания и публикации

13.30 – 14.30 Обедна почивка

14.30 – 15.40 Сесия „Обществено здраве и здравен мениджмънт“ / „Дентална медицина“ Зала 3

14.30 – 14.40 Проучване нагласата на майките на момичета в предпубертетна възраст относно ваксинацията против рак на маточната шийка. **Весела Иванчева**

14.40 – 14.50 Подходи за повишаване на физическата активност – добри практики за превенция и оценка на мускулно-скелетни дисфункции. **Самуела Давидова**

14.50 – 15.00 Рискови фактори асоциирани с оклузивни съдови заболявания на ретината. **Синан Алтикадир**

15.00 – 15.10 *The role and impact of telemedicine in reinventing healthcare management.* **Amita Singaravelou /English/**

15.10 – 15.20 Дигитални или конвенционални отпечатъци, кое да изберем? **Ебру Рамаданова**

15.20 – 15.30 Приложението на гингивалните мезенхимни стволови клетки при пародонтална регенерация – литературен обзор. **Михаела Евтимова**

15.30 – 15.40 Дискусия

Събота, 20 април 2024

Зала 5

08.30 – 10.00	Сесия „Сомнология“ – 1 част	Зала 5
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08.30 – 08.40 РЕМ поведенчески нарушения при пациенти с ранна паркинсонова болест. **Виктор Карадийски**

08.40 – 08.50 Продължителност и качество на съня според самооценка сред българската популация. **Тодор Георгиев**

08.50 – 09.00 Ролята на мелатонина при загубата на коса. **Лидия Тодоррова**

09.00 – 09.10 Многоликото нарушение в невротрансмисията на синдрома на неспокойните крака. **Красимир Аврамов**

09.10 – 09.20 Обективните полисомнографски параметри непълно отразяват субективното подобрене при пациенти с бруксизъм по време на сън, лекувани с ботулинов токсин – представяне на два случая. **Анастасия Желева**

09.20 – 09.30 Хипнично главоболие. **Дана Стоянова**

09.30 – 09.40 Размерът има ли значение за съня? Сравнение между една нощ и две нощи запис на дишането по време на сън относно техния капацитет да диагностицират и оценяват тежкото на сънната апнея – пилотно проучване. **Димитър Тасков**

09.40 – 09.50 Домашен срещу лабораторен множествен тест за латентност на съня в диагностиката на нарколепсията – пилотно проучване. **Петър Чипев**

09.50 – 10.00 Събудната мечта – ефективност на моно- и комбинираната терапия с натриев оксибат и pitolasant при шест подрастващи с нарколепсия тип 1 в България – едноцентров опит. **Петър Чипев**

10.00 – 10.30	Кафе пауза
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12.00 – 12.45	Пленарна лекция <i>Prof. Blasé Billack, PhD</i> <i>To Teach or to Do Research – That is the Question</i>	Зала 2
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12.45 – 13.30	Пленарна лекция <i>Дончо Минков</i> <i>AI в полза на научните изследвания и публикации</i>	Зала 2
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13.30 – 14.30	Обедна почивка
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14.30 – 16.30	Сесия „Сомнология“ – 2 част	Зала 5
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14.30 – 15.30 Нарколепсия и други централни нарушения с хиперсомнолентност – **кръгла маса**

15.30 – 16.30 Отвъд „лесната диагноза“ сънна апнея – **кръгла маса**

- P1** Review of anatomic variations of the median nerve in the carpal tunnel. **Mihail Tokmakov**
- P2** Fibroadenoma's day out. **Gergana Trenova**
- P3** Adverse effects of Libtayo (cemiplimab) in the endocrine clinical practice – two cases of autoimmune hypophysitis during treatment for squamous cell carcinoma. **Ekaterina Babadzhanova**
- P4** Study of the antioxidant effect of bioflavonoid fustin isolated from *Cotinus coggygria* heartwood in acute rat models of organ damage. **Danail Pavlov**
- P5** The *Cotinus coggygria* heartwood-derived flavonoid fustin exerts an anti-inflammatory activity in different animal models. **Antoaneta Georgieva**
- P6** Trichoscopy in the diagnosis of alopecia areata. **Lidiya Todorova**
- P7** Microbiological diagnosis and treatment strategy for invasive *Candida glabrata* infections. **Milena Rupcheva**
- P8** Anthropological comparison of dimensions of dental crowns between Bulgarian and Indian population. **Usman Khalid**
- P9** Atypical pneumonia – a case study. **Nikola Vardev**
- P10** Prolactinoma – a case study. **Milena Zdravcheva**
- P11** Homeopathy – a successful approach to seasonal allergies (review). **Emi Dueva**
- P12** A patient with three metachronous cancers occurring over a period of three years and the clinical importance of investigating potential neoplastic growth during follow-up. **Marin Kanarev**
- P13** A comparative analysis of pharmaceutical care education in Bulgaria and France. **Radiana Staynova**
- P14** Casein-fucoidan nanocomposites as a drug delivery system for daunorubicin. **Nikolay Zahariev**



Youth Scientific Association "Asclepius"

SCIENCE and YOUTH

ABSTRACTS

Auditorium complex, MU-Plovdiv

19–21 April 2024

I. Surgical Session

ACUTE MESENTERIC ISCHEMIA CLINICAL PRESENTATION AND MANAGEMENT – A REVIEW

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Introduction: Acute Mesenteric Ischemia is caused by the sudden interruption of blood supply to the intestine, leading to cellular damage, mesenteric infarction, intestinal necrosis, leading to an acute inflammatory process and death. With the increase in average life expectancy, acute mesenteric ischemia represents one of the threatening abdominal conditions. Three main arteries that supply blood to the small and large bowel are the coeliac trunk, superior mesenteric artery and inferior mesenteric artery. Any insufficiency of blood flow within mesenteric circulation leading to blockage of metabolic demands of the bowel potentially leads to a catastrophic outcome and requires emergency intervention in acute settings. **Aim:** Introduce the topic of Acute Mesenteric ischemia with associated co-morbidities and current medical and surgical management guidelines. **Resources and methods:** Search was conducted using four databases PubMed, SCOPUS, Ovid EMBASE, MEDLINE. **Discussion:** Advancement in endovascular approaches along with radiological techniques gives essential time for emergency surgical management. However, the challenge lies in the initial diagnosis and individualized medical management. Principle goals of management lie in early Resuscitation, Rapid Diagnosis, and early Revascularization before significant progress happens toward systemic inflammatory response. Further treatment decision lies in which type of acute mesenteric ischemia is presented and at what stage the condition is diagnosed. Different types of Acute Mesenteric Ischemia have different management guidelines and it also depends on associated complications. **Conclusion:** Early intervention can stop the progress of the condition leading to a full recovery of the patient. The focus needs to be on early diagnosis and individualized treatment.

Keywords: acute mesenteric ischemia, embolism, bowel ischemia, bowel infarction, MeSH

ABDOMINAL ACTINOMYCOSIS COMPLICATED WITH INTESTINAL OBSTRUCTION, PERITONEAL ABSCESS, AND EXTENSIVE ABDOMINAL FIBROSIS – A RARE CASE PRESENTATION

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Background: Abdominal actinomycosis is an uncommon chronic suppurative disease caused by *Actinomycosis israelii*, which results in infiltrative abdominal mass lesions, which are often indistinguishable from malignancy. We aim to present a rare case of actinomycosis complicated with intestinal obstruction, terminal ileum perforation and extensive abdominal fibrosis. **Case presentation:** A 71-year-old man presented with squeezing abdominal pain. Palpation of the abdomen revealed acute peritoneal signs. A computed tomography scan of the abdomen revealed distended intestinal loops, an abscess in the right lower quadrant, abdominal and pelvis mass lesions. Laparotomy was performed and as an operative finding was established inflammatory process of the terminal ileum with perforation of the intestine, right iliac fossa abscess, and mass lesion that infiltrated the anterior abdominal wall, retroperitoneal space and pelvis which was indistinguishable from malignancy. Resection of the inflamed intestinal segment and drainage of the abdominal abscess was performed and a specimen from the mass lesion was also obtained. Histological examination of the resected intestinal segment and abdominal mass revealed a colony of actinomyces and a mixed inflammatory response. **Conclusion:** We present a rare case of abdominal actinomycosis that is complicated with intestinal obstruction, peritoneal abscess, and extensive abdominal fibrosis. The clinical interest of the presented case is a severe progression of this uncommon chronic suppurative infectious disease.

Keywords: *abdominal actinomycosis, intestinal obstruction, mass lesion, peritoneal abscess*

A COMBINATION OF TWO LOCALIZATION METHODS FOR MULTIFOCAL, POSTNEOADJUVANT, NONPALPABLE BREAST CANCER

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Background: Multifocal and multicentric breast lesions are becoming more common as a result of advances in imaging methods. Neoadjuvant chemotherapy in certain biological subtypes has shown remarkable results leading to a high percentage of complete clinical and pathological response to therapy. The combination of multifocal, non-palpable tumors that are subject to preoperative therapy suggests the use of modern localization techniques to perform breast-conserving surgery. **Aim:** To present a case in which two different localization techniques were used for wide local excision of 3 multifocal breast cancer lesions with complete clinical response. **Case presentation:** A 76-year-old post-menopausal woman is presented with 2 cm palpable lump in the upper outer quadrant of her left breast, which was seen on mammography. Ultrasound examination defined two more lesions (0.5, 0.6 cm) located in the axillary tail of the breast. Core needle biopsy confirmed multifocal triple-negative breast cancer. Marker clips were introduced in each tumour under sonographic guidance, before initiating neoadjuvant therapy. After systemic therapy, complete clinical response was vindicate in two of three cancers. Because of poor visibility of markers in the lateral tumours, guidewires were introduced under sonographic control. Intraoperative ultrasound was used in order to excise the medial cancer and wires guide the excision of the lateral clips. **Conclusion:** The use of localisation techniques in patients with postneoadjuvant multifocal breast cancer is mandatory in order to plan surgical treatment and to obtain negative margins.

Keywords: *breast cancer, triple-negative, neoadjuvant, breast-conserving surgery, intraoperative ultrasound*

MENINGOENCEPHALITIS CAUSED BY MEDULLOBLASTOMA IN ADULTHOOD: CASE REPORT

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Introduction: The medulloblastoma is a type of malignant neoplasm in the cerebellum. It comprises less than 1% of central nervous system tumors found in adults. The development of meningoencephalitis is a result of the migration of tumour cells to the meninges of the brain which can cause a number of neurological complications. **Aim:** The aim of this report is to present a rare case of cerebellar cancer in adulthood causing meningoencephalitis and to evaluate the diagnostic and therapeutic techniques. **Materials and methods:** We present a 45-year-old male patient who has entered the neurosurgery clinic with a long-lasting severe headache. MRT showed evidence of a tumour in the posterior cranial fossa engaging the first cervical neurons. Neurological status determined intracranial hypertension. Biopsy examination found sections expressing a cancerous formation causing a chronic meningoencephalitis in the right hemisphere of the cerebellum. The patient's treatment included a craniotomy under general anaesthesia and a biopsy of the malignant formations. **Results and discussion:** The surgery was successful and postoperative complications were not observed. Follow-up examinations proved a significant improvement. Surgical resection and craniospinal irradiation are promising methods of managing the disease. **Conclusions:** Meningoencephalitis resulting from a medulloblastoma is a complication which may occur in adulthood and surgery is its only effective treatment.

Keywords: medulloblastoma, meningoencephalitis, rare case

FIBROADENOMA'S DAY OUT

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In the first 7 weeks of embryonal development 2 symmetrical lines from the axillar region towards the inguinal zone develop – the so called milk lines. Eventually by week 9 of embryonal development they become rudimental but in some cases (less than 0.5% of the population) ectopic breast tissue could be observed. The most common localization is the axilla, second most common is the vulvar region. Fibroadenoma is the most common benign breast tumor in adolescent and young women. It is believed that this tumor is a consequence of increased breast tissue sensitivity to estrogen. Vulval fibroadenoma is an example of a rare condition with few reported cases in the medical literature. We present a case of a 40-years-old woman who complained of burden and uncomfortable feeling in the vulvo-vaginal region for the last 3 months and this feeling worsened during the last month. Physical examination revealed a mass on the left major labia, 4.5 cm in diameter without any inflammatory or other secondary changes. The differential diagnosis includes vulvar cysts such as Bartholin gland cyst, condyloma (genital wart) and papillary hidradenoma. The gross and histological examination proved to be a pericanalicular fibroadenoma. Better knowledge of such rare variants is a prerequisite for applying more informative and advanced methods of examination and therefore adequate therapeutic approach which would reduce the complications.

Keywords: vulval fibroadenoma, ectopic breast tissue, pericanalicular fibroadenoma

BASALOID SQUAMOUS CELL CARCINOMA OF THE ANAL REGION – CASE REPORT

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Anal squamous cell carcinoma (SCC) is the most common malignant epithelial tumour arising within the anal canal and perianal region, frequent associate with HPV infection. Basaloid squamous cell carcinoma is an aggressive subtype with a tendency to recur and metastasize to regional lymph nodes, showing overlapping histological features with basal cell carcinoma but having different therapeutical strategy. We present a case of 64 years old female complaining of rectal discomfort, constipation, tenesmus and change in stool caliber with pencilthin stools for the last 3 months. Colonoscopy showed anorectal nodular mass constricting the lumen of the bowel. Surgery was performed and the histological examination of the tumor showed plexiform pattern and palisading of small undifferentiated cells with central necrosis of tumor nodules. The differential diagnosis based on the morphology included basal cell carcinoma and basaloid squamous cell carcinoma. The correlation between the histological features and the results from the immunohistochemical analysis are important for this distinction and definite diagnosis.

Keywords: anal squamous cell carcinoma, basaloid squamous cell carcinoma, basal cell carcinoma

ISOLATED CYSTIC LYMPHANGIOMATOSIS OF THE SPLEEN IN A PATIENT WITH DIABETES MELLITUS AND HYPERTENSION

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Isolated cystic lymphangiomatosis of the spleen is an extremely rare pathology with diffuse proliferation of anastomosing lymphatic vessels. It is thought to be the result of abnormal development and usually appears in childhood. It is most often an element of systemic lymphangiomatosis. We present a rare case of a 38-year-old woman with diabetes and hypertension who was admitted to the Surgical Department with a history of intermittent abdominal pain for one month. The pain has a sharp and sudden onset and is localized in the left upper quadrant of the abdomen, radiating to the back. Sometimes it is accompanied by nausea and vomiting. Ultrasonography showed an enlarged spleen with multiple well-demarcated and variable-sized hypodense cystic lesions. The largest lesion measures 2.5x3 cm. The liver shows fatty degeneration. No similar cystic lesions were found in the liver, kidneys, or lungs. No enlarged lymph nodes were found in the patient's abdomen, pelvis or chest. A splenectomy was performed operatively. Macroscopically, the spleen is enlarged, 20/18/10 cm. Subcapsular and on a section in the middle of the parenchyma, there are numerous small honeycomb-like cystic lesions filled with clear contents. Microscopically, multiple cystic spaces filled with eosinophilic fluid are observed. No evidence of abscess formation or granuloma formation was found. Immunohistochemistry was performed with CD31, CD34, CD68 and D2-40.

Keywords: isolated cystic lymphangiomatosis of the spleen, splenomegaly, hypertension

ARTHROSCOPIC TREATMENT FOR CARTILAGE DAMAGE OF THE KNEE

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Purpose: To present arthroscopic treatment as a method of minimally invasive approach for initial cartilaginous changes of the knee joint.

Material and methods: For the period from June 2013 – July 2023, in the Clinic of Orthopedics and Traumatology at the University Hospital "St. George" Plovdiv were performed diagnostic and therapeutic arthroscopy of the knee joint in 563 patients. 382 women and 181 men, aged from 43 to 72 years old. Joe Tippett's classification was used to grade the cartilage changes found in the knee joint during the minimally invasive procedure. In end-stage cartilage damage, it was mainly applied the abrasive arthroplasty technique. **Results:** 360 patients diagnosed with grade I – VI cartilage damage had complete recovery of the knee joint function. In another 152 of them with established grade VII and VIII, the condition improved with resolution of joint pain, increased range of motion, and resolution of chronic synovitis. In 42 of the patients there was no change in the joint condition, while in 9 others the condition even worsened. **Conclusion:** Arthroscopy of the knee joint is a minimally invasive surgical intervention aimed at preventing and preserving the joint from progression of osteoarthritis of the knee, as well as delaying the onset of irreversible bone changes in the joint.

Keywords: *arthroscopic procedure, abrasive arthroplasty, cartilage damage*

MORPHOLOGIC CHANGES IN CARPAL TUNNEL SYNDROME

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Introduction: Carpal tunnel syndrome (CTS) is the most common compression neuropathy of the upper extremities. The median nerve is compressed under the flexor retinaculum due to primary and secondary changes. Primary CTS is polyetiological while the etiology of idiopathic CTS is unknown. Histologic changes in the subsynovial connective tissue of the flexor tenosynovium (SSCT) of patients with CTS have been investigated, but their clinical and prognostic importance is unclear. Very important is the fact that the retrospective design of many previous studies does not allow correct evaluation of the pre-operative changes in relation to following therapy and prognosis. **Aim of the study:** The aim of the study were the histologic changes in the tenosynovial tissue in ten surgically treated patients for carpal tunnel syndrome and median nerve compression. Tissue samples of the synovial connective tissue under the median nerve were studied for pathologic changes. **Results and discussion:** The results showed reactive chronic synovitis, synovial hypertrophy, island-like fibrosis and hyalinosis. Histologically the samples were stained with Hematoxylin and Eosin, PAS reaction was performed for histochemical investigation with Shift method, and Van Gieson and Congo Red were used in order to rule out amyloidosis. **Conclusion:** We would suggest evaluation of the tenosynovial tissue under the flexor retinaculum after retinacular release. In case of inflammation, hypertrophy or mas effect, the surgeon must perform partial tenosynovectomy in order to decrease the volume of the carpal tunnel or to prevent the recurrence possibility.

Keywords: Carpal tunnel, histopathology, median nerve, synovium

REVIEW OF ANATOMIC VARIATIONS OF THE MEDIAN NERVE IN THE CARPAL TUNNEL

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Introduction: Carpal tunnel syndrome is the most common entrapment neuropathy. Median nerve compression due to increased pressure in the carpal tunnel leads to impaired function of the hand and discomfort and paresthesia. Surgical division of the transverse carpal ligament is a method of choice for the treatment of the condition due to common conservative treatment failure. **Aim of the study:** This paper aims at reviewing the most important anatomic variations of the median nerve in the carpal tunnel and their implication on surgical treatment of the disease. **Material and methods:** A review of literature was performed and the median nerve variations were described and summarized. Surgical importance and influence on treatment outcome were emphasized. **Results and discussion:** Different results have been reported on the frequency of median nerve variations. They are summarized in Lanz classification and the clinical importance of the different groups for treatment outcome is discussed. **Conclusion:** Anatomic variations of the median nerve in the carpal tunnel are frequent and may become a major obstacle on treatment outcome in patients who undergo surgery. Detailed knowledge on related anatomy is extremely important in every day surgical practice.

Keywords: anatomic variations, median nerve, carpal tunnel, surgery, complications

ACUTE ABDOMEN DUE TO SPONTANEOUS RUPTURE OF ADRENAL GLAND METASTASIS AS INITIAL CLINICAL MANIFESTATION OF LUNG CANCER – RARE CASE REPORT

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Background: Suprarenal glands are a common site for metastasis of lung cancer. These metastases are usually solitary, asymptomatic and diagnosed incidentally during staging of patients with lung cancer. Symptomatic suprarenal gland metastases at the time of initial lung cancer diagnosis are extremely rare. Our **aim** is to present a case of lung cancer with initial clinical presentation of acute abdomen caused by massive retroperitoneal hemorrhage as a result of spontaneous rupture of unilateral huge adrenal metastasis. **Case presentation:** We present a 66-year old male patient with sudden onset of severe abdominal pain. Rebound tenderness and rigidity of abdomen were established on physical examination. Massive liquid collection in retroperitoneal space, tumor mass of the right suprarenal gland, free intraperitoneal liquid and tumor of the right lower lung lobe were revealed by computed tomography. Massive right-sided retroperitoneal hemorrhage, intraperitoneal blood collection and necrotic tumor of the right adrenal gland were established by laparotomy on emergency. Histological examination of specimen taken from the adrenal gland tumor revealed metastasis of squamous cell lung carcinoma **Conclusion:** Our case is unique because it presents a quite rare initial expression of metastatic lung cancer – massive retroperitoneal hemorrhage due to rupture of huge adrenal metastasis. We consider that this publication might be useful for practice.

Keywords: *acute abdomen, retroperitoneal hemorrhage, adrenal metastasis, lung cancer*

ADVANTAGES AND DISADVANTAGES OF HORMONAL INTRAUTERINE DEVICES – LITERATURE REVIEW

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Introduction: In 1976, the FDA approved the manufacture of the first progestin-releasing intrauterine system in the United States. The second intrauterine system was approved in 1990 and has since been used in more than 120 countries around the world. Nowadays, a number of publications have been accumulated on the contraceptive effect of the devices and on their non-contraceptive benefits related to the antiproliferative action on the endometrium, which determines the main advantages of the pessary. Other studies focus on the unwanted effects of hormonal intrauterine devices. **Aim:** The aim of this study is to evaluate the literature and present a review about the advantages and disadvantages, indications and contraindications of levonorgestrel-releasing intrauterine systems. **Resources and methods:** A literature search of PubMed data base was conducted. Used keywords were: hormonal intrauterine devices; levonorgestrel-releasing intrauterine system. **Results and discussion:** More than 190 publications were found for the last 3 years, which reflect the interest of researchers over the years and the relevance of the problem today. **Conclusion:** The review of the literature on the subject provides up-to-date information from the reviewed studies on the advantages of levonorgestrel-releasing intrauterine pessaries and the extended indications for their use in gynecological practice. New publications related to the side effects of intrauterine systems are also indicated.

Keywords: *hormonal intrauterine devices, levonorgestrel-releasing intrauterine system*

PEDIATRIC ORBITAL TUMORS: AN ILLUSTRATIVE CASE REPORT WITH A REVIEW OF DIFFERENTIAL DIAGNOSIS

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Orbital tumors are relatively rare in the pediatric population and are among the most undesirable causes of childhood proptosis. This report aims at presenting the case of an infant with unilateral proptosis, followed by a concise review of the differentially diagnostic aspects of pathological orbital masses in children, highlighting their diversity and the importance of their timely diagnosis. The patient is a female, the first of twins, born at 37 weeks of gestation with a body weight of 2160 g. Neonatal O2 therapy was applied due to RDS. She first presented to the University Eye Clinic at the age of 5 weeks, due to proptosis of the right eye noticed by her parents. Eyeball motility, as well as all structural and functional aspects of the eye, were unaffected. Contrast CT showed a lobulated, contrast-enhancing formation in the right retrobulbar space, ~16 mm axially, enveloping the optic nerve, engaging the extraocular musculature, and pushing the bulb ventrolaterally, with contrast-enhanced MRI reaffirming the finding. A biopsy (ideally excisional, if possible) was recommended, but parents have insofar refused. Considering the extreme diversity of orbital mass-occupying lesions, their forms can range from clinically and pathologically benign entities, such as hemangiomas and dermoid cysts, to extremely aggressive rhabdomyosarcomas, neuroblastomas and Ewing's sarcoma metastases, among numerous others. This report serves as a demonstrative case showcasing the extremely broad differential diagnosis of pediatric orbital tumors and as an educational resource on said topic.

Keywords: *pediatric, orbital tumor, differential diagnosis*

A RARE CASE OF INTRACRANIAL MULTIPLE MYELOMA MIMICKING MENINGIOMA

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Background: Multiple myeloma is a neoplastic proliferation of plasma cells that represents almost 2% of all cancer diagnoses worldwide. Plasma cell disorders can manifest as several lesions – multiple myeloma, or a single lesion – solitary plasmacytoma. Plasmacytoma may affect the soft tissues or the bones, such as skull, spine, pelvis and ribs. **Case presentation:** We present a case of a 68-year-old female patient who was transferred to the emergency department with complaints of headache, difficulty in speaking and impaired movements of right limbs. The emergency computed tomography revealed extra axial intracranial mass, resembling meningioma. The patient was diagnosed with multiple myeloma approximately 1 years prior, and had received several courses of chemotherapy. The patient underwent surgical treatment and the tumor was totally resected. The histological result was consistent with multiple myeloma. **Discussion:** The intracranial involvement of multiple myeloma is a very rare complication that presents in about 0.7–4.6% of cases. It usually results as an extraosseous spread from hematogenous dissemination or adjacent skull lesions, as was in our case. Such expansive growth of multiple myeloma represents a challenging differential diagnosis to physicians and requires multidisciplinary approach of treatment.

Keywords: *multiple myeloma, plasmacytoma, meningioma, CNS, surgery*

THE USE OF DIFFUSION TENSOR IMAGING FOR ASSESSMENT OF WHITE BRAIN MATTER CHANGES IN TRAUMATIC BRAIN INJURY – A LITERATURE REVIEW

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Introduction: Diffusion tensor imaging (DTI) is a specific neuroimaging modality, used to detect microstructural abnormalities in the cerebral white matter in patients with traumatic brain injury, which are non-detectable by other standard imaging modalities such as computed tomography and conventional magnetic resonance imaging. DTI images and results can also be used to create 3D images (tractographies) of the brain interconnections most commonly damaged in brain injury. **Aim:** The aim of the current study is to conduct a contemporary literature review for the use of DTI for assessment of white brain matter changes in traumatic brain injury. **Materials and methods:** A detailed search has been conducted using the databases of Scopus, Web of Science, Google Scholar and PubMed. **Results:** Confirmation of the importance of DTI in cases of brain injury is achieved. **Conclusion:** The social role of brain injury defines the need to determine the structural substrate of the neurological impairments of these patients. The results from imaging studies such as DTI provide scientific evidence for the mechanisms of development of long-term neurological and cognitive dysfunctions. Thus, neurosurgeons will be empowered to introduce more efficient and targeted therapeutic and rehabilitation protocols that aim to reduce the long-term neurological deterioration and improving the quality of life of these patients.

Keywords: *TBI, DTI, tractography, white matter, quality of life*

GALLSTONE ILEUS: A RARE FORM INTESTINAL OBSTRUCTION – CASE STUDY

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Introduction: Intestinal obstruction from gallstone impaction is a rare occurrence, accounting for less than 0.5% of mechanical bowel obstruction cases. This condition is often diagnosed late due to its rarity and nonspecific clinical presentation. **Case report:** A 71-year old female patient was transferred to the surgical department with vomiting, epigastric bloating and abdominal pain. Due to the history of cholelithiasis and episodes of acute cholecystitis a CT scan, abdominal and endoscopic ultrasound were performed. The latter showed signs of small stones in the gallbladder, pneumobilia and distended small intestine. A decision for emergency laparotomy was taken revealing a jejunal distension due to a 6-centimetre gallstone trapped distally with intact bowel wall and no signs of peritonitis. Longitudinal enterotomy with consecutive transverse two-layer suture of the intestine was performed. **Discussion:** The gallstone ileus is a rare condition affecting predominantly elderly patients. The most common mechanism is through chronic inflammation of the gallbladder causing biliary-enteric fistula although other mechanisms involving passage of the calculus through the ampulla of Vater are also described. Due to the infrequency of the condition and the more common diseases presenting at that age group the diagnosis is sometimes delayed or even made during surgery. A number of diagnostic radiographic signs have been described but the most sensitive imaging modality is the computed tomography. The treatment is primarily operative although the surgical approach varies depending on the patient's current overall condition, the severity of the bowel obstruction and the type of biliary-enteric fistula.

Keywords: gallstone ileus, bowel obstruction, emergency surgery, laparotomy

DEVELOPMENT OF INGUINAL HERNIOPLASTY

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Hernia is one of the diseases that haunted humanity from its very beginning to the modern times. Undoubtedly, the evolution of surgical techniques has led to a significant reduction in the frequency of complications and recurrences. Despite the progress of medical science and the improvement of surgical instrumentation, the “ideal” hernioplasty, guaranteeing the absence of recurrence and postoperative complications, is still being sought. The history of surgery for hernia has gone through many stages of development. That includes ancient era, the era of the start of herniology, the anatomic era, the era of repair under tension, and the era of tensionless repair. A new section and the next step in the development of surgical methods affecting the treatment of inguinal hernias are laparoscopic and robotic surgery. Despite the progress in the surgical treatment of this common pathology, the universal method guaranteeing the absence of recurrence and complications is still being sought.

Keywords: *inguinal hernia, hernioplasty, laparoscopic hernioplasty*

ABNORMAL UTERINE BLEEDING IN PERIMENOPAUSAL WOMEN – DIAGNOSTIC-THERAPEUTIC APPROACH – LITERATURE REVIEW

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Introduction: Perimenopause is the period between the first symptoms of diminished ovarian function, usually beginning in the early forties, lasting up to two years after the final menstrual period. Abnormal uterine bleeding (AUB) commonly occurs among women in perimenopause. It is characterized by excessive bleeding in terms of duration, frequency, or volume, leading to a decline in quality of life and psychological health. For women with structural uterine issues, hysterectomy, often conducted using minimally invasive techniques, provides lasting relief from symptoms and is linked to sustained enhancements in quality of life and sexual function. In the last three decades, various uterus-preserving therapies have emerged as substitutes for hysterectomy.

Aim: The aim of this study is to evaluate the literature and present a review about diagnostic-therapeutic approach by perimenopausal women with abnormal uterine bleeding. **Resources and methods:** A literature search of PubMed data base was conducted. Used keywords were: abnormal uterine bleeding in perimenopausal women.

Results and discussion: More than 30 publications were found for the last 3 years (2020–2023), which reflect the interest of researchers over the years and the relevance of the problem today. **Conclusion:** The review of the literature on the subject provides up-to-date information from the reviewed studies on the impact of different diagnostic-therapeutic methods on quality of life and personalized treatment options for perimenopausal women with abnormal uterine bleeding (AUB).

Keywords: *abnormal uterine bleeding, perimenopausal women*

II. Biomedical Session

OBJECTIVE POLYSOMNOGRAPHIC PARAMETERS INCOMPLETELY REPRESENT SUBJECTIVE IMPROVEMENT IN PATIENTS WITH SLEEP BRUXISM TREATED WITH BOTULINUM TOXIN – TWO CASE REPORTS

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Introduction: Local administration of botulinum toxin A (BTX) is a novel therapeutic approach for patients with sleep bruxism, but data on its clinical efficacy and effects on various sleep parameters remains obscure. **Aim:** This report compares the objective changes in sleep structure and bruxism intensity with the subjectively reported improvement of sleep quality and daily symptoms after administration of BTX.

Materials and methods: Two female patients, aged 45 and 28, presented with complaints of morning headache, jaw stiffness and teeth clenching. They underwent unattended, homebased polysomnography and were diagnosed with sleep bruxism. Patient one had bruxism index (BI) of 8.4/h and patient two – BI of 3.3/h. Sleep structure was mildly impaired in both with decreased REM-sleep percentage. Local injection of 30 units BTX in each masseter muscle and 20 units in each temporal muscle was applied, followed by additional polysomnographic evaluation thirty days after treatment. **Results and discussion:** Albeit both patients reported significant improvement regarding complaints and sleep quality, the objective measurement showed improvement only for patient 1 (posttreatment BI = 4.3/h). Considerable aggravation was found for the second patient with BI increasing to 4.6/h. However, sleep architecture was restored in both patients with REM stage normalization. **Conclusion:** The following report indicates that standard objective sleep measurements are insufficient to assess the positive clinical outcome in patients with sleep bruxism. Further investigation is needed to evaluate the benefits of the treatment.

Keywords: sleep, bruxism, botulinum toxin, polysomnography

THE POSSIBILITIES OF A NON-CONTRAST ENHANCED ABBREVIATED MRI PROTOCOL FOR BREAST CANCER DETECTION

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Purpose: The role of the contrast-enhanced abbreviated MRI protocol for breast cancer detection is recognized by all radiologists. However, the establishment of a non-contrast enhanced abbreviated MRI protocol (NCEA-MRI) will save radiologist time, reduce both patients' stress, downside gadolinium-related side effects and may decrease the amount of invasive procedures. **Methods and materials:** This retrospective study includes 64 patients for the period January, 2022 – December, 2022, who had breast-related symptoms and underwent MRI. Their scans were reanalyzed by excluding the contrast-enhanced sequences. Distinguishing benign from malignant solid lesions relied only on diffusion-weighted images (DWI) and macroscopic signs such as shape, margins and architectural distortion from T2-weighted images (T2WI) and T1-weighted images (T1WI). **Results:** The total of solid lesions in the 64 MRIs were 96, after histopathological verification 80 (83.3%) of the lesions were benign and 16 (16,7%) were malignant. From both groups 9 (9.4%) lesions were suspicious on the NCEA-MRI and further examination was needed. After the biopsy 3 (33.4%) of them turned out to be fibroadenomas and 6 (66.6%) – cancers. **Conclusion:** We are optimistic that NCEA-MRI protocol will be able to provide reliable results and thus in the future it can be implemented in the screening and diagnostic strategy for breast cancer. Limitations A small number of patients was included, which can interfere the outcome of our study and a larger clinical trial is needed for further validation of the results

Keywords: MRI, breast, cancer

THE COTINUS COGGYGRIA HEARTWOOD-DERIVED FLAVONOID FUSTIN EXERTS AN ANTI-INFLAMMATORY ACTIVITY IN DIFFERENT ANIMAL MODELS

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Introduction: The widely used medicinal plant *Cotinus coggygria* contains a high concentration of polyphenols including fustin. **Aim:** The aim of the present study was to investigate the anti-inflammatory effect of fustin in different experimental models using male Wistar rats.

Materials and methods: The isolation of fustin from *C. coggygria* heartwood was performed by high-performance liquid chromatography, and nuclear magnetic resonance spectroscopy was used for its purification. The anti-inflammatory and gastro-enteroprotective activities of fustin were investigated in the following *in vivo* models: carrageenan-induced acute hind paw inflammation, indomethacin-induced gastric ulceration and trinitrobenzene sulfonate-induced colitis. Fustin was applied daily orally at doses 10 and 20 mg/kg. **Results and discussion:** Fustin reduced the edema induced by the intraplantar injection of λ -carrageenan at 30th and 60th minute thus preventing the first phase of acute inflammation, probably by blocking prostaglandin synthesis. In the ulcer model, fustin was able to ameliorate the histopathological indices of mucosal damage and inflammation. Fustin was able to alleviate some of the histopathological indices in the colitis model as well. In addition, the immunohistochemically-determined expression of NF- κ B in gastric and intestinal mucosa was reduced, pointing to possible anti-inflammatory effect. **Conclusion:** The anti-inflammatory effect of fustin probably accounted for the protective effects observed in different animal models of inflammation and organ damage.

Keywords: *Cotinus coggygria*, fustin, anti-inflammatory activity, animal models

Acknowledgement: This study is supported by the Bulgarian National Science Fund, Ministry of Education and Science, Grant number KP-06-N43/6/2020.

ASSESSMENT OF ANTIMICROBIAL SUSCEPTIBILITY OF STAPHYLOCOCCUS AUREUS NASAL ISOLATES FROM PRECLINICAL MEDICAL STUDENTS AT THE MEDICAL UNIVERSITY OF PLOVDIV

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Introduction: Preclinical medical students reflect the community and may act as reservoirs of bacteria such as *Staphylococcus aureus*. The nasal carriage may be responsible for this. *S. aureus* can develop resistance to various antimicrobial agents. **Aim:** Examination of nasal carriage among preclinical medical students. Detection of methicillin-resistant *Staphylococcus aureus* (MRSA) rate and inducible resistance to clindamycin (iMLS). Comparison of the results with relevant study conveyed in 2019. **Materials and methods:** Nasal swabs from 512 medical students were tested. The identification was done by using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). Antibiotic susceptibility testing was done by the Kirby-Bauer method and BIOMIC V3 system. **Results and discussion:** The staphylococcal carriage rate in 2023 was 29.3% and in 2019 – 21.5%. No statistical significance was found between Bulgarian and International students in 2023. From 2019 to 2023 international students demonstrated increased carriage. **Conclusion:** Preclinical medical students share the same rate of *S. aureus* colonization as the general population. This data would be of interest to further delineate the trend of *S. aureus* nasal carriage and MRSA.

Keywords: *Staphylococcus aureus*, nasal carriage, medical students

TRICHOSCOPY IN THE DIAGNOSIS OF ALOPECIA AREATA

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Introduction: Alopecia areata (AA) is one of the most common hair loss disorders. The prevalence of the disease is 0.1% – 0.2% of the general population. AA is a T-cell mediated autoimmune condition characterized by non-scarring hair loss that may affect only parts of the scalp, the entire scalp or parts of the body. AA may manifest as a single episode or may have a relapsing course. Dermoscopy of the hair and scalp is known as trichoscopy: a useful method for diagnosing and monitoring hair and scalp disorders, as well as monitoring the effect of the applied treatment.

Aim: To make a review of the literature on the topic of trichoscopy in the diagnosis of alopecia areata.

Materials and methods: PubMed publications were searched using the following keywords: "trichoscopy", "alopecia areata". A total of 143 publications published between 2008 and 2023 were reviewed.

Results and discussion: The presence of exclamation mark hairs, black dots, triangular hairs, broken hairs, and pointed hairs in the alopecic patches indicates disease activity. One of the most common trichoscopic features of AA are the yellow dots – empty follicular openings filled with keratin and sebum. They predominates in long-standing, inactive disease. Short vellus hairs are also common. Hair regrowth phase includes: upright regrowing hairs and circle hairs. Diagnosis should be based on the coexistence of several trichoscopic findings rather than the presence of a single sign.

Conclusion: Trichoscopy is a useful method for diagnosing and monitoring of AA, as well as for follow-up after treatment.

Keywords: *alopecia areata, diagnosis, trichoscopy, dermoscopy, hair loss*

HYPOTHALAMO-PITUITARY-GONADAL AXIS IMBALANCE AND ITS ROLE IN PCOS PATHOGENESIS

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Polycystic ovary syndrome (PCOS) is a prevalent and distressing endocrine disorder with an unclear aetiology. It's characterized by hormonal imbalance causing irregular periods and the presence of small cysts on the ovaries. PCOS is a heterogenous disorder with multifactorial mechanisms including genetics, hyperandrogenism, obesity, insulin resistance, increased pro-inflammatory cytokines, oxidative stress, and impaired neuronal circuits and hormonal regulation. It's very common during reproductive age and leads to decrease in the quality of life with a risk of infertility. Knowing different aspects of its pathogenic mechanism will help to target the root cause for their stimulation and hence preparing better treatment regimen. Our review will focus on understanding the imbalance of steroid hormone feedback to the hypothalamo-pituitary-gonadal axis and its role in PCOS pathophysiology. The ovarian function in all mammals is controlled by the gonadotropin-releasing hormone (GnRH) neurons. GnRH stimulates the secretion of the gonadotropins from the pituitary gland, subsequently controlling gonadal steroid hormones secretion. These hormones provide negative feedback through sensitive neuronal network in the brain. In PCOS, regulatory mechanisms are impaired by different mechanisms. Elevated androgens levels and impaired arcuate GABA neurons regulation interfere with progesterone negative feedback. Obesity and insulin resistance activates GnRH neurons insulin receptors leading to increased GnRH pulsatile secretion. Regardless, PCOS multifactorial nature makes administering proper treatment a challenging issue. Our review highlights the importance of identifying the phenotype of PCOS, hence tailoring an individualised clinical care.

Keywords: PCOS, pathogenesis, GABA neurons, hyperandrogenism, insulin resistance

LACTATE AS A MODERN TOOL OF EXERCISE PHYSIOLOGY – A REVIEW OF THE LITERATURE

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Introduction: Lactate is a key molecule in exercise metabolism. In the last two decades there has been a revolution in the understanding of its role – from a byproduct of hypoxic muscles to a major energy resource and a signaling molecule – ‘lactormone’. **Aim:** The aim of this review is to compile all the up-to-date information that is available on the general metabolism of lactate, but also the specific use that exercise physiologists, coaches and athletes can get out of lactate measurements, lactate-based training zones and periodization of training sessions. **Materials and methods:** Three databases were searched for this review – PUBMED, Google Scholar and Science Direct. **Results and discussion:** Since the revolution in the understanding of lactate’s role in normal metabolism and disease in the late 20th century, more evidence has been assembled regarding the specific part it plays in exercise. From the vast body of knowledge was developed the concept of training intensity distribution into zones according to the level of blood lactate. The end goal of training to a specific lactate level or ‘threshold’ is the increased utilization of lactate as an energy source by active muscles and ultimately better performance, which has been backed up by the achievements of numerous athletes, training according to this concept. **Conclusion:** Lactate is established as a valuable training tool, but nevertheless it is part of an evolving scientific field, which changes rapidly and an updated look at the science behind lactate-based training can be beneficial to athletes overall.

Keywords: lactate, exercise, threshold, OBLA, LT

THE SEEMINGLY HIDDEN ROLE OF RIGHT VENTRICULAR DYSFUNCTION IN THE PATHOPHYSIOLOGY OF SUDDEN CARDIAC DEATH AMONG ELITE ATHLETES

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Introduction: Sudden cardiac death (SCD) has been acknowledged as a significant cause of mortality among apparently healthy elite athletes. Traditionally, much focus has been directed towards the role of the left ventricle and its pathophysiology. Yet, emerging research highlights importance of right ventricular dysfunction in the development of sudden cardiac death. **Aim:** This review aims to explore new findings about the role of right ventricular dysfunction regarding the pathogenesis of sudden cardiac death in elite athletes. **Material and methods:** A search in the PubMed database was performed utilizing the following keywords: sudden cardiac death and elite athletes, sudden cardiac death, and right ventricle. Twenty-five articles were selected. **Results and discussion:** Endurance exercise places a disproportional load on the right ventricle, both physically and metabolically, due to it's thinner chamber wall, relative to the left ventricle. This seems to contribute to pro-arrhythmic right ventricular remodeling. Furthermore, right ventricular dysfunction is observed following intense endurance exercise, evidenced further by inversely correlated elevation of biomarkers such as Troponin and B-type natriuretic peptide. Moreover, morphological changes to the right ventricle may not be entirely reversible as opposed to left ventricular changes as seen in athletic heart syndrome. **Conclusion:** Sudden cardiac death is a leading cause of mortality in elite athletes, despite routine screenings and annual medical evaluations. This indicates a gap in our comprehension of the underlying pathogenesis and underlines the need for further research in this area.

Keywords: *sudden cardiac death, right ventricular dysfunction, right ventricle, elite athletes, sports medicine*

ANTHROPOLOGICAL COMPARISON OF DIMENSIONS OF DENTAL CROWNS BETWEEN BULGARIAN AND INDIAN POPULATION

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Introduction: Dental profile consists of specific individual characteristics related to the teeth and their size. They can help in estimation of age, sex, race, socio-economic status, personal habits, oral and systemic health, occupation and dietary status of the person. Variability observed in the human dentition provides a theoretical basis for the individualization of human dentition. Numerous factors can contribute to variation in tooth size but probably the combination between genetic factors and environmental influences leads to the differences between populations. The **aim** of the present study is to evaluate the variations of dental dimensions between Bulgarians and Indians.

Materials and methods: The study included 232 Bulgarians aged 20–40 years. Vestibulolingual and mesiodistal dimensions of teeth were measured by Dentistry Sliding Vernier Caliper and analyzed with SPSS 23.0.

Results: We found significant differences in mesiodistal dimensions of maxillary canines, premolars and molars and mandibular incisors and premolars between Bulgarians and Indians. Some of them were with high degree of significance. **Conclusion:** Our results revealed that odontometric dimensions vary in different population and therefore it is necessary to determine specific population values in order to make identification possible.

Keywords: dental dimensions, dental profile, population-specific, Bulgarians

EXPLORING THE EFFECTS OF HEATED TOBACCO PRODUCTS ON RESPIRATORY HEALTH – A COMPREHENSIVE LITERATURE REVIEW

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Introduction: More than 1.3 billion people around the world are current tobacco users. Due to the fact that smoking is a significant risk factor for a number of chronic conditions, more people are looking towards alternatives to nicotine consumption. Heated tobacco products (HTPs) are a new class of devices, used to deliver nicotine by heating instead of burning the tobacco, therefore supposedly omitting most of the harmful effects of cigarette smoke. **Aim:** The aim of this article is to review the current knowledge regarding HTPs use and their effect on pulmonary health. **Materials and methods:** PubMed and Scopus searches were utilized, using the keywords “heated tobacco products”, “respiratory health” and “pulmonary function”, in order to find relevant articles. **Results and discussion:** The effects of HTPs on the respiratory system have been examined mostly using in vitro methods, with limited clinical data. In-vitro studies have found that exposure to HTP aerosol produces comparable inflammatory response to conventional cigarette smoke and has similar destructive effects on the respiratory epithelium and smooth muscle cells. Human trials including HTPs have produced conflicting results, regarding the long-term effects on respiratory health. HTP use has also been associated with acute and potentially life-threatening conditions like acute eosinophilic pneumonia. **Conclusion:** Increasing number of people are switching from conventional cigarettes to HTPs every year. However, the long-term effects of HTPs on pulmonary health are not well established. More research is needed to determine the potential risks that HTPs pose to the users' pulmonary health.

Keywords: *heated tobacco products, respiratory function, smoking, pulmonary health*

CALPAINS AS BIOMARKERS OF CARDIOVASCULAR RISK IN PATIENTS WITH ISCHEMIC HEART DISEASE

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Introduction: Cardiovascular diseases are among the leading causes of disability and a third of the causes of death worldwide. The leading cause of their appearance, development, and complications is atherosclerosis. The search for rapid and qualitative diagnostic markers remains an important problem for cardiology. Calpains are calcium-dependent stress-responsive intracellular proteases and are responsible for cell signaling, apoptosis, exocytosis, mitochondrial metabolism, and cytoskeletal remodeling. Impaired expression of various members of the calpain family and reduced activity of their inhibitor calpastatin are observed in various pathologies. This family of enzymes has been shown to play an important role in the pathogenesis of atherosclerosis, diabetes mellitus, liver, and several other diseases. To date, 15 members of the calpain family have been discovered, 10 of which are expressed in the heart. They are divided into 2 groups, conventional (1, 2, 3, 8, 9, 11, 12, 14) and non-conventional (5, 6, 7, 10, 12 and 15), based on the content of penta-EF in the structure of domain IV. Calpain 1 and 2 have the most pronounced proatherogenic role. They are responsible for monocyte and macrophage chemotaxis, smooth muscle cell migration, vascular fibrosis, and calcification. Their overactivation weakens the barrier function of vascular endothelial cells. Calpain-10 is involved in the development of type 2 diabetes and polymorphisms in their gene are associated with an increased risk of developing this disease. The review aims to focus attention on certain members of the calpain family as markers of cardiovascular risk.

Keywords: *calpains, biomarkers, cardiovascular diseases*

INFLAMMATION AND AUTOPHAGY MARKERS IN NAÏVE RHEUMATOID ARTHRITIS PATIENTS

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Rheumatoid arthritis (RA) is an autoimmune disease with systemic manifestations. Severe oxidative stress, inflammation and dysregulated autophagy are discussed in the pathogenesis of the disease. The aim of the study is to examine protein and gene levels of novel markers of inflammation (YKL-40), autophagy and tissue remodeling (LAMP-1 and LAMP-2) in RA patients. Twenty naïve RA patients and ten controls were involved in the study. Conventional parameters related to inflammation such as – CRP, RF, ESR were examined. All patients were assessed by ultrasonography. Plasma YKL-40 and LAMPs levels were determined by ELISA. Gene expression was evaluated by qPCR. Higher plasma YKL-40 levels in RA patients compared to the control group were found. We detected decreased LAMP-1 concentration in patients and no difference in LAMP-2 levels between patients and healthy individuals. No change in YKL-40 and LAMPs gene expression levels was found. Clinical parameters were altered in all RA patients. A feeble correlation was found between CRP and YKL-40. The results showed the presence of inflammation in newly diagnosed RA patients. The significantly higher plasma YKL-40 could be used to distinguish both healthy controls from RA patients and indicated its participation in the inflammatory process. The difference in YKL-40 protein and gene expression levels may reflect the impact of local joint production even at early stages of RA. Most probably autophagy and tissue remodeling are not affected in naïve patients but might be activated during disease progression.

Keywords: YKL-40, LAMPs, Rheumatoid arthritis

COGNITIVE IMPAIRMENT IN EARLY STAGES OF PARKINSON'S DISEASE

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Introduction: Parkinson's disease (PD) is a common neurodegenerative condition characterized by motor and nonmotor symptoms. Among non-motor features the most significantly contributing to the patients' disability are cognitive decline and dementia. **Aim:** To evaluate the cognitive functions in newly diagnosed, treatment naïve patients with early PD. **Materials and methods:** The study comprised 28 newly diagnosed patients with PD according to the Movement Disorder Society – Parkinson's Disease (2015) criteria. The severity of motor impairment was evaluated by Unified Parkinson's Disease Rating Scale (UPDRS). The cognitive functions were assessed by Montreal Cognitive Assessment (MOCA) and Mini Mental State Examination (MMSE) tests. **Results:** More than 2/3 of the patients showed abnormally low score on cognitive tests (92,9% on MOCA and 78,6% on MMSE). Moderate negative correlation was found between MOCA results and age of the patients ($r_{xy} = 0,553$, $p = 0,002$), and MOCA results and the age at the onset of the disease ($r_{xy} = 0,528$, $p = 0,004$). No significant correlations were found between the MMSE score, age of the patients, the age at disease onset and the duration of the disease. **Conclusion:** A large part of patients with newly diagnosed PD have different degree of cognitive dysfunctions. The age of the patients and the age at the disease onset can contribute to increased cognitive impairment in the early stages of Parkinson's disease.

Keywords: cognitive impairment, Parkinson's disease, non-motor symptoms, dementia

VIRAL PNEUMONIA IN THE EARLY POSTOPERATIVE PERIOD – POSTMORTEM MORPHOLOGICAL FINDINGS

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Nosocomial infections are one of the leading causes of in-hospital mortality with bacterial pathogens being most common. In surgical patients usual sources of infections are the surgical site and infectious complications after invasive procedures. We report a case of 26-years old male with no known comorbidities admitted to the hospital for elective pilonidal cyst removal. The surgical intervention was performed under spinal anesthesia and underwent with no complications. On postoperative day one unexplained fever was noted. The differential diagnosis in the intensive care unit included sepsis from postoperative surgical site infection or post spinal meningitis and empirical antibiotic therapy was started. Over the next two days rapidly progressing multiorgan failure refractory to all treatment led to the patient's death. Autopsy was performed revealing severe pulmonary pathology with the histological picture of viral pneumonia with features of respiratory syncytial virus.

Keywords: viral pneumonia, respiratory syncytial virus

STUDY OF THE ANTIOXIDANT EFFECT OF BIOFLAVONOID FUSTIN ISOLATED FROM COTINUS COGGYGRIA HEARTWOOD IN ACUTE RAT MODELS OF ORGAN DAMAGE

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Introduction: The medicinal plant *Cotinus coggygria* has a high content of polyphenols, including the dihydroflavonol fustin, which is poorly studied in preclinical experiments. The antioxidant effects of total extracts from *C. coggygria* leaves and heartwood have been relatively well documented. The **aim** of this study was to explore the antioxidant activity of fustin in experimental pharmacological models of organ damage in Wistar rats. **Materials and methods:** Fustin was isolated from *C. coggygria* heartwood and purified by high-performance liquid chromatography and NMR-spectroscopy. The *in vivo* studies were conducted on three acute rat models of oxidative stress: indomethacin-induced gastric ulceration ($n = 30$, fustin dose 10 mg/kg); paracetamol-induced hepatotoxicity ($n = 48$, fustin doses 5 and 10 mg/kg) and trinitrobenzene sulfonate (TNBS)-induced colitis ($n = 30$, fustin dose 20 mg/kg). Biochemical analyses of malondialdehyde (MDA) and superoxide dismutase (SOD) levels in blood serum and organ homogenates were performed. **Results and discussion:** Fustin exerted tissue protective action but did not change significantly MDA levels in blood serum and organ homogenates, demonstrating the absence of an effect on lipid peroxidation in all three models of organ damage. Fustin treatment restored the colon activity of SOD in the experimental TNBS-induced colitis. Most probably, this antioxidant effect may result from its ability to increase intracellular antioxidant defense by gene expression regulation. **Conclusion:** The observed *in vivo* tissue protective action of fustin in rat models of organ damage is not due to its antioxidant properties.

Keywords: *Smoke-tree heartwood, Cotinus coggygria, Fustin, Wistar Rats, Antioxidant effect*

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ADVERSE EFFECTS OF LIBTAYO (CEMIPLIMAB) IN THE ENDOCRINE CLINICAL PRACTICE – TWO CASES OF AUTOIMMUNE HYPOPHYSITIS DURING TREATMENT FOR SQUAMOUS CELL CARCINOMA

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Introduction: Libtayo (cemiplimab) is an Immune checkpoint inhibitor (ICI) used to treat squamous cell carcinoma and non-small cell lung cancer (NSCLC). ICIs have resulted in a variety of side effects that involve the endocrine system, most commonly thyroiditis, hypophysitis, Type 1 diabetes, adrenalitis, and central diabetes insipidus. We present two clinical cases – 65-year-old patient with squamous cell carcinoma, treated with cemiplimab, who presented to the clinic with destructive thyrotoxicosis in the background of autoimmune thyroid disease and subsequent development of secondary hypocorticism. The other patient was started on Libtayo in relation to accompanying squamous cell carcinoma and carcinoma of the parotid gland. On admission, we registered primary hypothyroidism and central hypocorticism as a consequence of possible autoimmune hypophysitis that was suspected after performing MRI of the brain. **Discussion:** Autoimmune hypophysitis is considered a rare condition, some reports estimate an incidence of 1 in 9 million individuals. ICI-associated hypophysitis and primary adrenal insufficiency lead to a permanent loss of adrenal function that is potentially lethal. Clinical manifestations of hypocorticism, such as fatigue, weakness, poor oral intake, low blood pressure, nausea and vomiting overlap with symptoms of malignancy and may remain unrecognized which delays timely treatment. **Conclusion:** We present clinical cases of two patients with secondary hypocorticism caused by Cemiplimab in order to emphasize the importance of routine screening for ICI-hypophysitis as it has the potential to prevent significant morbidity and mortality.

Keywords: *Libtayo, Immune checkpoint inhibitor, Secondary hypocorticism, Autoimmune hypophysitis*

PROTEIN-PROTEIN INTERACTIONS OF MAST CELLS IN ASD

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disturbance, diagnosed in early childhood. It is associated with varying degrees of dysfunctional communication and social skills, repetitive and stereotypic behaviors. Regardless of the constant increase in the number of diagnosed patients, there are still no established treatment schemes in global practice. Many children with ASD have allergic symptoms, often in the absence of mast cell (MC) positive tests. Activation of MCs may release molecules related to inflammation and neurotoxicity, which contribute to the pathogenesis of ASD. The aim of the present paper is to search for a relationship between MCs and associated key molecules and immune pathways involved in the pathogenesis of autism. PPI network and enrichment analyzes were performed using receptor information and secreted molecules from activated MCs identified in ASD patients. Our results revealed interactions of MCs with molecular pathways, cytokines, basic marker molecules for MCs degranulation, and various receptors. The established relationships between ASD and MC's activation, as well as the involved molecules and interactions, are important for elucidating the pathogenesis of ASD. This could help the development of effective future treatments for autistic patients by discovering new therapeutic target molecules.

Keywords: ASD, mast cells, mediators, neuroinflammation

NONBACTERIAL THROMBOTIC ENDOCARDITIS – THE PATH FOR THE DIAGNOSIS

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Introduction: The nonbacterial thrombotic endocarditis is a rare disease often associated with hypercoagulable states such as systemic lupus erythematosus, antiphospholipid syndrome or advanced malignancy like adenocarcinoma. Clinical manifestation is frequently associated with an embolic incident. **Aim:** To describe a clinical case of nonbacterial endocarditis as a result of undiagnosed antiphospholipid syndrome and high suspicion for systemic lupus. Materials and methods: We present a case of 55 years old woman, who was admitted to the cardiology clinic due to persistent fevers up to 39 degrees for two months, arthralgias and myalgias. As a comorbidity, reported Crohn's disease, for which remission was achieved on Mesalazine therapy. **Results and discussion:** Transthoracic and transesophageal echocardiography showed vegetation of the aortic valve, without any presence of valve dysfunction. In the presence of triple-negative blood cultures, persistence of fevers, and the presence of histologically proven autoimmune disease, further investigations were performed, which proved antiphospholipid syndrome and high clinical suspicion for systemic lupus. After consultation with a rheumatologist and administration of Methylprednisolone, the patient remained permanently afebrile. The patient was referred to a rheumatology clinic for further treatment. In patients with "suspected infective endocarditis" with formed vegetation and negative blood cultures, nonbacterial thrombotic endocarditis should be considered, due to a difference in therapeutic behavior. Anticoagulant therapy is the first line of treatment for nonbacterial endocarditis, because of the increased risk of systemic embolism, rather than antibacterial therapy. **Conclusion:** Treatment of the underlying disease in nonbacterial thrombotic endocarditis is key to the patient's short- and long-term prognosis.

Keywords: Nonbacterial thrombotic endocarditis (NBTE); Libman-Sacks endocarditis (LSE); Systemic lupus erythematosus (SLE); Antiphospholipid syndrome (APS)

BLOOD MICROBIOME ANALYSIS IN PULMONARY SARCOIDOSIS PATIENTS

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Evidence suggests that microbiome dysbiosis is linked to pulmonary sarcoidosis, as indicated by bronchoalveolar lavage metagenomics. However, this method is invasive and limited to specialized centers. In contrast, venous blood collection is simpler and widely accessible. We hypothesize that the blood microbiome likely interacts with lung microbiota due to extensive capillary-alveoli contact; thus, it presents a less invasive option for studying sarcoidosis-associated microbiome changes. Our aim was to characterize the specific genera of blood microbiota that are enhanced in patients with pulmonary sarcoidosis. We extracted and sequenced microbial DNA from lysed blood samples, comparing 16S metagenomic sequencing data from 7 pulmonary sarcoidosis patients against 22 healthy controls. After data cleaning and taxonomic identification, we evaluated the metagenomic profiles of individuals and subjected them to statistical analysis. This revealed six bacterial genera: Veillonella, Prevotella, Cutibacterium, Corynebacterium, Streptococcus, and Comamonas – that were either unique to or notably prevalent in the blood samples of sarcoidosis patients. This study introduces a validated approach for evaluating the composition and diversity of the blood microbiome in individuals with rare diseases, such as sarcoidosis. By exploring the blood microbiome, we aim to deepen our understanding of the origins and progression of these diseases, potentially leading to the discovery of new, personalized treatment options.

Keywords: Lung diseases, Sarcoidosis, Microbiome, Metagenome analysis, Venous blood

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EPIGENETIC AND MORPHOLOGICAL ASPECTS OF HEALTHY AGING WITH FUNCTIONAL FOODS ENRICHED IN GAMMA-AMINOBUTYRIC ACID AND POLYPHENOLIC COMPOUNDS

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The aging is a relatively new problem in human history. The main objective of the project is to study the effect of functional foods and beverages enriched in biologically active compounds in *in vitro* and *in vivo* models of aging by the epigenetic modulation of the α -Klotho gene. This includes the development and characterization of functional foods and beverages enriched with gamma-aminobutyric acid and polyphenolic compounds, investigating the effect of the developed functional foods and beverages on delaying the aging process in *in vitro* models of aging and investigating the subtle molecular pathways of influencing some of the hallmarks of cellular aging, including the epigenetic modulation of the α -Klotho gene, studying the effect of functional foods and beverages on *in vivo* rat models with healthy experimental animals undergoing spontaneous aging by examining cognitive, sensory, locomotor and other physiological functions after supplementation, as well as an in-depth analysis of the morphological, molecular and epigenetic mechanisms of the antiaging effect in the kidney and the brain. Given the multidisciplinary nature of the project, which requires the conduct of phytochemical, microbiological, epigenetic, biochemical and medical research, its implementation will be carried out by three organizations. The topicality and importance of the topic derive from the fact that healthy aging is among the most significant social and economic challenges of the 21 century, It's novelty and originality derive from the fact that in the world literature there are only a few studies on the influence of nutritional components on the expression of the Klotho gene.

Keywords: *aging, functional foods and beverages, gamma-aminobutyric acid, polyphenolic compounds, Klotho gene*

PROLACTINOMA – A CASE STUDY

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Prolactinoma is a tumor of the adenohypophysis, originating from the lactotrophic cells, which chronically secretes prolactin in abnormally high levels and causes gonadic dysfunction. Usually, the adenoma presents itself with galactorrhea, oligorrhea, amenorrhea and/or anovulation with shortened luteal phase, severe premenstrual syndrome, low libido, mild hirsutism, and seborrhea. This case report presents how even though the patient presents with regular menstrual cycle and normal sex hormone levels, the presence of ovulatory bleeding, which could appear to be a gynecological issue, might be the debut of an underlying endocrinological condition. We present a young woman, whose main symptom is ovulatory bleeding, which has gone from slight spotting to severe hemorrhage for 5–7 days a week over the years. Broad spectrum of hormonal assays was made such as prolactin, macroprolactin, pituitary-gonad and thyroid hormone levels. The results showed drastically elevated prolactin levels. A magnetic resonance imaging was done. A tumor was found with parameters of a microadenoma (8.9 mm transversal, 5.1 mm craniocaudal and 3.5 mm sagittal). In a differential diagnostic are discussed a Polycystic Ovary Syndrome, Idiopathic hyperprolactinemia, or Autoimmune hypothyroidism, due to the probability of Hashimoto antibodies creating complexes with prolactin, resulting in macroprolactin. In conclusion, a symptom of bleeding during ovulation can be related to an endocrine disturbance such as hyperprolactinemia, which is not a classical and common symptom.

Keywords: *prolactinoma, ovulatory bleeding, prolactin*

MICROBIOLOGICAL DIAGNOSIS AND TREATMENT STRATEGY FOR INVASIVE CANDIDA GLABRATA INFECTIONS

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Introduction: *Candida glabrata* is an opportunistic pathogen and the second or third most common causative agent of candidiasis depending on the site of infection. This pathogenic fungus is a therapeutic problem due to a constant decrease in antifungal susceptibility. Treatment for *C. glabrata* infections is challenging since the pathogen frequently develops resistance to several echinocandins and azoles, especially fluconazole. As a result, immunocompromised patients have a significantly higher mortality rate from *C. glabrata* infections. The aim of this study was to explore the scientific literature to summarise the recommended approaches for microbiological diagnosis and therapeutic approaches in patients with invasive *C. glabrata* infections.

Materials and methods: A PubMed search on the relative available literature with keywords: *Candida glabrata*, invasive infections, and treatment was performed. Articles that investigated the treatment of invasive *C. glabrata* infection were included, as well as the European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations.

Results and discussions: According to EUCAST and the references, the recommended antifungals for *C. glabrata* antimycogram are micafungin, anidulafungin, caspofungin, fluconazole, and amphotericin B. In recent years there has been an increase in resistance of *C. glabrata* to azoles and echinocandins. This poses a serious therapeutic problem as it eliminates treatment options for invasive *C. glabrata* infections in immunocompromised patients.

Conclusion: To tackle the problem of increasing antimycotic resistance and mortality in invasive *C. glabrata* infections, it is necessary to discover novel therapeutic approaches and markers that distinguish invasive from superficial candidiasis.

Keywords: *Fungal infection, invasive mycotic infection, antifungal treatment*

ATYPICAL PNEUMONIA – A CASE STUDY

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Pneumonia is an infection of the lower respiratory tract that involves the airways and parenchyma, with consolidation of the alveolar spaces. The causative agents may be viruses, bacteria, fungi. Atypical pneumonias are most often caused by intracellular microorganisms and are characterized by a milder and “atypical” clinical picture. Atypical pneumonia describes patterns typically more diffuse or interstitial than lobar pneumonia. The causative agents may be: Chlamydia pneumoniae, Chlamydia psittaci, Mycoplasma pneumoniae and viruses. Mycoplasma pneumoniae is most common after age 5 and is most prevalent in late summer and fall. We present a clinical case of a 13-year-old boy with fever, cough and pain in the left thoracic region. After physical examination a mildly hyperemic throat has been established. The rest of the parameters of the physical examination were normal. On radiography a right upper lung paramediastinal oval formation with a heterogeneous structure and mortared X-ray density with unsharp outlines and reduced transparency of the adjacent lung parenchyma was found. On CT scan, consolidation of the parenchyma of the second and third segments of the right lung was found. On ultrasonography, evidence of pneumonia was detected. PCR of sputum proved the causative agent – Mycoplasma pneumoniae. This case illustrates the difficulty in diagnosing atypical pneumonias. Knowledge of the most common causative agents of atypical pneumonias is critical for making the correct diagnosis and choosing the right treatment.

Keywords: *atypical pneumonia, Mycoplasma pneumoniae, consolidation, oval formation*

PRESCHOOL CHILDREN AND PULMONARY FUNCTION TESTING – A NEW OPTION FOR BETTER DIAGNOSTICS

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The diagnostics and follow-up of the obstructive lung diseases in young children under 6 years of age are always been a challenge. The Forced oscillation technique (FOT) is effortless alternative of spirometry and is proven to be sensitive method of testing. The purpose of this study is to demonstrate the success rate of FOT compared to the traditional Spirometry in preschool age. 20 healthy children aged 3–6 were enrolled in this study. They performed both FOT (RESMON PRO) and Spirometry (Vitalograph) test. The forced oscillation technique applies an external oscillatory signal in order to determine the response of the respiratory system. It requires only tidal breathing and a total of three technically acceptable measurements, whereas the spirometry test needs a lot of instructions, effort and time. All 20 healthy patients tried to perform FOT and Spirometry in order to evaluate the success rate of the two examinations. All children at the age of 3 couldn't perform the spirometry, and the total success rate for spirometry was no more than 50%. In comparison near 90% performed FOT successfully. Some children couldn't execute the FOT due to two main reasons: crying out of fear and laughing. The child's laughter was mainly caused by the oscillations which create a tickling sensation in the child's oral cavity and chest. The technique of forced oscillations is an extremely effective, effort-independent and informative method in the diagnosis of obstructive diseases, even at the young age of less than 6 years.

Keywords: *Forced oscillation technique, spirometry, airway obstruction, children*

CASE REPORT: CEREBRAL CALCIFICATION AS A RESULT OF PRIMARY HYPERPARATHYROIDISM CAUSED BY PARATHYROID ADENOMAS THAT IMITATES FHAR'S DISEASE

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Cerebral calcifications are classified into 3 groups: physiological, idiopathic (including Fahr disease) and secondary to calcium metabolism alterations. The most common causes of these calcifications with a striatum-pallidus-dentate distribution are the calcium–phosphorus metabolism disorders: hypoparathyroidism, pseudohypoparathyroidism, pseudo-pseudohypoparathyroidism and hyperparathyroidism. The association of basal ganglia calcifications and primary hyperparathyroidism is exceptional. This is a very rare consequence of hyperparathyroidism. A 45-year-old man was admitted to the Neurosurgery clinic with a closed craniocerebral injury – concussion, and symptoms of headache and loss of balance. A Brain CT scan was performed, on which it was found calcifications on the basal ganglia, the tentorium and subtentorially around the cerebellum. Tests were done for: serum calcium (which levels were above normal), phosphate (which levels were below normal), vit D (which levels were normal), and PTH (which levels were elevated). The patient was treated symptomatically for the condition of concussion and sent for further diagnostic tests. From these tests, it was concluded that the patient had a diagnosis of parathyroid adenomas, which were the cause of primary hyperparathyroidism with elevated levels of calcium and PTH. The differential diagnosis of Fahr's disease was rejected and it was concluded that the cerebral calcifications were the result of elevated serum calcium levels.

Keywords: case report, cerebral calcification, parathyroid adenoma, hyperparathyroidism

ACUTE MYELOID LEUKEMIA DIAGNOSED DURING PREGNANCY: A CASE REPORT

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Introduction: Acute myeloid leukemia (AML) occurring during pregnancy is not a common medical event. Its treatment is significant clinical challenge, regarding the therapy-associated risks both for the mother and the fetus and in addition raises a serious question whether the pregnancy should be continued. AML is often complicated with infection, bleeding and placental dysfunction. On the other hand all cytostatic agents are teratogenic therefore maternal health must be paramount. **Case presentation:** We report a case of 28-year-old pregnant female in 14-week of gestation presenting with classical findings of AML proven by the presence of blasts cells in peripheral blood and bone marrow. Flowcytometry confirmed AML. Abortion on medical indications was performed in consideration of the progressive course of the disease. Standard induction "7+3" and consolidation chemotherapy HDAC were administered and the patient achieved hematological remission. Donor search found HLA – matched unrelated donor. The patient underwent allogeneic stem – cell transplantation followed by donor lymphocyte infusion and a second stem cell transplant from the same donor because of progressive evolution of the disease. Unfortunately AML relapsed again after second transplant and the patient died. **Discussion and conclusion:** Simultaneous establishment of pregnancy and life-threatening diagnosis such as AML requires individual approach. Evidence obtained so far are insufficient for determining a causative association between pregnancy and hematological cancers. Many questions are still open regarding the cessation of pregnancy, the possibility to preserve the fetus and postpone chemotherapy and the option for cord blood stem cell collection.

Keywords: Acute myeloid leukemia (AML), Pregnancy, Abortion on Medical Indication

III. Pharmacy and Pharmacotherapy Session

PREPARATION OF OPTIMIZED GEL MODEL WITH TETRACYCLINE-LOADED LIPOSOMES FOR TREATMENT OF BACTERIAL SKIN INFECTIONS

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Introduction: Skin infections are some of the most common medical conditions. The treatment of bacterial dermal infections includes the use of antibiotics, which can be administered orally or topically. Tetracyclines are often used in the therapy. **The aim** of the present study was to formulate a semi-solid gel form with tetracycline-loaded liposomes, for topical administration of tetracycline. **Materials and methods:** liposomes were prepared using egg-yolk phosphatidylcholine, cholesterol and Kolliphor p188, by thin-layer hydration technique, followed by extrusion, in order to obtain liposomes with appropriate size. Four models were prepared with varying concentrations of phosphatidylcholine, cholesterol, emulsifier and tetracycline. The formulated liposomes were purified from unentrapped drug by dialysis and characterized in terms of particle size, surface morphology, drug loading and encapsulation efficiency using dynamic laser scattering, scanning electron microscopy and UV-Vis spectroscopy. Semi-solid formulation was obtained using Carbomer 934, gelled with triethanolamine. *In vitro* drug release was performed via diffusion through dialysis membrane at $32\text{ C}^{\circ} \pm 5\text{ C}^{\circ}$. The obtained results were used to determine the drug release kinetics. **Results and discussion:** The formulated vesicles were spherical in shape, showing relatively high drug encapsulation efficiency and suitable size at around 200 nm. After incorporation in the hydrogel, prolonged drug release was observed. Based on the achieved results, a promising formulation was proposed for topical treatment of bacterial skin infections.

Keywords: hydrogel, tetracycline-loaded liposomes, bacterial skin infections

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CASEIN-FUCOIDAN NANOCOMPOSITES AS A DRUG DELIVERY SYSTEM FOR DAUNORUBICIN

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The aim of this study was to develop casein/fucoidan nanocomposites via polyelectrolyte complexation and subsequent nano spray drying and to evaluate their potential for daunorubicin delivery. 3 (k-p) fractional factorial design was applied to estimate the effect of the independent variables (casein-fucoidan ratio, crosslinker concentration and spray intensity) over the dependent variables (production yield, particle size and zeta potential). Furthermore, the optimal production parameters for the preparation of blank nanocomposites were estimated. Based on an optimized "placebo" model of casein-fucoidan nanocomposites, three batches of daunorubicin-loaded particles were synthesized at varied crosslinker concentration and spray intensity. The obtained structures have average particle size within the range 355 ± 9 nm to 407 ± 8 nm, zeta potential from -30.61 ± 1.05 mV to -32.9 ± 1.35 mV and production yield between $77.39 \pm 4.24\%$ and $92.51 \pm 4.89\%$. Drug loading was between $3.25 \pm 1.04\%$ and $4.85 \pm 0.82\%$ and encapsulation efficacy was in the range from $44.02 \pm 1.80\%$ to $61.07 \pm 2.24\%$. Delayed drug release was observed in all three batches, being more prominent in the batch that was crosslinked with 3% glutaraldehyde solution.

Keywords: *fractional factorial design, casein/fucoidan nanocomposites, polyelectrolyte complexation, spray drying*

Acknowledgements: This research was funded by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria project number BG-RRP-2.004-0007-C01.

CANCER TREATMENT WITH BENZAMIDES: ACHIEVED PROGRESS AND FUTURE PERSPECTIVES

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Introduction: Epigenetic therapy and epigenetic drugs are considered new “nuclear weapons” for different types of cancer. One of the therapeutic approaches for cancer treatment is the inhibition of histone deacetylases (HDACs). Chidamide is the first synthetic histone deacetylase inhibitor (HDACi) that belongs to the class of benzamides. It was approved by drug authorities in China (2014) and Japan (2021) and is currently used for the treatment of peripheral T-cell lymphoma.

Aim: This study was focused on elucidating the current state of knowledge about the potential of benzamides and benzamide derivatives as HDACi. **Materials and methods:** This study was based on a literature survey of publications between 2000 and 2024. We searched the Scopus, Web of Science, and PubMed databases using different combinations of keywords. **Results and discussion:** Our results systemize (a) approved drugs, such as benzamides and their derivatives worldwide; (b) the current status of the ongoing trials; and (c) chemical classification of the benzamide derivatives with potential activity according to the pharmacophoric model. Moreover, different structural factors from enzyme–drug interactions shed light on the important interactions of HDACi–HDACs systems. **Conclusion:** These results can be used as a starting point for a deeper understanding of the molecular mechanisms involved in HDAC inhibition and for the design of new potent and selective benzamide and benzamide derivatives for different types of HDACs.

Keywords: HDACs, HDACi, cancer, benzamides, benzamide derivatives

ARE HERBAL MEDICINES SAFE DURING PREGNANCY AND BREASTFEEDING? – ANALYSIS OF REGISTERED HERBAL MEDICINES IN BULGARIA

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Introduction: Despite being considered natural, herbal medicines may pose risks, especially during pregnancy and breastfeeding, as their safety profile is often not available or incomplete. The pharmacological effects of herbal medicines derive from different biologically active compounds, potentially leading to adverse effects or interactions with commonly prescribed and nonprescription medicines. **Aim:** This study aims to analyze the Summaries of Product Characteristics (SmPCs) of registered nonprescription herbal medicines in Bulgaria, focusing on the information regarding safety during pregnancy and lactation. **Methods:** The list of registered nonprescription medicines in Bulgaria, as of January 24th, 2024, was obtained from the Bulgarian Drug Agency's (BDA) website and analyzed. Herbal medicines were identified from the list, and their respective SmPCs were investigated. Data concerning the effects on human fertility, usage in women of childbearing potential, and specific recommendations for use during pregnancy and breastfeeding were extracted and evaluated. **Results:** A total of 92 nonprescription herbal medicines were included in the BDA list as of January 24th, 2024. Among these, 44.57% were contraindicated (not recommended) for use during pregnancy and breastfeeding, 51.08% lacked sufficient information, and only 4.35% were allowed to be used in these special populations. **Conclusion:** The majority of registered herbal medicines lack comprehensive safety information for pregnancy and breastfeeding. This knowledge gap may contribute to the inappropriate use of these products by pregnant and lactating women and perpetuate the misconception of their absolute safety.

Keywords: pregnancy, lactation, herbal medicines, pharmacovigilance, Summaries of Product Characteristics

RP-HPLC METHOD FOR SIMULTANEOUS DETERMINATION OF PARACETAMOL, DICLOFENAC SODIUM AND OMEPRAZOLE IN TABLET DOSAGE FORM

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Introduction: The combination of analgesics is a strategy to achieve therapeutic goals, such as facilitating patient compliance, simplifying prescribing, etc. Combination of nonsteroidal anti-inflammatory drugs with a proton pump inhibitor omeprazole is beneficial as it suppress gastric acid secretion. **Aim:** The aim of this study is to develop and validate simple, precise and accurate reverse-phase high performance liquid chromatographic (RP-HPLC) method with isocratic elution mode for simultaneous determination of paracetamol, diclofenac sodium and omeprazole in tablet dosage forms.

Materials and methods: The chromatography was carried out on a C18, 250 mm x 4.6 mm, 5 µm column with acetonitrile:water:0.5 triethylamine (85:10:5 v/v/v) as a mobile phase, at a flow rate of 1.0 ml/min, with detection at 240 nm.

Results: This paper described the elaboration of simple and fast analytical procedure for assay of paracetamol, diclofenac sodium and omeprazole in tablets by RP-HPLC. The method was validated for the parameters like specificity, linearity, precision, accuracy, LOD and LOQ. **Conclusion:** The results of the studies showed that the proposed chromatographic procedure is rapid, precise and accurate, which can be applied for the routine assessment of described drugs in tablets.

Keywords: paracetamol, diclofenac sodium, omeprazole, RP-HPLC, validation

CHEMICALLY MODIFIED SYSTEMS FOR DRUG IMMOBILIZATION (REVIEW)

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Introduction: Long-acting drug formulations ensure maintenance of the desired therapeutic concentration in the body for a long period of time. One of the delayed release methods is through immobilized drug delivery systems where the drug substance is included in the polymer chain or linked to it by chemical bonds. **Objective:** Overview of the application of chemically modified systems for the immobilization of drugs. **Materials and methods:** A review of published articles on the subject was performed in Google Scholar, Scopus, Pubmed. **Results and discussion:** In chemically immobilized systems, the release of the drug is the result of the polymer chains depolymerization or the destruction of the bonds between the polymer and the drug. In this connection, the surface of the polymer must be compatible with the drug, and we have different methods of immobilization. It is generally accepted that drugs must possess aldehyde, carboxyl or hydroxyl groups. The use of additional cross-linking agents allows the expansion of the range of chemical groups to be immobilized. Both natural polymers such as chitosan, alginate, dextran and synthetic polymers-polyamides, polystyrene and polyacrylamide can be used as immobilization matrices. Chemically immobilized systems are used as a method for delivering a number of enzymes, antitumor agents, nucleic acids in gene therapy, vaccines into the body. The possibilities of prolonging the release of cytostatics, steroids and other medicinal substances such as ranitidine have also been studied. **Conclusion:** The development of immobilized systems is a promising method for the modified release of drugs but at the same time it creates a number of challenges that can be resolved with further studies.

Keywords: *immobilized systems, polymers*

GREEN SYNTHESIS OF MAGNETIC NANOPARTICLES – PREPARATION AND CHARACTERIZATION

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Green synthesis is an environmentally friendly and cost-effective method for the preparation of nanoparticles with theranostic and multimodal therapeutic applications. This approach is in line with the principles of green chemistry, significantly reducing the environmental impact associated with conventional chemical syntheses. Moreover, it enhances the biocompatibility of nanoparticles, making them more suitable for biomedical applications. The use of natural extracts in the synthesis process not only facilitates the reduction and stabilization of nanoparticles but also introduces functional groups onto their surfaces, enhancing their therapeutic potential. The aim of this study was the preparation of magnetic nanoparticles by reduction of ferrous and ferric ions with plant extract. The synthesized nanoparticles were characterized to determine their size, morphology, and magnetic properties, in addition to verifying the presence of bio-organic compounds from the plant extract on the nanoparticles' surfaces. The results confirm the efficacy of the green synthesis approach in the production of nanoparticles with good magnetic and structural properties, that hold promise for a range of environmental and biomedical applications.

Keywords: *magnetic nanoparticles, green synthesis, IONPs, iron oxide*

BULGARIAN MEDICINAL PLANTS USED IN THE TREATMENT OF DIABETES MELLITUS

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Introduction: Diabetes is a global health problem and the number of diabetic patients is constantly increasing. Conventional antidiabetic therapies are associated with high costs and limited efficiency. They do not help as much as expected and for that reason new compounds with antidiabetic activity are sought. Lately, medicinal substances with natural origin are found out which are with potential to be used for therapy of diabetes. They are most commonly found in plants and their parts. They are not expensive and safer than conventional antidiabetic medications. **Aim:** The aim of this review article is to familiarize with the antidiabetic properties of Bulgarian medicinal plants and their parts used for the preparation of medicinal forms. **Materials and methods:** The survey includes literature available in the databases of PubMed. **Results and discussion:** The subject of consideration in this article are walnut, galega, dandelion, burdock, nettle and garlic. Antidiabetic compounds were found in these plants. Some of them were tested in diabetic rats and they show a good antidiabetic activity. **Conclusion:** Plants are a good source of antidiabetic compounds. They are a new alternative for treatment. However, further studies are needed in order to confirm the antidiabetic potential of these plants

Keywords: *diabetes mellitus, medicinal plants, treatment, bulgarian*

SPECIFIC MARKETING AUTHORIZATION PROCEDURES FOR EARLY ACCESS TO NEW MEDICINES IN EU: A RETROSPECTIVE ANALYSIS (2015–2023)

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Introduction: The European Union (EU) pharmaceutical legislation establishes regulatory mechanisms aimed at facilitating a more flexible and accelerated scientific evaluation process for marketing authorization applications. Early access procedures are designed to expedite access to therapeutic areas with high unmet medical needs or lacking satisfactory treatment alternatives. **Aim:** This study aims to analyze the early access procedures within the EU in terms of quantity and types, and to categorize the medicinal products authorized under these procedures by therapeutic areas. **Materials and methods:** A retrospective analysis of the European Medicines Agency's (EMA) annual reports was conducted for the period 2015 to 2023. Early access procedures were categorized by number and type (conditional marketing authorization, approval under exceptional circumstances, and accelerated assessment). Medicinal products subject to these procedures were further classified by therapeutic areas. **Results:** In the years 2016 and 2017, the largest number of medicinal products underwent accelerated assessment procedures ($n = 7$ for both years). In 2021, the number of medicinal products receiving conditional marketing authorization remained consistent with that of 2020 ($n = 13$). This suggests a growing urgency due to the COVID-19 pandemic and an increased demand for expedited responses to unmet therapeutic needs. Approvals under exceptional circumstances peaked in 2020 and 2022 ($n = 5$ for each year). In 2023, eight medicines were recommended for conditional marketing authorization. Additionally, one medicine was authorized under exceptional circumstances, and three medicines received a recommendation for marketing authorization following accelerated assessment. The primary therapeutic areas in 2023 were oncology, neurology, cardiology, and hematology.

Conclusion: Analysis indicates that medicinal products authorized for early access procedures between 2015 and 2023 predominantly belong to therapeutic areas such as neurology, hematology, endocrinology, oncology, and immunology, reflecting the expansion of these approaches into broader medical fields.

Keywords: EU, EMA, conditional marketing authorization, approval under exceptional circumstances, accelerated assessment

DEVELOPMENT AND CHARACTERIZATION IDEBENONELOADED LIPOSOMES FOR TARGETED DRUG DELIVERY TO THE COLON

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Introduction: Inflammatory bowel disease is a term including two conditions (Crohn's disease and ulcerative colitis), characterized by chronic inflammation of the gastrointestinal tract (GIT). Prolonged inflammations usually result in different GIT damages. Inflammatory bowel disease treatment can be either pharmacological (anti-inflammatory drugs, immune system suppressors, antibiotics, etc.) or non-pharmacological (probiotics, antioxidants, vitamins and supplements).

The aim of this study was to obtain idebenone-loaded liposomes and incorporate them in a gastro-resistant formulation.

Materials and methods: Liposomes were prepared with conventional thin-layer hydration followed by ultrasonication and extrusion to obtain population with an appropriate size.

Liposomes were characterized in terms of size and ζ -potential and were purified from the unentrapped drug using the dialysis method. Furthermore, liposomes were coated, using low molecular weight chitosan, which was cross-linked with glutaraldehyde.

Results and discussion: significant increase in the size of the liposomes was observed, as well as ζ -potential change – from negative to positive which was a sign of the successful coating of the liposomes. *In vitro* drug-release study was performed in a dialysis bag. Based on the obtained results, a promising model of gastro-resistant idebenone-loaded liposomes was selected, for the delivery of idebenone to the bowels.

Keywords: idebenone-loaded liposomes, inflammatory bowel disease, colon drug delivery

Acknowledgements: This research was funded by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria project number BG-RRP-2.004-0007-C01.

LOZENGES WITH MUCOADHESIVE BENZYDAMINE-LOADED LIPOSOMES FOR TREATMENT OF ORAL INFLAMMATIONS

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Introduction: Benzydamine is a widely used nonsteroidal anti-inflammatory drug for treatment of multiple conditions of the mouth and throat. Besides its anti-inflammatory effect, it also possesses anaesthetic and analgesic properties. **The aim** of this study was to formulate and characterize lozenges, containing benzydamine-loaded mucoadhesive liposomes for local treatment of oral inflammations.

Materials and methods: Benzydamine-loaded liposomes were prepared by the ethanol-injection method. Three models were prepared with varying concentrations of phosphatidylcholine, cholesterol and Kolliphor p188. Furthermore, the liposomes were purified from the unentrapped drug, using the dialysis method. Liposomes were characterized in terms of particle size, shape, drug loading and encapsulation efficiency using laser diffraction scattering, scanning electron microscopy and UV-vis spectroscopy. Optimal model was selected based on morphology and maximum encapsulation efficiency. Subsequently, liposomes were coated with sodium alginate in concentration 0.25%. Coated liposomes were lyophilized using mannitol as cryoprotectant and included in lozenges by tabletting. **Results and discussion:** Obtained tablets were characterized in terms of their pharmacopoeial control parameters – uniformity of mass, mechanical strength and friability. The produced tablets were at an average weight of 0.500 g. They showed relatively high mechanical strength and low friability index. *In vitro* release study was performed using dissolution tester, paddle type with modifications and sustained drug release was observed. Obtained data demonstrate that the proposed model tablets can be considered as an enhanced drug delivery system, with improved properties, providing mucoadhesion and sustained drug release for the effective treatment of oral and throat inflammations.

Keywords: mucoadhesive liposomes, oral inflammation, lozenges

Acknowledgements: This research was funded by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria project number BG-RRP-2.004-0007-C01.

A COMPARATIVE ANALYSIS OF PHARMACEUTICAL CARE EDUCATION IN BULGARIA AND FRANCE

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Introduction: Pharmaceutical care is now recognized as an indispensable aspect of pharmacy practice. To ensure pharmacists can effectively fulfil their primary mission, pharmacy students must acquire theoretical knowledge, practical skills, and competencies. Across many European countries, pharmaceutical care has been successfully integrated into pharmacy curricula for over two decades. **Aim:** This study aims to compare the pharmaceutical care courses at the Faculty of Pharmacy, Medical University of Plovdiv, Bulgaria, and the Faculty of Pharmacy, Aix-Marseille University, Marseille, France. **Materials and methods:** The curricula of the faculties of pharmacy at the Medical University of Plovdiv, Bulgaria, and Aix-Marseille University, Marseille, France, were analyzed and compared. Our research focused on the pharmaceutical care syllabi, types of theoretical and practical classes offered, and teaching and evaluation methods employed. **Results:** Pharmaceutical Care is a compulsory course studied in the 8th semester of the fourth year of the pharmacy curriculum at the Faculty of Pharmacy, Medical University of Plovdiv. Teaching and evaluation methodologies include brainstorming, clinical case-solving, and role-plays. In France, there are two disciplines equivalent to Pharmaceutical Care. Teaching methods encompass problem-based learning, e-learning, clinical case-solving, and self-training through viewing recorded cases. **Conclusion:** There are both similarities and differences in pharmaceutical care education between Bulgaria and France. While France offers two distinct classes for this discipline compared to one in Bulgaria, the pedagogical approaches vary. Nonetheless, both disciplines strive to provide accurate knowledge to pharmacy students.

Keywords: Bulgaria, France, pharmaceutical care, pharmacy education

NASAL NANOCOMPOSITE MICROSPHERES FOR TARGETED DRUG DELIVERY TO THE BRAIN

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Introduction: The development of nanocomposite microspheres with optimal bioadhesive and biopharmaceutical properties is a technological challenge, the successful implementation of which is a prerequisite for the creation of an innovative and easy-to-use drug delivery system for nasal administration of drugs. **The aim of the study:** Development of nanocomposite microspheres as a model drug delivery system with potential for targeted delivery of idebenone in the central nervous system. **Materials and methods:** Emulsion solvent evaporation method was used for nanoparticles preparation. Three models of Idebenone-loaded nanoparticles were developed and the influence of molecular weight on entrapment efficiency was investigated. The model with the highest entrapment efficiency was incorporated into sodium alginate microspheres obtained by spray drying. The biopharmaceutical behavior and biological activity of idebenone included in nanocomposite microspheres was investigated. **Results and discussion:** The composite structures ranged in size from $6.05 \pm 1.78 \mu\text{m}$ to $7.37 \pm 2.4 \mu\text{m}$, suitable for nasal administration. Incorporation of Idebenone in composite microspheres did not result in a change in its antioxidant activity. A synergistic effect was found in the antioxidant activity of idebenone and sodium alginate. Drug release from the composite structure was delayed compared to the release from the nanoparticles. **Conclusion:** The applied emulsion/solvent evaporation technique and spray drying are suitable for obtaining idebenone-loaded nanocomposite microspheres with optimal size for nasal administration. There are no chemical interactions between the drug and the polymers and that indicates their compatibility.

Keywords: nanocomposite microspheres, idebenone, nasal administration

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IV. Therapeutic Session

DRUG APPROACH IN POST-COVID HIGH-GRADE VENTRICULAR ARRHYTHMIAS – A CASE REPORT

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A 50-year-old man who, 6 years ago, due to hypertrophic cardiomyopathy with obstruction and severe mitral regurgitation with normal coronary anatomy, underwent volume surgery-resection of the interventricular septum a modo Morrow and mitral valve prosthesis with Carbomedics 29. All the time he was taking 2.5 mg Bisoprolol and 49 monotopic ventricular extrasystoles for 24 hours. 1 year ago, the patient experienced a moderate-severe COVID-19 viral infection. A few weeks later, an arrhythmia debuted – 8,447 ventricular extrasystoles – monotopic, 114 ventricular couplets, 25 ventricular volleys, 3 episodes of ventricular tachycardia. Therapeutically, Bisoprolol, Sotalol, Amiodarone without and with Bisoprolol, Mexitil are used without effect. Due to resistance to the therapy, an adreno-magnetic resonance of the heart was performed with the aim of ablating the focus responsible for the ventricular arrhythmias – limited areas of fibrosis in the depth of the basal septum and in the lateral wall of the left ventricle subepicardial – of a non-ischemic type. In the desperate search at that time for a medicinal solution, the classic in beta blockers was included as an antirhythmic effect – Propranolol in a gradual increase in the dose up to 3 times of 40 mg. In a few weeks, the ventricular rhythm disturbances were reduced to physiological ones. And for several months, the patient is again on 5 mg Bisoprolol. Post-covid fibrosis appears to be no less a risk factor for ventricular arrhythmias than heart surgery. Despite the availability of many antiarrhythmic drugs such as Propranolol should not be neglected with his membrane-stabilizing effect.

Keywords: *cardiomyopathy, arrhythmia, Propranolol, antiarrhythmic drugs, ventricular arrhythmias*

ADMINISTRATION OF BOTULINUM TOXIN FOR A PATIENT WITH RAYNAUD'S SYNDROME: A CASE REPORT

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Raynaud's syndrome is a paroxysmal vasospastic disorder of the digital arteries after exposure to cold or stress. It manifests with pain, swelling, stiffness, and hypesthesia. Severe manifestations are associated with the appearance of trophic ulcers. The criteria for primary Raynaud's syndrome include attacks of peripheral vascular vaso-spasm caused by cold or stress, symmetrical engagement of both hands, lack of tissue necrosis or gangrene, absence of another main disease, normal findings of capillaroscopy and etc. The most common indications for administration of botulin toxin include focal dystonias, spastic increased muscle tone with contractures in central hemi- and paraparesis in stroke, multiple sclerosis, brain injuries, treatment of pain, involuntary muscle hyperactivity of a non-dystonic character, in strabismus and nystagmus and aesthetic medicine. We report a clinical case of a 48-year-old female patient with Raynaud's syndrome. We have placed 70E, distributed to both hands 35E Botulin toxin Type A "Xeomin". Improvement was noticed on day 3, with the warming of the hands, without swelling and pain with duration of the effect over 3 months.

Keywords: Case report, botulinum toxin, raynaud's syndrome, toxin

UNILATERAL PARALYSIS OF THE ABDUCENS NERVE AS AN ISOLATED MANIFESTATION OF CEREBRAL VENOUS SINUS THROMBOSIS

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Introduction: Cerebral venous sinus thrombosis (CVST) is a rare condition characterized by obstruction of cerebral venous sinuses. While common symptoms include headache, encephalopathy and seizures, diplopia is unusual. **Case presentation:** We report a case of a 17-year-old boy with isolated unilateral abducens nerve palsy as a sign of CVST. The patient presented with bitemporal headache, vomiting, and subsequent left-eye curvature, double vision, and blurred vision. Neuroimaging revealed partial thrombosis of the superior sagittal sinus and loss of blood flow in draining veins. Papilledema was observed and the thrombophilia panel showed elevated homocysteine due to androgen intake. The application of an increased dose of Clexan, vitamin B6, B12 and folic acid led to a complete reverse development of the clinical symptoms (including papilledema) and a significant improvement in the results from the neuroimaging after 3 months from the start of the treatment. **Conclusion:** Unilateral abducens nerve palsy in CVST is rare, emphasizing the need to consider it in the differential diagnosis. Neuroimaging plays a crucial role in diagnosis, and risk factors such as homocysteinemia and androgen intake should be assessed.

Keywords: *Cerebral venous sinus thrombosis, unilateral abducens nerve palsy, diplopia, homocysteinemia, androgen intake*

HOMEOPATHY – A SUCCESSFUL APPROACH TO SEASONAL ALLERGIES (REVIEW)

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Introduction: Allergy is the fourth chronic disease according to the WHO. By 2050, 50% of the population will suffer from at least one type of allergy. Between 20% and 30% of the population in each country is affected by hay fever (according to WHO data). 20% of the population in Bulgaria suffers from this problem. **Objective:** Overview of the application of homeopathic remedies in the therapy of seasonal allergies.

Materials and methods: A review of published articles on the topic in the Google Scholar, Scopus, Pubmed databases was performed.

Results and discussion: In search of effective and maximally sparing therapeutic methods, the contribution of homeopathy to control, treatment and prevention is confirmed by a number of studies. In this review we will consider the practical benefit of knowing and applying this therapeutic method as an independent or complementary to the main treatment. Studies have shown the advantages of homeopathic remedies compared to conventional allergic rhinitis therapy. Homeopathic Medications demonstrate a particularly pronounced effect on the symptoms of allergic rhinitis, especially on nasal obstruction. Management of hay fever with homeopathy should begin about a month before the usual manifestation of the disease. Homeopathic treatment can be symptomatic, pathogenetic and terrain. Among the most commonly used preparations are Poumon histamine, Apis mellifica, Pol-lens, Allium cepa, Nux vomica and others. **Conclusion:** The knowledge and proper application of homeopathy in allergic rhinitis can improve the quality of life and be successfully included in prevention and therapy without the risk of side effects and contraindications.

Keywords: *seasonal allergies, homeopathy*

CONCOMITANT JAK-2 AND BCR-ABL1 EXPRESSION IN A PATIENT WITH CHRONIC MYELOID LEUKEMIA. CLINICAL EVOLUTION AND CARDIAC IMPACT

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Introduction: Double expression of Philadelphia chromosome and JAK-2 mutation in chronic myeloid leukemia (CML) patients is an uncommon condition. Little is known about the clinical evolution, best treatment modalities and the outcome of these patients. On the other hand, JAK2V617F mutation alters endothelial function and promotes a large spectrum of cardiovascular complications.

Case presentation: We present a case of a 63 years old male patient diagnosed with CML in 2017 with hyperleukocytosis, left shift, splenomegaly and Philadelphia chromosome transcripts. Standard therapy with Imatinib was initiated, but in 1-year suboptimal molecular response was registered. Therapy was switched to second – generation TKI – Nilotinib. In 2021 while in MMR 5.0 log, patient manifested headache and arterial hypertension. Lab tests showed significantly elevated Hb, Ery, Hct and PLT while WBC and Differential formula were within normal ranges. Molecular tests proved JAK-2 mutation. Because of hypertension and arrhythmia, the patient was admitted in the Cardiology department. Arterial hypertension, ischemic heart disease, tachyfrequent atrial fibrillation, conduction disturbances, high grade aortic valve stenosis and multiple occlusions of peripheral vessels were found. TAVI was performed along with antihypertensive and anti-arrhythmic therapy. Nilotinib was replaced by Bosutinib to reduce cardiotoxicity. Currently patient is still in MMR 5.0 log, but JAK-2 mutant allele burden is increasing, and cardiovascular diseases is dominant.

Discussion and conclusion: There are no therapeutic standards for CML double positive for M-BCR-ABL and JAK-2. An unsolved problem is the impact of JAK-2 mutation on cardiovascular system.

Keywords: CML, JAK-2 mutation, cardiovascular complications

LEFT VENTRICULAR NONCOMPACTI ON CARDIOMYOPATHY IN COMBINATION WITH ATRIAL SEPTAL ANEURISM AND DEFECT – BETTER OR WORSE?

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Introduction: Left ventricular noncompaction cardiomyopathy (LVNC) can occur in isolation or coexist with other cardiac and/or systemic anomalies. **Aim:** We describe the case of a woman who presented with heart failure for the first time at 42 years of age. **Material and methods:** The diagnosis was LVNC. Transthoracic echocardiography showed a trabeculated, sponge-like appearance of the ventricular apical and inferolateral segments as well as atrial septal aneurism in combination with atrial septal defect (ASD) and left to right shunt.

Results and discussion: After guideline based titrated medical management of heart failure, the patient was asymptomatic at follow-up examinations. The closure of the ASD was discussed. A decision for preserving the restrictive, left-to-right shunt as a natural method to reduce the degree of left atrial hypertension was made. We believe that left atrial decompression improves the atrioventricular interaction and global hemodynamic function. Reducing left atrial pressure and enlargement may be the answer why the incidence of atrial fibrillation is influenced, too. In addition, secondary pulmonary hypertension should be reduced by direct impact on the pulmonary congestion. In **conclusion** the case of LVNC in combination with atrial septal aneurism and ASD is a model of natural hemodynamic compensation of heart failure.

Keywords: *noncompaction cardiomyopathy, atrial septal defect, treatment*

THE IMPACT OF ASBESTOSIS ON WORKERS' HEALTH – A CLINICAL CASE

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Introduction: We want to present a clinical case of a 76-year-old patient diagnosed with Asbestosis. More than 40 years ago he practiced a occupation related to asbestos exposure. The diagnosis was made 20 years after cessation of occupational contact with asbestos. The respiratory symptoms were triggered unexpectedly and cannot be linked to another lung disease. The progression of symptoms worsened the patient's quality of life. **Goal:** The aim is to raise awareness about the risk factors from the work environment. A purposefully taken occupational history could guide the diagnostic thinking of general practitioners towards the early diagnosis of this type of pneumoconiosis. **Materials and methods:** To describe this clinical case, the data from the patient's medical documentation and the results of functional and imaging lung tests were used. **Results and discussion:** Patients and doctors underestimate the importance of occupational history. They might not have information about the risk factors in the different occupations. The patient presented by us was in this situation. He didn't have information or suspected that the production activity he was performing was risk factor for his health. Exposure to asbestos, even after cessation can trigger a severe lung disease that significantly worsens the quality of life of the patients. **Conclusion:** Information about the occupational route and a targeted occupational history are of key importance for the diagnosis and prevention of dust lung diseases. They contribute to the early and accurate diagnosis of pneumoconiosis and can improve the quality of life of those affected.

Keywords: *occupational disease, asbestosis, risk factors*

TRAIT MINDFULNESS AND THE EXPERIENCE OF STUTTERING

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Introduction: Mindfulness-based interventions are increasingly recommended as part of a comprehensive stuttering treatment despite the gap in the literature regarding the trait mindfulness of people who stutter and potential effects on stuttering treatment response. **Aim:** To determine levels of trait mindfulness in people who stutter and compare to people who do not stutter to understand whether or when mindfulness-based interventions may be appropriate as part of a comprehensive stuttering treatment program. Additionally, relationships among characteristics of stuttering (i.e., experiential avoidance, repetitive negative thinking, inattention characteristics) and trait mindfulness were explored to provide evidence for efficacious and individualized stuttering treatment options. **Materials and methods:** Seventeen adults who stutter and 17 adults who do not stutter completed the Five Facet Mindfulness Questionnaire (FFMQ) to measure trait mindfulness to accomplish the first research aim. A subset of 16 adults who stutter from the first aim took an online battery of assessments related to characteristics of stuttering to accomplish the second research aim.

Results and discussion: People who stutter did not differ significantly in their total FFMQ scores compared to people who do not stutter. The strongest associations were found between trait mindfulness and experiential avoidance, suggesting the potential benefits of a non-avoidance approach in stuttering therapy. **Conclusions:** These findings suggest the critical examination mindfulness-based interventions for people who stutter. This also suggests the necessity to comprehensively understand the characteristics of stuttering specific to the client and how those contribute to their overall experience of stuttering.

Keywords: *mindfulness, experience of stuttering, experiential avoidance*

A PATIENT WITH THREE METACHRONOUS CANCERS OCCURRING OVER A PERIOD OF THREE YEARS AND THE CLINICAL IMPORTANCE OF INVESTIGATING POTENTIAL NEOPLASTIC GROWTH DURING FOLLOW-UP

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Thanks to increased survival rates in patients bearing oncological malignancies due to recent developments in anti-cancer therapies and diagnostic techniques, observation of clinical cases of metachronous cancers is more common and can provide more in-depth knowledge of their development and, as a result, help clinicians apply suitable therapy. This unusual case of three metachronous tumors presented the opportunity to follow their occurrence, progression, and treatment thoroughly. A 77-year-old male presented with carcinoma ventriculi of the pylorus region, which was surgically removed via subtotal stomach resection and subsequent treatment and dynamic follow up at an oncologic ward, until a CT scan revealed a new neoplastic growth suspicion in the area of the urinary bladder which was later histologically confirmed. Following yet another radical treatment, the patient was, once again, dynamically monitored in an oncology ward with regular CT scans and tumor markers. However, elevated tumor markers prompted a PET/CT scan, which was indicative of a new neoplastic growth in the region of the stomach cardia. It was diagnosed as an adenocarcinoma infiltrating the esophagus. After biopsy, the histology showed that while similar to the first gastric neoplasm, it was, once again, a different primary tumor site. In conclusion, this case report highlights the importance of patient follow-up and studying recurring neoplastic growth. Despite the absence of symptoms, clinicians should maintain a high level of suspicion when evaluating the patient data and choosing the most suitable therapy.

Keywords: carcinoma, follow-up, metachronous, neoplastic growth, recurrence

A CLINICAL CASE OF ISOLATED RIGHT-SIDED INFECTIVE ENDOCARDITIS

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Introduction: Right-sided infective endocarditis (IE) accounts for 5% to 10% of all cases and is most commonly associated with intravenous drug use, intracardiac devices, and central venous catheters, which have become increasingly used in recent years. Isolated right-sided IE in the absence of the mentioned predisposing factors is extremely rare. **Objective:** To describe a clinical case of isolated right-sided IE in the absence of usual predisposing conditions. **Material and methods:** We present a 72-year-old man with a history of recurrent fever of 2–3 months, despite several courses of antibiotic treatment, with a typical inflammatory laboratory constellation. With suspicion of IE, he was admitted to the Cardiology Clinic for clarification. **Results:** Laboratory data revealed inflammation and anemia. X-ray showed evidence of bilateral pulmonary infiltrative changes and pleural effusions. Transthoracic echocardiography visualized a large and mobile vegetation of the tricuspid valve, with severe regurgitation. *Staphylococcus aureus* was isolated from blood cultures. A definite IE of the tricuspid valve was diagnosed. With an indication for early surgical treatment, the patient underwent surgery and prosthetics with a biological tricuspid valve prosthesis. Intraoperatively, a perimembranous ventricular septal defect was diagnosed and corrected. Postoperatively, another 30 days of antibiotic treatment was administered. **Discussion:** Clinical suspicion is key to making the diagnosis of IE and choosing the most appropriate therapeutic strategy. The presence of a congenital heart malformation with a left-to-right shunt explains the unusual isolated right-sided involvement. **Conclusion:** In cases of isolated right-sided IE, the possibility of congenital heart disease with left-right shunt should be considered.

Keywords: right-sided IE, congenital heart disease, diagnostics

TREATMENT STRATEGY IN A RANDOM HEART FAILURE PATIENT – IT IS ALWAYS A CHALLENGE!

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Introduction: Treatment of heart failure with reduced ejection fraction (HFrEF) has been clearly defined in recent international guidelines. Official recommendations do not fully address every possible scenario in real clinical practice. **Aim:** We describe the case of a 58 years old male patient referred for a cardiology consultation before cataract surgery after an ECG. **Material and methods:** Transthoracic echocardiography showed a dilated, remodeled left ventricle, with segmental wall motion abnormalities and severe mitral regurgitation. Coronary angiography revealed chronic occlusion of right coronary artery and stenosis of circumflex artery. At that stage a referral for cardiac surgery was done and the patient asked for second opinion. Cardiac magnetic resonance was used for assessment of myocardial viability. **Results and discussion:** After heart team discussion a strategy for guideline based titrated medical management of heart failure was chosen. The patient was asymptomatic at follow-up examinations. The full spectrum of guideline recommended treatment was introduced. A two stage percutaneous revascularization was undertaken. After two months of follow-up the patient was in stable sinus rhythm, with improved left ventricular function and mitral regurgitation. **Conclusion:** In complex cases with secondary mitral regurgitation, decision-making isn't always straightforward. The Heart Team is essential to determine the best individualized management, starting from optimized pharmacological evidence based treatments.

Keywords: HFrEF, secondary mitral regurgitation, treatment

CONTAINED RUPTURE OF THE THORACIC AORTA MIMICKING MEDIASTINAL MALIGNANCY: A CASE REPORT

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The rupture of an aneurysm of the thoracic aorta (TAA) is a rare life-threatening emergency with a high mortality rate if the condition is not promptly diagnosed and treated. In a classic aortic rupture scenario the tearing or bursting of the aorta leads to massive internal bleeding, causing a sudden drop in blood pressure and rapid hemorrhagic shock. In this paper we present a rare case of a 71-year-old male patient with back pain and peripheral edema. Computed tomography (CT) images were taken and a posterior mediastinal mass measuring 8.5 cm x 6.1 cm, that was compressing the esophagus, was found. The boundaries between the tumor and the aortic structures were hard to discern. The differential diagnosis included lymphoma, sarcoma or a primary esophageal tumor. Contrast-enhanced CT revealed a contained rupture of the thoracic aorta, limited by surrounding structures and a thrombotic sheath, which explained the stable hemodynamics of our patient. This rare case underscores the importance of considering aortic pathology, specifically the possibility of a contained rupture, in patients with atypical mediastinal masses. We emphasize the role of contrast-enhanced CT and demonstrate that the awareness of this rare condition is crucial for accurate diagnosis and appropriate management.

Keywords: Contained rupture, thoracic aorta, mediastinal mass, aortic pathology

V. Somnology Session

OBJECTIVE POLYSOMNOGRAPHIC PARAMETERS INCOMPLETELY REPRESENT SUBJECTIVE IMPROVEMENT IN PATIENTS WITH SLEEP BRUXISM TREATED WITH BOTULINUM TOXIN – TWO CASE REPORTS

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Introduction: Local administration of botulinum toxin A (BTX) is a novel therapeutic approach for patients with sleep bruxism, but data on its clinical efficacy and effects on various sleep parameters remain obscure. **Aim:** This report compares the objective changes in sleep structure and bruxism intensity with the subjectively reported improvement of sleep quality and daily symptoms after administration of BTX.

Materials and methods: Two female patients, aged 45 and 28, presented with complaints of morning headache, jaw stiffness and teeth clenching. They underwent unattended, homebased polysomnography and were diagnosed with sleep bruxism. Patient one had bruxism index (BI) of 8.4/h and patient two – BI of 3.3/h. Sleep structure was mildly impaired in both with decreased REM – sleep percentage. Local injection of 30 units BTX in each masseter muscle and 20 units in each temporal muscle was applied, followed by additional polysomnographic evaluation thirty days after treatment. **Results and discussion:** Albeit both patients reported significant improvement regarding complaints and sleep quality, the objective measurement showed improvement only for patient 1 (posttreatment BI = 4.3/h). Considerable aggravation was found for the second patient with BI increasing to 4.6/h. However, sleep architecture was restored in both patients with REM stage normalization. **Conclusion:** The following report indicates that standard objective sleep measurements are insufficient to assess the positive clinical outcome in patients with sleep bruxism. Further investigation is needed to evaluate the benefits of the treatment.

Keywords: *sleep bruxism, botulinum toxin, polysomnography*

REM BEHAVIORAL DISORDER IN DRUG NAÏVE PATIENT WITH PARKINSON'S DISEASE – A CASE REPORT

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Introduction: In contrast to most neurological disorders, prodromal markers of Parkinson's disease (PD) exhibit remarkably variegated array, which also includes Rapid Eye Movement Behavioral Disorder (RBD). **Aim:** This case report aims at exemplifying the profile of a drug naïve PD patient who manifests with RBD and commenting on the distinct polysomnographic findings. **Materials and methods:** A 71-year-old male patient presented with symptoms highly indicative of PD. He was evaluated using the Unified Parkinson's Disease Scale (UPDRS), Montreal Cognitive Assessment Test (MOCA) and Parkinson's Disease Sleep Scale (PDSS). Due to complaints of vivid dreams and dream enactment, the patient underwent full unattended home-based polysomnograph (PSG), following approved RBD protocol.

Results: The patient scored 2 points on Part I, 6 points on Part II, 13 points on part III of UPDRS, on MOCA test – 22 points and 6 points on PDSS. The PSG findings revealed decreased sleep efficiency – 70.2% and impaired sleep macroarchitecture with REM percentage of 18.7%. Although the periodic leg movements (PLM) index was notable at 16.9/h, the arousal index was 13.5/h with only 2.7/h associated with PLM. There was no indication for clinically relevant respiratory events. Supporting the diagnosis of RBD was the absence of REM atonia.

Conclusion: The presence of RBD not only antedates the development of PD, but also remains clinically relevant sleep disturbance in patients after diagnosis. Moreover, RBD persists as an unexploited prodrome that can delineate the population at risk for PD as well as be a potential indicator of disease-modifying therapy.

Keywords: *REM behavioral disorder, drug naïve PD, polysomnography*

THE MULTIFACETED PERTURBATION IN THE NEUROTRANSMISSION OF RESTLESS LEGS SYNDROME – A CONCISE REVIEW

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Introduction: The pathophysiological intricacy of restless legs syndrome (RLS) unambiguously manifests both in the diverse but apparently disconnected treatment strategies and the response to them. The pathogenesis involves a multilayered interplay of neurotransmitters in the striatum. **Aim:** This review explores the contemporary putative relationships in the dynamics of four major neurotransmitters (dopamine, glutamate, opioids, adenosine) and their receptors in RLS pathogenesis. **Material and methods:** A structured search was conducted in the database of PubMed and Web of Science. The following keywords were applied: “restless legs syndrome”, “neurotransmission” and “striatum”. We included articles published in the last ten years to provide an organization of the current state of knowledge. **Results and discussion:** Advances in the understanding of the pathogenesis in RLS suggest that the observed striatal presynaptic hyperdopaminergic state is secondary to a striatal hyperglutameric state, induced by brain iron deficiency. Moreover, at the level of the synaptic interface in the striatopallidal and striatonigral neurons exist interaction and heteromerization of specific subtypes of adenosine and dopamine receptors (D1R, D2R). Recent evidence established the efficacy of a blocker of the adenosine reuptake transporters in alleviating subjective symptoms and objective findings and thus further confirmed the presence of adenosine dysfunction in RLS. Additionally, μ -opioid receptor (MOR) agonists are known to mitigate symptoms in treatment-resistant patients or in those with augmentation. Striosomal D1R-MOR heteromers are speculated to be the substrate for this response. **Conclusion:** Integration of the proposed pathogenetic hypotheses could provide a convergence toward a unified understanding of RLS occurrence and development.

Keywords: *restless legs syndrome, neurotransmission, striatum*

THE ROLE OF MELATONIN IN HAIR LOSS

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Introduction: Until recently, melatonin has been considered a hormone regulating the circadian day-night rhythm. However, it modulates hair follicle growth and pigmentation. Anagen hair follicles are important sites of extrapineal melatonin synthesis. Melatonin is suggested to play a role in hair-cycle control and to down-regulate both apoptosis and estrogen receptor expression. **Aim:** To make a review of literature on the topic of the role of melatonin in hair loss. Materials and methods: We searched through PubMed and Google Scholar publications using the following keywords: "melatonin", "hair loss". A total of 54 publications published between 1988 and 2024 were reviewed. **Results and discussion:** A total of 9 studies were selected, with evidence of melatonin use in subjects with different types of hair loss. Most studies reported improved scalp hair growth, density, and hair shaft thickness among melatonin users. Topical melatonin dosage is 0.0033% or 0.1% solution/once-daily for and 1.5 mg twice-daily oral melatonin supplementation. It is suggested that melatonin plays a role in hair cycle regulation, because hair follicle is extrapineal melatonin source and peripheral melatonin target tissue. The intrafollicular melatonin synthesis and signaling is suspected to control endogenously hair growth by keratinocyte apoptosis modulation and by desensitizing the follicle to estrogen signaling. Melatonin may also counteract testosterone-induced cell actions. **Conclusion:** There is evidence to support melatonin use for hair growth, in people with hair loss conditions. Further studies should include more patients and investigate the mechanism of action.

Keywords: *melatonin, hair loss, alopecia, androgenetic alopecia, trichology*

DOES SIZE MATTER IN SLEEP? COMPARING ONE NIGHT TO TWO NIGHTS RECORDINGS OF BREATHING DURING SLEEP IN THEIR CAPACITY TO DIAGNOSE AND GRADE SLEEP APNEA – A PILOT STUDY

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Introduction: Out-of-center sleep tests (OCSTs) were included as a possible option for measuring the number of events per hour of recording in the diagnostic criteria for obstructive sleep apnea. OCSTs are often prone to give false negative or false positive results due to poor signal quality and inability to measure total sleep time accurately.

Aim: The aim of this study was to test whether OCST in two consecutive nights can lead to greater reliability in diagnosis and severity grading. **Materials and methods:** We analyzed 20 OCST recordings performed in two consecutive nights in patients with high pre-test risk for obstructive sleep apnea. Signal quality and polygraphic variables as apnea/hypopnea index (AHI) were measured after manual scoring of both nights. Results from the first night were compared to the second night and also to the mean values of the two nights taken as a whole. Difference in indexes greater than 10 was considered significant. **Results:** In most studies ($n = 12$) first night results were comparable to second night results in terms of diagnostic capacity for obstructive sleep apnea (AHI) and signal quality. Mean results for the two nights taken as a whole were comparable to the first night results in 14 recordings. There was no missed diagnosis from the first night in all 20 recordings. Improper severity grading might appear with only one-night of OCST. **Conclusion:** Longer recordings of breathing during sleep with OCST might lead do better severity grading in obstructive sleep apnea, but it's not changing the true-positive rate.

Keywords: OCST, AHI, sleep apnea, diagnostics

AT-HOME VERSUS IN-LAB MULTIPLE SLEEP LATENCY TEST IN DIAGNOSING NARCOLEPSY – A PILOT STUDY

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Introduction: In-laboratory multiple sleep latency test (MSLT) is the main instrumental test to diagnose narcolepsy according to the criteria of the International Classification of Sleep Disorders. Nevertheless it has variable normative values, a high false negative results rate and hard to perform, time-consuming protocol. **Aim:** The aim of the study was to compare results between standard in-lab MSLT and a new ambulatory MSLT protocol using a self-applied polysomnographic device in 5 patients diagnosed with narcolepsy type 1 (NT1). **Materials and methods:** Five treatment naïve patients (3 females) diagnosed with NT1 by a standard protocol with 1 week actigraphy, 1 night of polysomnography and a MSLT were tested with a new ambulatory protocol with 1 week of actigraphy, 2 nights of home polysomnography and an at-home MSLT using a Nox A1 Self-applied somnography (SAS) device. Mean sleep latency and number of sleep-onset REM periods (SOREMPs) were measured by both MSLT protocols and results were compared. Actigraphy and polysomnography variables were also compared between protocols in all patients. **Results:** Studied patients (mean age 37.4) had comparable results from in-lab and at-home MSLT in terms of mean sleep latency and number of SOREMPs, both tests confirming unequivocally their diagnosis. No major mistakes were encountered from the self-appliance of the SAS device, except for one patient not being able to start the recording and needing to repeat the test. All patients reported better comfort with the ambulatory test. **Conclusion:** At-home self-applied MSLT give comparable results to standard in-lab MSLT for diagnosing narcolepsy.

Keywords: MSLT, polysomnography, narcolepsy

A DREAM COME TRUE – EFFECTS OF MONO- AND COMBINATION THERAPY WITH SODIUM OXYBATE AND PITOLISANT IN SIX BULGARIAN ADOLESCENTS WITH NARCOLEPSY TYPE 1 – A SINGLE CENTER EXPERIENCE

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Introduction: Sodium Oxybate (SO) and Pitolisant are considered first line treatment for patients with narcolepsy type 1 (NT1) by current European guidelines. Both drugs are not imported in Bulgaria. **Aim:**

The aim of this study is to share a single center experience with SO and Pitolisant treatment of six Bulgarian adolescents with NT1. **Materials and methods:**

Six patients (2 males) in adolescence were prescribed SO and Pitolisant. All of them received SO for a period of time. Two patients were also prescribed Pitolisant as second medication. All patients had initial assessment by Epworth sleepiness scale (ESS) and actigraphy when they were diagnosed. A second assessment was made when they have reached therapeutic dose of the medications. ESS score and actigraphy variables (mean sleep efficiency, mean sleep latency, inter-daily variability, etc.) were compared before and after treatment. **Results:** All patients (mean age 15 years) received SO. Dose was titrated gradually to 6–7 grams per night. Four patients received SO for more than 1 year. The other 2 patients have stopped SO due to Health Insurance reimbursement issues. Five patients had a marked improvement in ESS score and actigraphy variables when they have reached therapeutic dose and the effect was sustained in time. One patient had no improvement. Two patients had Pitolisant added to treatment with SO. They have shown greater improvement compared to the patients on monotherapy. **Conclusion:** First line treatment of NT1 with SO and Pitolisant in Bulgaria is possible and leads to a marked improvement in patient's condition.

Keywords: Narcolepsy, Sodium Oxybate, Pitolisant, Adolescent

SELF-REPORTED SLEEP DURATION AND SLEEP QUALITY AMONG BULGARIAN ADULTS – A POPULATION-BASED CROSS-SECTIONAL STUDY

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Introduction: Information from population-based studies, focused on sleep quality and quantity, can be a useful tool when evaluating well-being and quality of life and could propose an approach in developing strategies for improvements in general health. **Aim:** The present study investigates self-reported sleep quality and duration among Bulgarian adults. **Materials and methods:** The study was conducted by a marketing research agency via an online survey platform among a sample of 600 adults aged 25 to 55, living in cities with a population of over 50,000 people and having internet access. The respondents filled out online questionnaires. Correlation analysis, T-test, ANOVA and post-hoc analyses were applied to analyze the results. **Results:** Over 70% of the respondents reported experiencing sleep problems with 72% having at least one awakening per night. The average sleep duration on business days is 6 h and 45 min, as opposed to the desirable of 8 h and 20 min. Self-defined “poor sleepers” showed higher levels of worry and anxiety compared to self-defined “good sleepers” ($p < 0.001$). People with body mass index (BMI) over 30 complain more of daytime sleepiness, sleep fragmentation and snoring, compared to those with $BMI < 25$ ($p < 0.001$). The “bad sleepers” tend to have adopted more improper behaviors before sleep in contrast to “good sleepers” ($p < 0.001$). **Conclusion:** Despite the limits of the survey, it confirms the presence of expected associations between impaired sleep quality, mood disturbances, daytime consequences and BMI. Expansion of the targeted population would provide foundations for improving awareness and structuring proposals for health policies.

Keywords: *sleep quality, sleep duration, population-based study, Bulgarian population*

HYPNIC HEADACHE

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Introduction: The relatively new delineation of the hypnic headache as separate nosological entity combined with its low prevalence renders it mostly obscure and underrecognized by physicians. It is characterized by attacks occurring exclusively during sleep, leading to awakenings and subsequently reduced sleep quality. **Aim:** The aim of this report is to underscore the need for heightened clinical suspicion and comprehensive evaluation to differentiate hypnic headache from other primary and secondary headache disorders. **Materials and methods:** A 42-year-old woman, previously diagnosed with migraine, presented with complains of multiple nighttime awakenings, accompanied by headache, at regular intervals of 90 minutes, nonrestorative sleep and snoring and witnessed apneas. She took up to 4 pills of non-steroid anti-inflammatory drug per night with limited effectiveness. A full unattended polysomnographic study (PSG) was performed. **Results and discussion:** The PSG data interpretation excluded the presence of sleep apnea. The patient-reported timing of the headaches coincided with REM episodes, which, added to their characteristics, were indicative of hypnic headache. The diagnosis was supported “ex juvantibus” by excellent response to caffeine treatment. Hypnic headache is not characterized by daytime episodes; therefore, we presume an overlap between hypnic headache and migraine in that case. **Conclusion:** The differential diagnosis of hypnic headache entails meticulous exclusion of secondary causes and consideration of overlapping features with other primary headache disorders. Despite the limited evidence-based guidelines for its treatment, the proposed therapeutic approach diverges from that of other types of headaches.

Keywords: *hypnic headache, sleep, primary headache*

VI. Public Health and Health Management Session

THE ROLE AND IMPACT OF TELEMEDICINE IN REINVENTING HEALTHCARE MANAGEMENT

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Introduction: Telemedicine has the potential to improve healthcare access and streamline physicians' workload. Despite its increased use, there is a lack of regulation, opening up questions about patient safety and guidelines for physicians. **Aim:** The aim of this review is to examine the benefits and drawbacks of telemedicine in its application in primary healthcare. **Materials and methods:** A search was conducted in Google Scholar, PubMed, and ScienceDirect Database as well as official webpages of governmental organisations by using keywords and word combinations. **Results and discussion:** In the digital age, there is an increasing reliance on technology to improve and enhance communication and the healthcare sector is no stranger to this. Studies have shown that since the advent of the Covid-19 pandemic, there has been an uptick in use of telemedicine consultations for diagnosis, management, and patient reviews in primary healthcare. Modern society in the West favours quick and easy access to all aspects of life, including medicine, and in several surveys reviewed, patients have shown a favourable opinion of telemedicine. There are, however, important limitations to telemedicine that mustn't be ignored due to the risk of patient harm. **Conclusion:** Telemedicine is a new approach to primary healthcare, providing patients in remote areas access to quality medical opinions that they would otherwise have been without. However, in this fast-paced digital world, more research is needed to clarify telemedicine's limitations so appropriate guidelines for its use can be drawn up to protect patient safety.

Keywords: *Telemedicine, primary healthcare, chronic diseases, diagnosis*

A SURVEY OF THE ATTITUDES OF MOTHERS OF PREPUBESCENT GIRLS ABOUT CERVICAL CANCER VACCINATION

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Introduction: Cervical cancer is a significant public health problem that requires priority attention. It is the second most common cancer among women aged 15 to 44 in Europe, but is potentially preventable in 99% of cases, provided early prevention is carried out. The high incidence and unfavorable prognosis of cervical carcinoma create a number of difficulties for modern public health care. In a number of countries in Europe and the world, traditions for the timely prevention of it have been established, which include vaccination of girls aged 10–13 years. **Objective:** To investigate the attitude of mothers of girls towards the primary prevention of cervical cancer, to determine their awareness of prevention methods, and to analyze their knowledge about vaccination. **Material and methods:** An anonymous online questionnaire on the Google forms platform was used. A total of 100 mothers of girls between the ages of 9 and 13 were surveyed. The research was conducted in the period December 2023 – January 2024. **Results and conclusions:** The awareness among mothers about the ways of human papilloma virus infection, the importance of cervical cancer and the possibilities of primary prevention is weak, according to the results of the conducted online anonymous survey. It is necessary to introduce information brochures, higher commitment on the part of GPs, midwives and obstetrician-gynecologists, as well as targeted promotional campaigns to increase the health culture of the population.

Keywords: vaccination, cervical cancer, prevention

APPROACHES TO INCREASE PHYSICAL ACTIVITY – GOOD PRACTICES FOR THE PREVENTION AND ASSESSMENT OF MUSCULOSKELETAL DYSFUNCTIONS

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Introduction: Using prevention to increase health benefits and achieve a higher level of population well-being is one of the goals of health care. Physical activity (sports, fitness training or various movement practices) is one of the main factors for primary health prevention. It is a determining factor in the fight against hypodynamia. According to Eurobarometer data from 2022, nearly half (48.3%) of young people in the low union lead a sedentary lifestyle. The purpose of the study is the detection of musculoskeletal disorders and the application of a program based on the Pilates method to improve motor activity in case of impaired posture. **Materials and methods:** The study covered 120 persons aged 5–57 years, it was conducted in November 2023 in the city of Plovdiv. It is used with sociological methods, history, examination in combination with high-quality tests for musculoskeletal disorders. **Discussion and results:** The main reasons for musculoskeletal dysfunctions are immobility and incorrect posture. Pathokinetic analysis showed dysfunctions mainly in the back, neck and shoulders. A program based on the Pilates method was drawn up in accordance with the findings of the functional examination. As a result of the systemic physical loads, positive structural-functional changes of the impaired function have been achieved. Kinesthetic therapeutic means are applied for the prevention of spinal distortions. **Conclusion:** Time spent in health-enhancing physical activity to improve physical and mental health is an investment in health care, which is why it is necessary to move to a model of healthy behavior and good.

Keywords: *physical activity, musculoskeletal dysfunctions*

RISK FACTORS ASSOCIATED WITH RETINAL VASCULAR OCCLUSIVE DISEASES

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Introduction: Retinal vascular occlusive diseases are associated with multiple risk factors, including cardiovascular diseases, and can cause visual dysfunction. Generally, they are classified into two types: retinal arterial occlusions and retinal venous occlusions. **Aim:** The study aims to identify risk factors associated with retinal vascular occlusive diseases and evaluate their impact.

Materials and methods: Forty-eight patients with established retinal vascular occlusive diseases registered between January and December 2023 participated in the study. Registration of the risk factors was done using a questionnaire.

Results: Among all patients, 81.3% were found to have systemic hypertension, 10.4% – had diabetes, 27.1% – had cardiovascular diseases, 8.3% had glaucoma, and 10.4% had registered malignant disease. Twenty-five percent were found to have dyslipidemia during laboratory tests. It is estimated that 27.1% of them smoke. **Conclusion:** Among the patients who have retinal vascular occlusive diseases, the leading risk factor was hypertension, followed by cardiovascular diseases, dyslipidemia, and smoking. Additionally, age appears to be a significant risk factor.

Keywords: *retinal vascular occlusive diseases, risk factors, retinal artery occlusion, retinal vein occlusion*

VII. Dental Medicine Session

THE APPLICATION OF GINGIVAL MESENHYMAL STEM CELLS IN PERIODONTAL REGENERATION – A LITERATURE REVIEW

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Introduction: Periodontal regeneration is the most desired outcome of periodontal treatment, but it cannot always be achieved. A variety of approaches and materials are used to achieve this goal. In recent years, the application of mesenchymal stem cells (MSCs) and in particular gingival mesenchymal stem cells (GMSCs) to achieve regeneration of periodontal tissues has been widely discussed. **Objective:** The aim of this review is to analyze the clinical benefit of using gingival mesenchymal stem cells to support the regeneration of affected periodontal tissues, by reviewing specialized scientific literature.

Methods: Full articles written in English and published in peer-reviewed scientific journals were analyzed. **Results:** Dental tissue-derived mesenchymal stem cells (MSCs), especially those from the gingiva, have attracted attention in the field of regenerative medicine due to their provenance, rapid proliferation rates, and genomic stability. Experiments show that the application of these cells helps the regeneration of periodontal tissue, including the formation of new periodontal ligament and bone. Although there are clinical trials on the use of these cells in the treatment of periodontitis, the results are still unclear.

Conclusion: Gingival mesenchymal stem cells are considered a powerful tool for regenerative therapy in periodontitis. Despite the promising results of the studies, in order to move to clinical trials, further efforts are needed to establish standardized procedures for the production of GMSCs, the selection of suitable donors and the identification of the right patient groups for treatment.

Keywords: *periodontal regeneration, gingival mesenchymal stem cells, periodontitis*

DIGITAL OR CONVENTIONAL IMPRESSIONS, WHICH ONE TO CHOOSE?

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Introduction: Dental impression are a negative copy of the teeth and oral tissues, into which gypsum or other die materials can be processed to create a positive model of the dental structures. Dentistry in our days generates new information every year and digital dentistry is becoming established and influential. Dentists should stay abreast of new technologies, some of the conventional materials and less time-consuming techniques remain widely used. It is important to ensure safely and effectively impressing the exact form of the oral tissues and provide optimal patient management. The accuracy of the impression is of paramount importance for the functionality and longevity of the prosthetic restoration. **Aim:** The aim of the study is to introduce and compare advantages and disadvantages of digital and conventional impressions. **Material and methods:** The study was done by researching and comparing different sources in publicly available scientific online databases (such as PubMed, Scopus, Science Direct). **Results and discussion:** There were significant differences among the digital and conventional impressions in the working time and processing steps. Patients and dentists stated that digital impressions were more comfortable than conventional techniques. **Conclusion:** Digital impressions resulted in a more time-efficient technique than conventional impressions. They are cheaper for the dentist after an initial big investment.

Keywords: advantages, disadvantages, impression materials, impressions, digital dentistry



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РЕЗЮМЕТА
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ABSTRACTS

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Тема: „Бърза микробиологична диагностика на генитални инфекции при жени и мъже – сравнителен анализ“

Ръководител на проекта: д-р Ели Христозова, дм¹

Водещ изследовател: д-р Зоя Рачковска¹

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5. УМБАЛ „Пълмед“, гр. Пловдив, Лаборатория по микробиология

Цел: Комплексен анализ на гениталната микрофлора при мъже и жени, диагностика на дисбиозни и полово-предавани инфекции и оценка ползите от едновременното прилагане на молекулно-биологични и класически микробиологични методи.

Материал и методи: Изследвани са 121 материали – 72 вагинални и 49 уретрални секрета с рутинни тестове и Femoflor Screen и Androflor Screen. Отделно 51 вагинални и цервикални секрети са изследвани за носителство на HPV (6,11,16,18) с HPV Quant-4.

Резултати: Чрез Femoflor Screen бяха направени две проучвания. При първия скрининг на симптоматични небременни жени показа, че 2/3 от пациентките до 30 години имат тежка дисбиоза от *G. vaginalis* (57.1%), а вагиналната кандидоза е водеща при жени с нормоценоза. Второто проучване откри като причина за най-честата кандидоза *C. albicans* (n = 13, 76%).

Androflor Screen показва, че при мъжете преобладаващата условно-патогенна миктофлора са стафилококи (n = -31,63%), а най-чест патоген е *C. trachomatis* (n = 6, 12%). Доказваха се смесени инфекции от *C. trachomatis* и *M. genitalium*, а при мъжете с

G. vaginalis се откри смесена инфекция или повишени нива на транзиторна флора.

При теста за човешки папиломен вирус преобладаваха жените със средно образование ($N = 23$, 45%), семейни ($n = 29$, 57%), с един сексуален партньор ($n = 27$, 52%). HPV-16 е доминиращ вариант с болестност от 9.8%.

Заключение: Класическите и съвременните PCR методи за скрининг на генитални инфекции трябва взаимно да се допълват поради необходимостта от комплексен подход в диагностиката и интерпретацията.

Приложение в практиката: Рутинно внедряване на фишовете в доболничната/болнична помощ. Предлага се комбинираното изследване да стане част от клинична пътека към клиниките по Урология и Акушерство и гинекология в УМБАЛ „Св. Георги“.

Научни публикации:

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Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Микробиом и патофизиология на депресия с коморбидност. Разстройства вследствие употреба на алкохол“

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Цел на проекта: Да се изследва диференциално диагностичната стойност на невроимунологични и невроизобразяващи маркери при депресия и разстройство вследствие употреба на алкохол.

Материал и методи: Изследвани са 3 пациента с Разстройство с употреба на алкохол коморбидно с Голямо депресивно разстройство, и 10 с Голямо депресивно разстройство.

Резултати: Депресията и в частност Голямо депресивно разстройство (ГДР) е сред заболяванията с най-висока социална значимост и е една от водещите причини за осъществяване на психиатрична консултация в амбулаторната практика. Съществува сериозна коморбидност между ГДР и Разстройство вследствие употреба на алкохол, достигаща 28%. Набирането на пациенти от популационна група с коморбидно Разстройство с употреба на алкохол и Голямо депресивно разстройство се оказа изключително трудно, поради което не бе достигнат заложения брой пациенти. Осъществяването на втората част от научното

изследване: имунологично изследване към момента на провеждане на проучването технически е невъзможно да се осъществи в България, в рамките на МУ-Пловдив или друго висше учебно заведение.

Заключение: В предварителните данни от проведените изследвания се повтарят търсените зависимости между биохимичните процеси в централната нервна система (регистрирани посредством спектроскопия) и патофизиологичните процеси (регистрирани посредством функционален МРИ), както и с периферния имунен отговор (чрез биологични тестове в периферна кръв).

Приложение в практиката: Предлага се използването на невроимунологични и невроизобразяващи маркери при депресия и разстройство вследствие употреба на алкохол.

Научни публикации:

1. Kakanakova A, Popov S, Maes M. Immunological Disturbances and Neuroimaging Findings in Major Depressive Disorder (MDD) and Alcohol Use Disorder (AUD) Comorbid Patients. In: Current Topics in Medicinal Chemistry, 2020, 20, 1-11.
2. The Handbook of Substance Misuse and Addictions: From Biology to Public Health. /Springer Nature. Обзор на база темата на проекта - Neuroimaging and alcohol use disorder (AUD) Prof. A. Kakanakova, Department of Psychiatry and Medical Psychology, Medical University Plovdiv, Faculty of Medicine, Plovdiv, Bulgaria.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Диагностични и прогностични генетични маркери при остри миелоидни левкемии“

Ръководител на проекта: проф. д-р Веселина Горанова-Маринова, дм^{1,4}

Водещ изследовател: Иван Желязков^{2,5}

Членове на изследователския екип: гл. ас. д-р Катя Сапунрова^{1,4}; гл. ас. д-р Васко Гръкланов^{1,4}; Христина Иванова^{1,4}; д-р Христо Иванов, дм^{2,5}; д-р Александър Линев^{2,5}; проф. д-р Вили Стоянова, дм^{2,5}; проф. д-р Жанет Грудева-Попова, дм^{1,3}

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Първа катедра по вътрешни болести, Секция по хематология
2. Медицински факултет, Катедра по педиатрия и медицинска генетика „Проф. д-р Иван Андреев“
3. Медицински факултет, Катедра по клинична онкология, Секция по медицинска онкология
4. УМБАЛ „Св. Георги“, гр. Пловдив, Клиника по клинична хематология
5. УМБАЛ „Св. Георги“, гр. Пловдив, Отделение по медицинска генетика

Цел: Да се проучи честотата на най-честите генетични мутации при новодиагностицирани пациенти с остра миелоидна левкемия (ОМЛ), установени с дигитален дроплет PCR и да се анализира тяхното прогностично значение.

Пациенти и методи: За периода 04.2020 г. – 04.2023 г. са проучени 83 пациенти с ОМЛ, мъже 38 (45.8%)/ жени 45 (54.2%) на средна възраст 59.4 ± 16.3 г. Установиха се следните генетични мутации: AML1-ETO (RUNX1-RUNX1T1) – при 8 (9.7%); PML-RAR α – 2 (2.4%), BCR-ABL1 – 1 (1.2%), SET-CAN – 1 (1.2%), MLL – 6 (7.5%), FLT-3 – ITD – 8 (9.7%), FLT-3 – TKD – 4 (4.8%), NPM – 7 (8.4%). Пациентите с установени генетични аномалии бяха сравнени с тези без мутации по демографски характеристики, подвариант на ОМЛ (de novo/вторична), клинично-лабораторни показатели, вида на проведеното лечение, терапевтичен отговор и обща преживяемост.

Резултати: Не се установи статистически значима разлика по демографски признания. Мутации MLL+, FLT-3+ и NPM + се установиха предимно при de novo ОМЛ. Най-висока честота на терапевтичен отговор се установи при пациентите с ОМЛ-М3, PML-RAR a+ (2/2), AML1-ETO при 6/8 и NPM+ при 5/6. Пациентите с FLT-3+ и MLL+ имат най-лоша прогноза: MS от 7 мес. и 2 мес. съответно. Тригодишната обща преживяемост при NPM+ е 64%, а при AML1-ETO – 48%.

Заключение: Данните от проведенния анализ потвърждават благоприятното прогностичното значение на NPM+, които се асоциират с висока честота на терапевтичен отговор и дълга преживяемост. Най-неблагоприятна прогноза потвърдихме при пациентите с мутации на MLL+, както и при FLT-3+, въпреки възможността за таргетна терапия.

Научни публикации: –

Оценка за изпълнение на проекта: *Проектът е приключил навреме.*



Тема: „Таргетно геномно профилиране за диагностика и поведение при колоректален карцином“

Ръководител на проекта: проф. д-р Вили Стоянова, дм^{1,2}

Водещ изследовател: ас. д-р Димитър Димитров¹

Членове на изследователския екип: проф. д-р Жанет Грудева-Попова, дм^{3,4}; д-р Христо Иванов, дм^{1,2}; д-р Габриела Райчева^{3,4}; д-р Нели Митева-Марчева, дм^{1,2}; д-р Александър Линев²; Иван Желязков²

Базова организация: Медицински университет – Пловдив

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4. УМБАЛ „Св. Георги“, гр. Пловдив, Клиника по медицинска онкология

Цел: Идентифициране на индивидуалния генетичен профил на тумора при пациенти с колоректален карцином и проследяване на концентрацията на специфичният за пациента прогностичен генетичен маркер в cfctDNA преди и в хода на терапията.

Материал и методи: Секвениране на преби cfDNA изолирани от 48 пациенти с КРК. Извърши се дизайн и синтез на праймери и сонди с последващо дигитален дроплет PCR за количествено определяне на иницииращата мутация.

Резултати: Осъществи се оптимизиране и валидиране на протокол за изолация от периферна кръв на cfDNA. Установиха се соматични и герминативни варианти значими за развитието, прогресията и лечението на колоректален карцином. Соматични мутации свързани с развитието и прогресия на КРК: ARID1A/c.3999_4001delGCA установен при 95% от пациентите с честота на мутантния алел между 2,13% – 4,02%; PARP4/c.3509C>T при 72% от пациентите честота между 6,11% – 21,26%; CBL/c.1380_1382delTGA при 95% от пациентите, честота между 1,96% до 3,54%; IRS2/c.2102_2104delCCG при 59% от

пациентите, честота 2,3% – 4,69%; GATA6/c.996_998delCCA се установи в 32% от пациентите с честота 4,4% – 5,26%. Герминативни варианти носещ повишен рисък от злокачествени заболявания: TP53/c.215C>G с честота от секвенираните пробы 75%; AURKA/c.169A>G – 74%. Герминативни варианти асоциирани с нежелани лекарствени реакции от химиотерапевтици: DPYD/c.85C>T с честота от секвенираните пробы 94%; SLC22A2/c.808T>G с честота от секвенираните пробы 85%.

Заключение: Провеждането на течна биопсия с последващо секвениране дава възможност за установяване на соматични и герминативни варианти.

Приложение в практиката: Течната биопсия има голям потенциал за приложение в диагностика, проследяване на ефекта от терапията и еволюцията на онкологичните заболявания.

Научни публикации:

1. Nelly Miteva-Marcheva, Gabriela Raycheva, Dimitar Dimitrov, Momchil Topalov, Hristo Ivanov. "Liquid biopsy – a sensitive tool for detecting variants in solid tumors", Сборник с научни доклади „Наука и младост“ 2022, 58-60. ISSN 1314-9229

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Преконцепционна грижа за повече здрави семейства“

Ръководител на проекта: проф. д-р Румен Стефанов, дм¹

Водещ изследовател: д-р Елеонора Христова-Атанасова, дм¹

Членове на изследователския екип: доц. Георги Искров, дм¹; доц. Ралица Райчева, дм¹; д-р Виктория Мандова, дм¹

Базова организация: Медицински университет – Пловдив

1. *Факултет по обществено здраве, Катедра по социална медицина и обществено здраве*

Цел: Подобряване здравната култура и информираността за семайно планиране и преконцепционна грижа на съвременното българско семейство.

Материал и методи: Проучването се проведе под формата на фокус групи сред 20 жени на възраст от 18 до 49 години през периода – май – юли 2022 г. Извадката включваща нераждали жени, бременни и родилки.

Резултати: Участничките смятаха, че интернет и техният акушер-гинеколог са единствените места, където могат да научат как да планират своята бременност. Само две от тях са обсъдили плановете си за преконцепционна грижа (ПГ) със своите лекари. Жените посочиха, че общопрактикуващите лекари (ОПЛ) трябва да бъдат по-активни в популяризирането на ПГ. Всички респонденти очертаха необходимостта от уеб-базирана образователна платформа, която да служи като основен източник на здравна информация за бъдещи семейства.

Заключение: Ролята и функциите на общопрактикуващите лекари в континуума на ПГ трябва да бъдат преразгледани. Препоръчват се целенасочени образователни мерки за всички заинтересовани страни, включително жени и общопрактикуващи лекари. В тази връзка нашата лесно достъпна, базирана на знания уеб платформа би могла да подобри осведомеността и възприятието на българските жени за ПГ.

Приложение в практиката: На база потребностите на целевата група бе изготвена информационна здравна уеб платформа с цел промоция на здраве на жени във фертилна възраст. Бяха закупени домейн и хостинг за период от 10 години (<https://iskamdete.eu/>).

Научни публикации:

1. Hristova-Atanasova E, Iskrov G, Raycheva R, Mandova V, Stefanov R. Preconception-Health-Related Attitudes of Bulgarian Women of Reproductive Age. *Healthcare (Basel)*. 2023 Mar 30;11(7):989. doi: 10.3390/healthcare11070989. PMID: 37046916; PMCID: PMC10094175. – IF 3.160, Q2

Оценка за изпълнение на проекта: *Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.*



Тема: „Фетална морфология. Развитие на феталния мозък. Физиология и патология на нервната система“

Ръководител на проекта: проф. д-р Таня Китова, дмн¹

Водещ изследовател: проф. д-р Таня Китова, дмн¹

Членове на изследователския екип: проф. д-р Екатерина Учкова, дм²; проф. д-р Кичка Велкова, дмн³; проф. д-р Магдалена Стоева, дм³; доц. Кристина Килова, дм⁴; д-р Ангел Тенев⁵; д-р Надер Ахмад⁵; д-р Атанас Даварски, дм⁶; Донка Попова³; д-р Мария Годуин-Кингсли⁵

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по анатомия, хистология и ембриология
2. Медицински факултет, Катедра по акушерство и гинекология
3. Комплекс по трансляционна невронаука
4. Факултет по обществено здраве, Катедра по медицинска информатика, биостатистика и електронно обучение
5. Медицински факултет
6. Медицински факултет, Катедра по неврохирургия

Цел: Чрез функционална магнитно резонансна томография (ФМРТ) на бременни жени да се направи оценка на физическото развитие на фетусите чрез изследване на мозъчните структури, черепа и вътрешните органи.

Резултати: Всички диагнози са резултат от мултидисциплинарен подход при доказване на мозъчни малформации, малформативни синдроми. Прилагането на функционалния ядрено-магнитен резонанс позволи да бъдат диагностицирани аномалии на ЦНС – 26%, като хидроцефалия и дефекти на нервната тръба у плода. Аномалиите на плацентата касаещи предлежанието и морфологията бяха диагностицирани в 52% от изследванията, 22% от изследваните с малформативни синдрома на плода. Беше събран материал за бъдещи научни изследвания и усъвършенствана методиката на изследване, която по-принцип е затруднена от движението на плода и големината на плода в различните гестационни седмици на изследване.

Заключение: Независимо от малкия размер на изследваната група, резултатите подкрепят прилагането на ФМРТ при съспектни патологични находки на централната нервна система на плода, установени чрез пренатално ехографско изследване. Потвърждаването и допълването на наличните малформации помага на родителите за вземане на окончателно решение за изхода на бременността и е важен етап в мултидисциплинарната диагностика на вродени аномалии, като дефекти на нервната тръба, хромозомни, сърдечни аномалии и редки синдроми.

Приложение в практиката: Получените резултати са с приложна и теоретична насоченост и могат да бъдат в помощ на пренаталната диагностика, ембриологичната наука, етапите на ембрио- и органогенезата.

Научни публикации:

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2. **Kitova T**, Uchikova E, Uchikov P, Kitov B. Sirenomelia Associated with VACTERL and VACTERL-H Syndrome. *Int. J. Morphol.*, 2020; 38(3):793–98. (**Impact factor 2019 - 0,494**). **Open access**.
3. **Kitova T**, Uchikova EH, Kilova KP, Belovejdov VT. Turner Syndrome Associated with Cerebellar Abnormalities. *J Anat Soc India* 2020; 69:252–55. (**Impact factor – 0.227**). **Open access**.
4. **Kitova T**, Kitov B, Angelova P, Uchikova E. Letter to the Editor regarding "Pentalogy of Cantrell: A Case Report of Probable Pentalogy of Cantrell in a Full-term Neonate" *Iranian Journal of Neonatology*. 2022 Jul; 13(3). DOI: 10.22038/IJN.2022.60232.2147 **Impact factor - 0.385 Q 4 SJR - 016**.
5. Kitova T, Angelova P, Uchicova E, Kitov B. Letter to Editor regarding: „Giant Cardiac Rhabdomyoma with Mixed Atrial Tachycardia and Nonsustained Ventricular Tachycardia in a Newborn with Tuberous Sclerosis“ *Ewha Med J* 2023; 46(2):eX <https://doi.org/10.12771/emj.2023.eX> **Web of Science Impact factor - 0.1**
6. M.J.Kingsley-Godwin, A.Tenev, E.Uchikova, K.Velkova, V.Belovezhedov, M.Stoeva. Evaluation of the Significance of MRI in the Prenatal Diagnosis of Neural Tube Defects. *Journal of Medical and Biological Engineering*.
7. E Uchikova, A.Tenev. Modern Aspects of Accurate Diagnosis of Neural Tube Defects *Iran J Public Health*, Vol. 52, No.3, Mar 2023, pp.662-664
8. **Kitova T**, Uchikova E, Uchikov P, Kitov B. Mermaid Syndrome Associated with VACTERL-H Syndrome. *Folia Medica* 2021; 63(2):272–276 DOI: 10.3897/folmed.63.e52900 **Open access**

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Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Анализ на експресивния и мутационен профил на протеин-кодиращи гени при деца със специфично езиково нарушение“

Ръководител на проекта: проф. д-р Иван Иванов, дм^{1,2}

Водещ изследовател: д-р Иглика Соткова, дм^{1,2}

Членове на изследователския екип: д-р Христо Иванов, дм^{1,3}; проф. д-р Вили Стоянова, дм^{1,3}; проф. д-р Илияна Пачева, дм^{1,2}; д-р Димитър Димитров¹; д-р Нели Митева-Марчева, дм^{1,3}; д-р Елена Тимова²; д-р Александър Линев, биолог³; Иван Желязков, биолог³; Юрка Донева, логопед

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по педиатрия и медицинска генетика „Проф. д-р Иван Андреев“
2. УМБАЛ „Св. Георги“, гр. Пловдив, Клиника по детски и генетични заболявания
3. УМБАЛ „Св. Георги“, гр. Пловдив, Отделение по медицинска генетика

Специфичното езиково увреждане (СЕН) е нервноразвитийно разстройство, засягащо 7% от децата в предучилищна възраст, характеризиращо се със забавено развитие на речта, въпреки нормален невербален интелект. Генетичната етиология на заболяването е сложна, включваща множество генетични и екологични рискови фактори.

Цел: Този проект има за цел да характеризира мутационния и експресионния профил на протеин-кодиращи гени при деца със СЕН.

Материал и методи: Проучването включва 40 деца със СЕН и 24 здрави контроли. Извършен е анализ на РНК секвениране и секвениране на целия екзом.

Резултати: Идентифицирани са 61 гена с диференциална експресия при деца със СЕН, свързани главно с имунитета и клетъчната регулация. GINS2 показва най-голямата разлика в експресията. В групата СЕН са идентифицирани около 330 варианта с глобална честота в gnomAD под 0,01%.

Заключение: Открити са значителни промени в генната експресия при деца със СЕН в сравнение със здрави контроли. Бяха идентифицирани променена експресия на GINS2 и дисрегулация на биологични пътища свързани с имунитета. Значителна част от вариантите, идентифицирани от екзомното секвениране, свързани с езикови дефицити при нашите пациенти, са замесени в пътища, свързани със сензорната обработка на звука. Вариантите в тези гени могат едва доловимо да попречат на нормалното развитие и функциониране на невронните мрежи в области, свързани с езиковите умения, което води до нарушени езикови способности. Необходими са допълнителни функционални изследвания, за да се разбере напълно връзката между тези варианти и СЕН.

Приложение в практиката: Внедрени са протокол за изолиране на РНК от периферна кръв и протокол за анализ на генна експресия с ddPCR.

Научни публикации:

- Соткова-Иванова И. Езикови нарушения: клинични и генетични аспекти. Хранене и развитие (Иванов И и Пилософ В), Медицински университет-Пловдив. ISBN 978-619-237-065-7
- Соткова И, Йорданова Р, Георгиева А, Тимова Е, Пачева И, Стоянова В, Попов Н, Въчев Т, Иванов И. Анализ на генната експресия при деца със специфично езиково нарушение-начални резултати. Педиатрия, 1: 2-6, 2023.
- Соткова И, Иванов Х. Генетична и молекулярна основа на езиковото нарушение – обзор. Педиатрия, 1: 7-9, 2023.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Черепно-мозъчна травма – алтернатива за бърза и надеждна диагностика“

Ръководител на проекта: доц. д-р Светлозар Спасов, дм¹

Водещ изследовател: д-р Стела Янчева^{1,5}

Членове на изследователския екип: доц. Мария Казакова, дб²;
доц. д-р Георги Павлов, дм³; доц. д-р Илия Биволарски, дм⁴;
д-р Иван Црънчев, дм^{1,5}; Валентин Дичев, дб²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по съдебна медицина и деонтология
2. Медицински факултет, Катедра по медицинска биология
3. Медицински факултет, Катедра по анестезиология, спешна и интензивна медицина
4. Медицински факултет, Катедра по обща и клинична патология
5. УМБАЛ „Св. Георги“, гр. Пловдив, Отделение по съдебна медицина

Цел: Изследване диагностичната стойност на p-Tau и NF-L като се изследва концентрацията им в ликвор и плазма, в паралел с β-APP в случаи с черепно-мозъчна травма (ЧМТ).

Материал и методи: Изследвани са плазма и ликвор от 20 случая на пациенти с изолирана ЧМТ и мозъчна тъкан от 12 починали от ЧМТ, като за контролна група се използваха 11 случая на починали от нетравматични причини.

Резултати: Нивата на pTau в плазма са по-високи при пациенти с ЧМТ. При изследване нивата на NF-L в ликвор и плазма се установиха по-високи нива на NF-L в контролната група, в сравнението с тези на пациенти с ЧМТ. При оценяване на значимостта на високите нива на NF-L и p-Tau в ликвор и плазма в изследваната група пациенти с неблагоприятен изход през първите 6 месеца след претърпяната ЧМТ, не се наблюдава статистически значима зависимост. При имунохистохимичното изследване на 4 участъка от главния мозък при починали от ЧМТ, се установи сигнификантно по-висока експресията на β-APP при по-голяма тежест на травмата.

Заключение: Повишените нива на рTau в плазма е индикация за налична ЧМТ в първите 24 часа. Нивата на NF-L в плазма и ликвор не могат да се използват за диагностика на ЧМТ в първите 24 часа. Имуноистохимичното изследване експресията на β -APP в мозъчната тъкан корелира с тежестта на травмата.

Приложение в практиката: Изследване на концентрацията на р-Tau в плазма може да послужи за ранна диагностика на ЧМТ при пациенти. Изследване на плазмения р-Tau и β -APP може да послужи при решаване на съдебно-медицински случаи с особена сложност.

Научни публикации:

1. Yancheva S., Spasov S., Pavlov G., Bivolarski I., Dichev V., Kazakova M., Tsranchev I. Tissue and fluid based indicators for traumatic brain injury. Science & Technologies. 2023, 1. 48-56.

Оценка за изпълнение на проекта: Проектът е приключен със значими, спрямо предвидените цел и задачи пропуски.



Тема: „Морбофункционални аспекти на тестикуларната спермато- и стероидогенеза в условията на мелатонинов дефицит“

Ръководител на проекта: проф. д-р Ивета Коева, дм¹

Водещ изследовател: д-р Дарина Барбутска, дм¹

Членове на изследователския екип: проф. д-р Катерина Георгиева, дм²; проф. д-р Яна Чекаларова³; д-р Анелия Петрова¹; д-р Деляна Давчева, дм⁴; Георги Нанов⁵

Базова организация: Медицински университет – Пловдив

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3. Българска академия на науките, Институт по невробиология
4. Медицински факултет, Катедра по клинична лаборатория
5. Медицински факултет, студент

Цел: Да се изследва ролята на мелатонина в процесите на тестикуларната спермато- и стероидогенеза при модел на мелатонинов дефицит на плъхове на различна възраст.

Материал и методи: Използваха се тестикуларни фрагменти от 5-, 16- и 20-месечни мъжки плъхове, разделени в две групи: след пинеалектомия и SHAM. Морфологичните изменения се проследиха чрез оцветяване с Хематоксилин и Еозин и Азан по Хайденхайн. Чрез имунохистохимия се установи експресията на Cyclin D1, Bcl6, BDNF/TrkB, SubstanceP, NeurokininB, tACE. Серумната концентрация на тестостерон, LH и FSH се проследи чрез ELISA – метод.

Резултати: С рутинна хистологична техника се установиха характерни възрастови промени в тестиса на плъх на 5, 16 и 20 месеца, като липсваше разлика между двете групи. Установи се статистически значимо повишаване на имуноекспресията на Cyclin D1 в Лайдиговите клетки /ЛК/ на 20-месечните пинеалектомирани животни. Демонстрира се по-изразена експресия на BDNF и TrkB в ЛК на животните с отстранена епифиза и при трите възрастови

групи. Установи се завишена имуноекспресия за NeurokininB и SubstanceP в тестиса на плъх след pineалектомия съответно 20 и 16 месеца след раждането. Открива се статистически достоверно повишаване на имунореактивността за tACE в ЛК на животните от контролната група при 5- и 16-месечни плъхове. Липсва статистически значима разлика в серумните нива на тестостерон, LH и FSH между групата на pineалектомитраните животни и SHAM-групата.

Заключение: Получените резултати потвърждават ролята на мелатонина в тестикуларната морфология и функция.

Приложение в практиката: Предлагане на по-ефективни подходи за въздействие на процесите на стареене и подобряване на качеството на живот на възрастното население.

Научни публикации:

1. Barbutska D., Aneliya Petrova, Iveta Koeva, Katerina Georgieva, Yana Tchekalarova, Georgi Nanov *Expression of BDNF in an experimental model of melatonin deficiency*, Scientific Works of the Union of Scientists in Bulgaria – Plovdiv, Series G. Medicine, Pharmacy and Dental Medicine, Vol. XXVII 2022, 80-83.
2. Barbutska, D., Aneliya Petrova, Iveta Koeva, Katerina Georgieva, Yana Tchekalarova, Georgi Nanov, Testicular Steroidogenesis after Pinealectomy-the Role of BDNF Signaling System. *Acta Morphologica et Anthropologica*, 29, 3-4.
3. Barbutska D., Aneliya Petrova, Yvetta Koeva, Katerina Georgieva, Yana Tchekalarova Georgi Nanov *Apoptosis in testicular steroid-producing cells in melatonin deficiency conditions – the role of Cyclin D1*, Scientific Research of the Union of Scientists in Bulgaria – Plovdiv, series B. Natural Sciences and Humanities, Vol. XXIII, ISSN: 1311-9192 (Print), ISSN: 2534-9376 (On-line), IXth International Conference of Young Scientists, 14-15 July 2022.
4. Petrova A., Darina Barbutska, Yvetta Koeva, Marin Kanarev, Katerina Georgieva, Yana Tchekalarova, Delyana Davcheva, Ekaterina Kisova, Nikola Kostadinov, *Morphology and functional aspects of testicular Leidig cells in melatonin deficiency conditions*, Scientific researches of the Union of Scientists in Bulgaria-Plovdiv, series B. Natural Sciences and the Humanities, Vol. XXIV, ISSN 1311-9192 (Print), ISSN 2534-9376 (On-line), 2023.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Биохимични маркери за оценка на остеointеграцията след поставяне на титанови импланти“

Ръководител на проекта: проф. Татяна Влайкова, дб^{1,3}

Водещ изследовател: ас. Теодора Станкова, дб¹

Членове на изследователския екип: д-р Иван Начков²; д-р Никола Стаменов²; гл. ас. Илиян Димитров¹; ас. Катя Стефанова¹; Таня Тачева³; Цветелина Атанасова⁴; Георги Георгиев⁵; Радка Чолакова²

Базова организация: Медицински университет – Пловдив

1. Фармацевтичен факултет, Катедра по медицинска биохимия
2. Факултет по дентална медицина, Катедра по пародонтология и заболявания на оралната лигавица
3. Тракийски университет, Стара Загора, Медицински факултет, Катедра по медицинска химия и биохимия
4. Факултет по дентална медицина, студент
5. Медицински факултет, студент

Цел: Да се изясни значението на ключови молекули, участващи в костния метаболизъм, като серумни биомаркери за биохимична оценка на степента на остеointеграция след поставяне на титанови зъбни импланти.

Материал и методи: Настоящото изследване обхваща общо 100 пациенти, на които са поставени титанови импланти. Пациентите са проследени на 1, 3/4 и 6 месеца чрез контролни рентгенографии и измерване на първична и вторична стабилност, въз основа на което са разделени в три групи: приели успешно имплант; развили периимплантит и отхвърлили имплант. Определени са серумните нива на показатели на костния метаболизъм, минералната обмяна и липидния профил.

Резултати: Пациентите, отхвърлили импланта, имат статистически значимо по-високи серумни концентрации на слабо карбоксилиран остеокалцин (UcOC), а по-ниски на остеопротегерин и магнезий, както спрямо успешно приели имплантите, така и спрямо развилиите периимплантит. Положителни корелации се установяват в нивата на остеопротегерин с магнезий, а на лиганда

на рецепторния активатор на нуклерен фактор-кВ (RANKL) с UcOC в цялата изследвана група. По-висок RANKL/остеопротегерин индекс и LDL-холестерол се регистрират при отхърлилите спрямо приелите импланта индивиди. И двете групи с постимплантарни усложнения имат по-високи концентрации на MMP-8. Не се регистрират статистически достоверни различия между трите сравнявани групи по отношение на серумните нива на 25-хидроксивитамин D, остеокалцин, фетуин-A, HDL-холестерол и калций.

Заключение: Установените разлики в серумните нива на остеопротегерин, RANKL, UcOC, MMP-8, както и корелациите им с параметри на костната и минералната обмяна, доказва потенциалната им роля в процеса на остеоинтеграция след поставяне на дентални импланти.

Приложение в практиката: Резултатите от настоящето изследване биха спомогнали при селектирането на пациентите и прогнозиране на отговора към имплантологичното лечение.

Научни публикации:

1. T. Atanasova, T. Stankova, A. Bivolarska, T. Vlaykova. Matrix metalloproteinases in oral health - special attention on MMP-8. *Biomedicines*. 2023; 11(6):1514.
2. T. Stankova, I. Nachkov, N. Stamenov, K. Stefanova. Possible implication of vitamin D in dental implantology. 4th International conference on multidisciplinary scientific studies proceeding book. 2022; 366-370.
3. T. Stankova, I. Nachkov, N. Stamenov, I. Dimitrov, K. Stefanova, A. Bivolarska, T. Vlaykova. Possible interplay between osteoprotegerin, RANKL and magnesium in the response to dental implants. *Biomedicines*. 2024; (под рецензия).

Оценка за изпълнение на проекта: *Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.*



Тема: „Анализ и оптимизация на протоколите за тъканна диференциация на човешки стромални клетки, добити от мастна тъкан, в хрущялна тъкан за нуждите на тъканиното инженерство, регенеративната медицина и хирургията“

Ръководител на проекта: д-р Регина Хатър, дм¹

Водещ изследовател: д-р Първан Войнов²

Членове на изследователския екип: гл. ас. Йордан Сбирков, дб³; проф. д-р Виктория Сарафян, дмн³

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по пропедевтика на хирургичните болести, Секция по пластично-възстановителна, естетична хирургия и термична травма
2. МБАЛ „УниХоспитал“, гр. Панагюрище
3. Медицински факултет, Катедра по медицинска биология

Цел: Да се осъществи анализ и оптимизация на протоколите за тъканна диференциация на човешки стромални мезенхимни клетки, добити от мастна тъкан, в хрущялна тъкан за нуждите на тъканиното инженерство, регенеративната медицина и хирургия.

Материал и методи: Установени клетъчни линии от мезенхимни стволови клетки; мастна тъкан от донори, постъпили в отделението по пластично-възстановителна хирургия по собствено желание за естетични процедури; изолиране на SVF (stromal vascular fraction) клетки от мастната тъкан; клетъчно култивиране; цитохимичен и хистохимичен анализ за индуциране на хондрогенеза чрез оцветяване за глюказамингликани с Alcian blue и Safranin O; RT-qPCR анализ на хондроцитни маркери.

Резултати: Апробирани са нови за университета и страната методи/лабораторни протоколи за: 1) изолиране и 2) култивиране *in vitro* на SVF клетки от мастна тъкан; 3) индуциране на хондроцитна диференциация; 4) цито/хистохимично и морфологично валидиране на хондроцитната диференция; 5) оптимизиране на протоколи за намножаване на диференциирани хондроцити. След

индуциране на хондроцитна диференциация за 3 седмици се наблюдава интензивно оцветяване с алцианово синьо и повищена генна експресия на хондроцитните маркери агрикан и Sox9. Освен това проектът предостави възможността за пилотни подготвителни дейности по предвиден за въвдеще втори етап – 3D биопринтиране на изолирани от мастна тъкан SVF клетки.

Заключение: Доказва се потенциала за *in vitro* диференциация на хондроцити от автоложна мастна тъкан, което създава възможност за акумулиране на хондроцитна маса за последващо 3D биопринтиране.

Приложение в практиката: Това е пилотно проучване, благодарение на което са разработени редица протоколи за лабораторната и научноизследователската практика, които ще послужат като основа на последващи проекти в областта на тъканното инженерство.

Научни публикации: –

Оценка за изпълнение на проекта: *Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.*



Тема: „Ефект на биомиметични самосвързващи се пептиди, флуориди и кариесна инфильтрация върху начални лезии по гладки повърхности в детската възраст“

Ръководител на проекта: проф. д-р Ани Белчева, дм¹

Водещ изследовател: ас. д-р Ирина Узунова-Райчева¹

Членове на изследователския екип: д-р Елица Венева, дм¹; д-р Таня Нихтянова-Графалска, дм¹; д-р Светла Петрова-Бучкова, дм¹; д-р Пламена Сапунарова, дм¹; д-р Костадин Георгиев, дм²; доц. Ра-лица Райчева, дм³; д-р Илиян Добрев, дм⁴; проф. Данчо Даналев⁵

Базова организация: Медицински университет – Пловдив

1. Факултет по дентална медицина, Катедра по детска дентална медицина
2. Факултет по дентална медицина, Катедра по оперативно зъболечение и ендодонтия
3. Факултет по обществено здраве, Катедра по социална медицина и обществено здраве
4. Университет по хранителни технологии – Пловдив, Катедра по микробиология
5. Химикотехнологичен и металургичен университет – София, Ка-тедра по биотехнология

Цел: Да се проучи ефекта от приложение на съвременни методи и средства за неоперативно лечение на начален кариес по гладки повърхности, въз основа на експериментални и клинични изследвания.

Материал и методи: За експерименталните задачи се изготвят 96 образци от екстракирани по ортодонтски показания премолари, разделени на случаен принцип в четири групи: Gr-P₁₁₋₄, Gr-CPP-ACFP, Gr-Icon, Gr-контролна. Изкуствените кариозни лезии се оценяват преди и след деминерализация и на двадесет и първия ден от приложение на pH-цикличен модел в биофилмреактор, чрез изследване на микротвърдост, СЕМ-анализ и конфокална микроскопия. В клиничната задача са включени 44 пациента с 176 начални лезии, лекувани и проследени за 12 месеца. За статистически анализ се използва ANOVA тест или непараметрични алтернативи.

Резултати: Получените експериментални данни с помощта на новосъздадения протокол показват, че всички тествани материали имат способността да подобрят състоянието на изкуствени емайлови лезии. Групата на SAP P₁₁-4 показва по-добър ефект в сравнение с CPP-ACFP, кариесна инфильтрация и контролната група, но без статистически значима разлика между тях ($p > 0.05$). Предварителните резултати от проведеното клинично проучване показват, че и трите средства подобряват състоянието на лезите в комбинация с инструкции за орална хигиена.

Заключение: SAP P₁₁-4, CPP-ACFP и методът на кариесна инфильтрация са ефективни средства за профилактика и неоперативно лечение на начални кариозни лезии по гладки повърхности в детската възраст.

Приложение в практиката: Сравнението между традиционната реминерализация, биомиметичната регенерация и инфильтрацията със смола като форми на неинвазивно превантитивно лечение дава възможност за избор на най-добър клиничен подход при лечение на началните кариозни лезии и управление на кариозния процес в детската възраст.

Научни публикации:

1. Irina Uzunova, Iliyan Dobrev, Dancho Danalev, Ralitsa Raycheva, Kostadin Georgiev, Svetla Petrova, Tanya Nihtianova, Ani Belcheva Synthesis of Fluorenated Analogues of Self-assembling Peptide P₁₁-4 and Study on P₁₁-4 Therapeutic Effect on Artificial Initial Enamel Lesions. Journal of Chemical Technology and Metallurgy, 58, 3, 2023, 577-586.
2. Irina Uzunova, Iliyan Dobrev, Dancho Danalev, Ralitsa Raycheva, Kostadin Georgiev, Svetla Petrova, Tanya Nihtianova, Ani Belcheva Comparative Evaluation of Microhardness on Artificial Enamel Lesions on Smooth Surfaces after Application of Three Contemporary Agents: an in-vitro Study. Published 20 Mar 2023 in Journal of IMAB – Annual Proceeding (Scientific Papers); vol.28, Supplement 12 SEEC & 32 IMAB, section Dental medicine, 41-44.
3. И. Узунова, Т. Нихтянова, С. Петрова, Р. Райчева, Д. Даналев, А. Белчева СРАВНИТЕЛНА ОЦЕНКА НА ДВА РЕМИНЕРАЛИЗИРАЩИ АГЕНТА ЧРЕЗ КОНФОКАЛНА МИКРОСКОПИЯ: ИН ВИТРО ПРОУЧВАНЕ. - Приета публикация за печат в Сборник „Научни трудове на Съюза на учените в България – Пловдив“, 2023 г.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Влияние на селективните модулатори на андрогения рецептор (SARMs) върху физическия работен капацитет на организма и страничните им ефекти при експериментални плъхове“

Ръководител на проекта: проф. д-р Николай Бояджиев, дм¹

Водещ изследовател: д-р Веселин Василев¹

Членове на изследователския екип: проф. д-р Катерина Георгиева, дм¹; проф. д-р Слави Делчев, дм²; проф. д-р Пепа Атанасова, дм²; гл. ас. д-р Фанка Гергинска, дм²; проф. д-р Таня Денева, дм³; д-р Десислава Арабаджийска³; Заки Абди⁴

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по физиология
2. Медицински факултет, Катедра по анатомия, хистология и ембриология
3. Медицински факултет, Катедра по клинична лаборатория
4. Медицински факултет, студент

Цел: Да се изяснят ефектите на SARMs в комбинация с тренировка за издръжливост и установяване на някои неблагоприятни ефекти при плъхове.

Материал и методи: Проведохме два експеримента с общо 80 плъха, използвайки субстанциите остатин и лигандрол.

Резултати: След осемседмичен прием на двете вещества, в съчетание с тренировка за издръжливост, установихме, че те понижават субмаксималната издръжливост на плъховете, но този ефект се прояви само в условия на тренировка. По отношение на максималната кислородна консумация, остатин не прояви ефект, а лигандрол понижи значимо $\text{VO}_{2\text{max}}$. Ефектът на лигандрол се прояви при нетрениращите плъхове, а при трениращите тренировката го неутрализира. Двете субстанции не повлияха максималното време до изтощение и максималната спринтова скорост. Лигандрол повиши силата на захват, докато остатин нямаше ефект. Остатин повиши генната експресия на миостатин в *m. gastrocnemius*, а лигандрол понижи експресията на VEGF-A, в

същия мускул. Остарин и лигандрол не повлияха кислород-пренасящия капацитет на кръвта или броя на кръвните клетки. Двете субстанции предизвикаха неблагоприятни промени в липидния профил като остатин повиши концентрацията на общия холестерол, докато лигандрол повиши и концентрацията на триглицеридите. Двата нестероидни представителя на SARMs понижиха серумната глюкозна концентрация на гладно. В рамките на експерименталния период от 8 седмици, остатин не повлия серумните концентрации на гонадотропните хормони и на тестостерона. Лиандрол прояви неблагоприятен ефект, понижавайки значимо концентрацията на FSH и предизвика тенденция за понижение на тестостероновата концентрация.

Заключение: SARMs понижават субмаксималната издръжливост и проявяват негативни ефекти върху липидния профил при мъжки плъхове.

Приложение в практиката: Получените резултати ще обогатят информацията за SARMs като кандидат-терапевтици при различни социалнозначими заболявания.

Научни публикации:

1. Gerginska F, Delchev S, Vasilev V, Georgieva K, Boyadjiev N. The selective androgen receptor modulator ostarine increases the extracellular matrix in the myocardium without altering it in the EDL Muscle. *Acta Morphologica et Anthropologica*, 2022; 29(3-4):45-48.
2. Komrakova M, Schilling AF, Lehmann W, Vasilev V, Georgieva K, Gerginska F, Boyadjiev N, Delchev S. Selective Androgen Receptor Modulators Combined with Treadmill Exercise Have No Bone Benefit in Healthy Adult Rats. *Pharmaceuticals (Basel)*. 2023 Sep 5;16(9):1249.
3. Vasilev V, Boyadjiev N, Deneva T, Arabadzhiyska D, Komrakova M, et al. Effects of Ostarine and Endurance Training on Some Functional, Hematological, and Biochemical Parameters in Male Rats. *Asian J Sports Med*. 2024;15(1):e138116. <https://doi.org/10.5812/asjsm-138116>.

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Изследване на NGAL в урина, като маркер за бъбречнаувреда при онкоболни деца провеждащи химиотерапия“

Ръководител на проекта: проф. д-р Мария Спасова, дм¹

Водещ изследовател: д-р Петя Маркова¹

Членове на изследователския екип: д-р Неофит Спасов, дм¹; проф. д-р Таня Денева, дм²; д-р Зейра Халил¹; гл. ас. Антония Янева, дм³

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по педиатрия и медицинска генетика „Проф. д-р Иван Андреев“
2. Медицински факултет, Катедра по клинична лаборатория
3. Факултет по обществено здраве, Катедра по медицинска информатика, биостатистика и електронно обучение

Цел: Да се изясни ролята на NGAL в урина като ранен маркер за остра бъбречнаувреда при онкоболни деца, провеждащи химиотерапия.

Материал и методи: Изследвани са 40 деца, общо 116 химиотерапевтични цикъла, като нивата на уринния NGAL се изследваха преди терапията и на 12 час след приключването ѝ. Изследвана бе и FEFi (фракционирана екскреция на фосфати) като маркер за настъпване на тубулнаувреда, резултат от нефротоксичност, както и 30 деца, приключили своето лечение преди повече от една година, за настъпило хронично бъбречно заболяване.

Резултати: Установи се, статистически значима разлика в нивата на NGAL преди и на 12-ия час след провеждане на химиотерапията при пациенти преминали втори ($Z = -2.908$, $p = 0.004$) и трети цикъл ($Z = -2.737$, $p = 0.006$), както и при тези с повече от 4 химиотерапевтични цикли ($Z = -2.678$, $p = 0.007$), но тези промени в нивата на NGAL останаха в референтни граници. Установи се, статистически значимо повишение на FEFi на 12-ия час, както след един, така и след повече от един химиотерапевтични цикли. При децата, приключили своята химиотерапия преди повече от

една година, стадий на ХБЗ (хронично бъбречно заболяване) чрез общоприетите критерии на KDIGO – eGFR и протеинурия, беше установено при 11 от 30 деца (36%), докато завишени стойности на NGAL едва при две от тях (6,6%).

Заключение: NGAL, като маркер за нефротоксичност, е неспецифичен и ненадежден. FEFi, е с висока специфичност за остра бъбречна увреда, включително и за субклинична такава, причинена от терапия с нефротоксични медикаменти

Приложение в практиката: Предлага се FEFi да бъде включена към рутинното проследяване на всички пациенти, провеждащи химиотерапия с нефротоксични медикаменти.

Научни публикации:

1. Петя Маркова, Мария Спасова, Полина Митева – Шумналиева, Нефротоксичност в педиатричната онкология, роля на новите биомаркери за диагностицирането ѝ, Списание Педиатрия, бр 2,2023, стр.27-30

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Изследване възможностите на електро-импедансната томография като клиничен метод при проследяване динамиката на белодробната увреда при пациенти с гръден травма на механична вентилация“

Ръководител на проекта: проф. д-р Чавдар Стефанов, дмн¹

Водещ изследовател: д-р Ивайло Минев, дм¹

Членове на изследователския екип: проф. д-р Николета Трайкова, дм²; д-р Теодора Гогова²; д-р Емral Късебекиров¹

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по анестезиология, специална и интензивна медицина
2. УМБАЛ „Св. Георги“, гр. Пловдив, Отделение по образна диагностика

Цел: Да се предложи методика за мониторинг в реално време на промените в белодробното контузионно огнище

Материал и методи: Изследвани са данните от проведени компютъртомографии (КТ) и електро-импеданс томографии (ЕИТ) на 10 пациенти с белодробна контузия, подложени на механична вентилация и хоспитализирани в Клиниката по анестезиология и интензивно лечение, при УМБАЛ „Св. Георги“ (Пловдив, България).

Резултати: Създаде се протоколизиран подход, отчитащ индивидуалните особености на пациента. След анализ на КТ обра зите се дефинира **ниво на интерес** и репери за позициониране на ЕИТ електродите. Първичните данни от ЕИТ се реконструират в контура на гръден кост на пациента. Пространствената морфологична чувствителност към разположението на белодробната контузия се определя чрез сравнителен анализ на белодробните зони от КТ и реконструирания ЕИТ образ от съответното ниво (индекс на съответствие > 0.82). По този начин се преодоляват ограниченията за позициониране на електродите на нива различни от първоначално препоръчаните от производителя и възникват

показания за клинична употреба при състояния, характеризиращи се с хетерогенно дисеминирани или единични лезии.

Заключение: Персонализираният подход позволява ЕИТ да предостави достатъчна пространствена резолюция на белодробната контузия, подобри наблюдението в реално време на белодробната функция и морфология и подпомогне оптимизацията на механичната вентилация, особено при случаи с хетерогенно дисеминирани или единични лезии.

Приложение в практиката: Протокол за персонализирано клинично приложение на ЕИТ, повишаващ информативната стойност на метода и подпомагащ оптимизацията на протективната механична вентилация.

Хибриден метод за образна диагностика и мониториране на патофизиологичните промени във вентилацията и перфузията при белодробна контузия.

Научни публикации:

1. И. Минев, В. Юкич, Т. Гогова, Н. Трайкова. Персонализиран подход при определянето на нивото на интерес при електро-импедансна томография на бял дроб. Известия по химия. ISSN 2534-9899 (под печат)

Оценка за изпълнение на проекта: Проектът е приключен със значими, спрямо предвидените цел и задачи пропуски.



Тема: „Изследване на биологична активност на синтезиран от природни аминокиселини DIQ [1-(2-chlorophenyl)-6,7-dimethoxy-3-methyl-3,4-dihydroisoquinoline], като произведен на папаверина“

Ръководител на проекта: доц. Илияна Стефанова-Кънчева, дб¹
Водещ изследовател: ас. Вера Гледачева¹

Членове на изследователския екип: гл. ас. Валери Славчев, дф¹; гл. ас. Мина Пенчева, дб¹; доц. Стоянка Атанасова, дх²; доц. Дарinka Димитрова, дм³; гл. ас. Кремена Сарачева, дм⁴

Базова организация: Медицински университет – Пловдив

1. Фармацевтичен факултет, Катедра по медицинска физика и биофизика
2. Пловдивски университет „Паисий Хилendarsки“, Катедра по органична химия
3. Медицински факултет, Катедра по фармакология и лекарствена токсикология
4. Фармацевтичен факултет, Катедра по фармакология и клинична фармакология

Цел: Да се изследва потенциалната биологична активност на новосинтезирана молекула DIQ[1-(2-chlorophenyl)-6,7-dimethoxy-3-methyl-3,4-dihydroisoquinoline], чрез действие върху биоелектротенеза и механична активност на изолирани гладки мускули от стомах, остра токсичност и влияние върху когнитивни и двигателни способности на плъхове, спрямо реперната молекула на папаверин.

Материал и методи: С разрешение на БАБХ и етична комисия при изследванията са използвани мишки албиноси ICR и плъхове порода Wistar. Приложените методи са: Синтез по Grunewald, „Изометрична регистрация на съкратителна активност на изолирани тъкани“; “Shuttle-Box Active Avoidance Test”; “Step-Down Passive Avoidance Test”.

Резултати: Като произведен на папаверина от природни аминокиселини бе синтезиран DIQ. Изчисленията *in silico* предположиха мускулнорелаксираща активност и ниска токсичност за

новосинтезираният изохинолин. Ex vivo приложението на DIQ релаксира гладкомускулни препарати от корпусната част на стомаха на плъх в концентрационния диапазон 10^{-7} ÷ 10^{-4} М. В условия на 42 mM KCl-деполяризация и субмаксимална концентрация DIQ ($5\cdot10^{-5}$ М) намалява тонуса на спонтанните мускулни съкращения с 41.04%, за разлика от реперната молекула на папаверин, предизвикваща 18.79% намаление. Новосинтезираната молекула доказва биологичноактивния си потенциал и при in vivo тест за обучение и памет. Значими подобрения в когнитивните функции на плъхове бяха установени при 5 mg/kg спрямо 10 mg/kg за папавериновия изохинолин.

Заключение: Доказаните непосредствен спазмолитичен ефект и ниска степен на токсичност за DIQ, получен като потенциален лекарствен агент, е от съществено значение за евентуалната му приложимост в рационалния лекарствен дизайн на нови съединения.

Приложение в практиката: Представените резултати разкриват възможностите на създадената изохинолинова молекула да проявява свойства на спазмолитик и да служи като модел за създаване на нови генерации биологичноактивни изохинолини с фармакологично значими свойства.

Научни публикации:

1. Milusheva M, Gledacheva V, Batmazyan M, Nikolova S, Stefanova I, Dimitrova D, Saracheva K, Tomov D, Chaova-Gizdakova V. "Ex Vivo and In Vivo Study of Some Isoquinoline Precursors. Scientia Pharmaceutica"; 2022; 90(2):37. <https://doi.org/10.3390/scipharm90020037>; Q2, SJR₍₂₀₂₂₎ 0,57; IF₍₂₀₂₂₎ = 2,5

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Епигенетичен и неврофункционален профил на фенотиповете инсомния“

Ръководител на проекта: доц. д-р Кирил Терзийски, дм¹

Водещ изследовател: д-р Тодор Георгиев¹

Членове на изследователския екип: доц. д-р Севдалина Кандиларова, дм²; доц. Николай Мехтеров, дб³; д-р Анелия Драганова, дм¹; проф. д-р Дора Златарева, дм⁴; ас. д-р Росица Паунова²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по патологична физиология
2. Комплекс по трансляционна невронаука
3. Медицински факултет, Катедра по медицинска биология
4. Медицински университет – София, Катедра по образна диагностика

Цел: Да се създаде епигенетичен и неврофункционален профил на фенотиповете инсомния (с нормална и със скъсена продължителност на съня).

Материал и методи: Изследвани са 35 пациента с хронично безсъние, 14 здрави контроли (продължава и в момента). На всеки е направена полисомнографска оценка на съня, изследвани са нива на експресия на миРНК и е направена функционална магнитно-резонансна томография (ФМРТ).

Резултати: След измерване експресията на 10 миРНК при пациенти с безсъние и здрави контроли, и провеждането на ФМРТ при тях, се установи понижена експресия на let-7 в бели кръвни клетки и на miR-125b в плазма при пациенти, страдащи от хронично безсъние, сравнено със здрави контроли. Интерпретация на тези резултати в светлината на медиаторите, регулиращи цикъла сън-бодърстване, е показателна за нарушение в посттранскрипционните ефекти на невромедиатора орексин, чиято активност е потенциално изменена при пациенти с безсъние. В допълнение, на ФМРТ бяха открити аберантни връзки в невроналните мрежи при пациенти – инхибиторни от дорзомедиалния

префронтален кортекс до задния гирус цингули и от медиалния префронтален кортекс към лявата инсула. Тези данни са в подкрепа на хипотезата за невъзможност да бъдат подтиснати невронални мрежи в състояние на покой, при пациенти страдащи от хронично безсъние.

Заключение: Изменения в експресията на микро РНК let-7 може да играе роля в посттранскрипционната регулация на орексина, което да доведе до повишени нива на бодърстване при пациенти с безсъние. Данните от фМРТ потвърждават неспособността на ЦНС да постигне състояние на покой при страдащите от инсомния.

Приложение в практиката: Предлага се алтернативна теория, изследваща причината за възникване на хронично безсъние.

Научни публикации:

1. SERUM MIRNA LEVELS AND FMRI-RESTING STATE FUNCTIONAL CONNECTIVITY AS NOVEL MARKERS FOR ASSESSING CHRONIC INSOMNIA DISORDER - Todor Georgiev, Krasimir Avramov, Aneliya Draganova, Kiril Terziyski - Pathophysiology Department, Medical University Plovdiv, Bulgaria. Scientific Works of the Union of Scientists in Bulgaria – Plovdiv. Series G. Medicine, Pharmacy and Dental medicine, Vol. XXVIII 236-246.

Оценка за изпълнение на проекта: *Проектът е приключен със значими, спрямо предвидените цел и задачи пропуски.*



Тема: „Оценка на общото водно съдържание и разпределението на телесните течности чрез електроимпедансен анализ в периоперативния период при големи хирургични интервенции“

Ръководител на проекта: проф. д-р Чавдар Стефанов, дмн^{1,2}
Водещ изследовател: д-р Емral Кьосебекиров^{1,2}

Членове на изследователския екип: д-р Ивайло Минев, дм^{1,2}

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по анестезиология, специалност интензивна медицина
2. УМБАЛ „Св. Георги“, гр. Пловдив, Клиника по анестезиология и интензивно лечение

Цел: да се оцени ефективността на целотелесна биоимпедансна спектроскопия(БИС) при мониториране на пре- и постоперативната дистрибуция на телесните течности и ефекта от инфузионната терапия(ИТ) при големи хирургични интервенции.

Материал и методи: Касае се за обсервационно, проспективно проучване на базата на вътрешуниверситетски проект № НО-12/2021 на МУ-Пловдив, включващо пациенти хоспитализирани в хирургични отделения на УМБАЛ „Свети Георги“ за планова оперативна интервенция. Биоимпедансните измервания бяха извършени 1 ч преди и след общата интубационна анестезия. При всички пациенти интраоперативно се приложиха стандартни техники за мониторинг, както и се следеше часова диуреза, обем на ИТ и обем кръвзагуба, на базата на което се изчисли и нетният баланс. За перспирацион инсенсибилис се прие загуба на течности в обем 0.5 мл/кг/ч. Анализирани са показателите Overhydration (OHY), Total body water (TBW), Extracellular water (ECW) и Intracellular water (ICW).

Резултати: В проучването бяха включени 40 пациенти (19 жени и 21 мъже) на средна възраст 59.15 ± 9.68 г. със среден ИТН 27.1 ± 4.3 кг/см². Средна продължителност на оперативните интервенции беше 189.75 ± 87.63 мин за 18 лапаротомии,

15 торакотомии и 7 краниотомии. Средният изчислен нетен воден баланс беше 1344.64 ± 533.02 мл. TBW, ECW, ICW и OHY се увеличиха от съответните 44.84 ± 10.38 л, 15.08 ± 3.35 л, 29.66 ± 7.29 л, -0.77 ± 0.84 на 46.38 ± 10.57 л, 16.62 ± 3.52 л, 29.76 ± 7.3 л, 1.28 ± 0.75 . Установи се корелация между кумулативния воден баланс и увеличението на TBW ($r = 0.41$, $p < 0.05$), ECW ($r = 0.47$, $p < 0.05$) и OHY ($r = 0.33$, $p < 0.05$), докато ICW се увеличи незначително ($r = 0.24$).

Заключение: БИС може да бъде полезен инструмент в комплексната оценка на ИТ. Методът намира все по-широко приложение при пациенти в периоперативния период.

Приложение в практиката: Предлага се използването на биоимпедансния анализ за обективна оценка на общото водно съдържание и разпределение на телесните течности

Научни публикации:

1. Е. Кьосебекиров, И. Минев, Ч. Стефанов, Д. Казаков, С. Николова, Е. Митковски, В. Стоилов, А. Проданов, Г. Павлов. Биоимпедансен анализ за оценка на телесните течности при големи хирургични интервенции, Анеестезиология и интензивно лечение 2023; 2: 3-6.

Оценка за изпълнение на проекта: Проектът е приключен със значими, спрямо предвидените цел и задачи пропуски.



Тема: „Мултипараметричен МРТ на пациенти с карцином на простатата – нови възможности за стадиране чрез системата PI-RADS 2“

Ръководител на проекта: проф. д-р Силвия Цветкова-Тричкова, дм¹

Водещ изследовател: д-р Любомир Червенков, дм¹

Членове на изследователския екип: доц. д-р Катя Дойкова, дм¹; д-р Александър Георгиев¹; доц. д-р Младен Дойков, дм²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по образна диагностика

2. Медицински факултет, Катедра по урология и обща медицина

Цел: Оценка на възможностите на мултипараметричния МРТ за откриване на рак на простатата

Материал и методи: Петдесет и трима пациенти на възраст от 44 до 82 години са изследвани за наличие на клинично значим простатен карцином. Методите за оценка включват GE Discovery 3T магнитно-резонансен томограф, серумни нива на простатен специфичен антиген (PSA), трансректална ултрасонография (TRUS) и 12-ядрена TRUS биопсия.

Резултати: mp-MRI показва 83,20% съответствие с TRUS биопсията: чувствителност 91,43% (76,90 – 98,20), специфичност 75,00% (34,90 – 96,80), положителни прогнозни стойности 94,10% (82,80 – 98,20) и отрицателни прогнозни стойности 66,70% (38,70 – 86,40). От пациентите, класифицирани 4 и 5 клас по системата за изобразяване на простатата и докладване на данни PI-RADS, 94,12% са имали положителна TRUS биопсия, както и 44,40% от пациентите класифицирани PI-RADS клас 3. Установено е, че PI-RADS е значим предиктор за положителна TRUS биопсия ($p = 0,009$).

Заключение: Според нашето проучване mp-MRI и TRUS биопсията имат високо ниво на съответствие за първоначалното откриване на простатен карцином. Включването на mp-MRI в диагностичния алгоритъм за откриване на простатен карцином може значително да намали броя на неправилните диагнози въз основа

на диагностика на база единствено серумни нива на PSA и/или подозителни физически и дигитални изследвания.

Приложение в практиката: Демонстрира се значимостта на мултипарметричното магнитно-резонансно сканиране в диагностичния алгоритъм на откриването на простатен карцином, както и необходимостта от стандартизирано описание на находките спрямо системата PI-RADS.

Научни публикации:

1. А. Георгиев, Л. Червенков, М. Дойков, К. Дойкова, С. Цветкова. Активна профилактика на рака на простатата с 3 Тесла магнитен резонанс. Преглед на литературата. Списание Рентгенология и Радиология ISSN 0486-400X, кн. 1 2022, pp 7 – 15
2. Doykov, M., Chervenkov, L., Tsvetkova-Trichkova, S., Doykova, K. and Georgiev, A. 2022. Assessment of the Utility of Multiparametric Magnetic Resonance Imaging for Initial Detection of Prostate Cancer. Open Access Macedonian Journal of Medical Sciences. 10, B (Jul. 2022), 1840–1845. DOI:<https://doi.org/10.3889/oamjms.2022.10401>.
3. Georgiev, A.; Chervenkov, L.; Doykov, M.; Doykova, K.; Uchikov, P.; Tsvetkova, S. Surveillance Value of Apparent Diffusion Coefficient Maps: Multiparametric MRI in Active Surveillance of Prostate Cancer. Cancers 2023, 15, 1128. <https://doi.org/10.3390/cancers15041128>.
4. L. Chervenkov, N. Sirakov, S. Tsvetkova, M. Stoeva, K. Doykova, A. Hilendarov, M. Peycheva, G. Kostov, M. Doykov. МАГНИТНО-РЕЗОНАНСНАТА ТОМОГРАФИЯ В МЕДИЦИНСКАТА ПРАКТИКА. Scientific works of the Union of Scientists in Bulgaria-Plovdiv, series G. Medicine, Pharmacy and Dental medicine, Vol.XXXVIII. ISSN 1311-9427 (Print), ISSN 2534-9392 (On-line) 2022., pp 147 – 150
5. Л. Червенков, М. Дойков, К. Дойкова, С. Цветкова, А. Георгиев А. Хилендаров, Г. Костов, А. Василска, М. Стоева, Н. Сирацов. МУЛТИПАРАМЕТРИЧЕН МРТ НА ПАЦИЕНТИ С КАРЦИНОМ НА ПРОСТАТАТА – НОВИ ВЪЗМОЖНОСТИ ЗА СТАДИРАНЕ ЧРЕЗ СИСТЕМАТА PI-RADS 2. Scientific works of the Union of Scientists in Bulgaria-Plovdiv, series G. Medicine, Pharmacy and Dental medicine, Vol.XXXVIII. ISSN 1311-9427 (Print), ISSN 2534-9392 (On-line) 2022., pp 151 – 156
6. L. Chervenkov, et al. Future of prostate imaging: Artificial intelligence in assessing prostatic magnetic resonance imaging. World Journal of Radiology, 2023, 15.5: 136. doi: 10.4329/wjr.v15.i5.136
7. Образна диагностика на мъжката урогенитална система – Л. Червенков, монография ISBN 978-619-237-121-0

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Нисковъглехидратна (кетогенна) диета при деца със затлъстяване“

Ръководител на проекта: проф. д-р Иван Иванов, дм¹

Водещ изследовател: д-р Иванка Паскалева, дм¹

Членове на изследователския екип: доц. д-р Нарцис Калева, дм¹; д-р Валя Маркова²; д-р Любов Чочкова¹; д-р Петя Маркова¹; д-р Цветелина Цветанова¹; д-р Димитър Илиев³; Божидар Буков⁴

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по педиатрия и медицинска генетика „Проф. д-р Иван Андреев“
2. Медицински факултет, Катедра по клинична лаборатория
3. Медицински факултет, Катедра по ендокринология
4. Медицински факултет, студент

Цел: Да се определи ефекта на „добре формулирана кетогенна диета“ при деца със затлъстяване, метаболитен синдром и инсулинова резистентност.

Материал и методи: Сто деца на възраст 7 – 18 години провеждат антропометрични, клинични, лабораторни и ехографски изследвания и са поставени на кетогенна диета за 16 седмици.

Резултати: Анализирани са резултатите на 58 пациента, преличили успешно срока на проследяване и преминали контролни изследвания. Отчетено е сигнификантно понижение на всички проследявани антропометрични показатели – тегло, ИТМ, съотношение обиколка на талия/ръст. След диетата пациентите са с подобрена инсулинова чувствителност (понижени средни нива на инсулин и HOMA-IR индекс, повишени QUICKI и адипонектин). Значимо е понижен броя пациенти с артериална хипертония, хепатостеатоза и метаболитен синдром. При всички 8 момичета със синдром на поликистозните яйчници се появи спонтанна менструация, а тестостеронът се понижи. В края на диетата пациентите имат подобрен липиден профил (понижени триглицериди, триглицериди/HDL, ароВ, атерогенен индекс на плазма и дебелина на каротидния интима-медиа слой. Пациентите с добър и среден

комплайънс към диетата имат съществено по-значимо подобре-
ние на проследяваните показатели. Страницните ефекти от ди-
етата са леки и неналагащи преустановяването ѝ.

Заключение: „Добре формулираната кетогенна диета“ дока-
зано намалява теглото и висцералното затлъстяване при деца.
Тя води до подобрена инсулинова чувствителност, обратно раз-
витие на метаболитния синдром, понижен кардиоваскуларния
risk и повлиява благоприятно състоянието на пациенти с арте-
риална хипертония, хепатостеатоза и синдром на поликистозните
яйчници при добра поносимост и леки странични ефекти.

Приложение в практиката: Предлага се използването на нис-
ковъглехидратна (кетогенна) диета като една от диетите при деца
със затлъстяване, инсулинова резистентност, метаболитен синд-
ром и съпровождащи коморбидности.

Научни публикации:

1. Паскаleva I. Кетогенна диета - същност и приложението ѝ в клинич-
ната практика. Сп.Педиатрия, Том LXIII, 1/2023 година
2. Паскалева И. Кетогенна диета - видове, странични ефекти, противо-
показания. Сп.Педиатрия, Том LXIII, 1/2023 година
3. Паскалева, Иванка Н., Тилов, Борис Г., Кингсли-Годунин, Мария Яна.
Приложение на нисковъглехидратна (кетогенна) диета при лечение
на затлъстяване и метаболитен синдром в детската възраст. Сп. Ендок-
ринология, том XXVIII, книжка 1/2023

**Оценка за изпълнение на проекта: Проектът е приключил
навреме, реализиран е успешно с добра публикационна ак-
тивност.**



Тема: „Диагностика на pemphigus чрез имунохистохимично изследване за имуноглобулин G4 на парафинови срези“

Ръководител на проекта: доц. д-р Цветана Абаджиева, дм^{1,3}

Водещ изследовател: д-р Жанета Желязкова, дм^{1,3}

Членове на изследователския екип: проф. д-р Веселин Беловеждов, дм^{2,4}

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по дерматология и венерология

2. Медицински факултет, Катедра по обща и клинична патология

3. Клиника по дерматология и венерология

4. УМБАЛ „Св. Георги“, гр. Пловдив, Отделение по обща и клинична патология

Цел: Да се оцени ползата на имунохистохимичното изследване за имуноглобулин G4 върху парафинови срези като диагностичен тест за пемфигус.

Материал и методи: Петдесет фиксирани във формалин парафинови блокчета от тъкан от 50 пациенти с пемфигус са подбрани по реда на прием на пациентите. Пробите са от хистопатологичния архив на Клиниката. Пациентите са предварително диагностицирани чрез директно имунофлуоресцентно и хистопатологично изследване. Петдесет фиксирани във формалин парафинови блокчета от тъкан от пациенти с булоznи дерматози различни от пемфигус са използвани като контроли. Имунохистохимично изследване за имуноглобулин G4 (IgG4) се извършва върху парафинови срези с дебелина 4 μm с анти-IgG4 антитяло. Позитивността се определя като ясна, интензивна, непрекъсната имунореактивност, локализирана в междуклетъчните връзки на кератиноцитите. Нахodka, която не отговаря на тези критерии се определя като отрицателна.

Резултати: Четиридесет и трима от изследваните пациенти са с пемфигус вулгарис и седем са с пемфигус фолиацеус. Четиридесет и девет (98%) биопсии от пациенти с пемфигус са

имунореактивни за IgG4, една (2%) биопсия от горен гръб от пациент с орален пемфигус показва отрицателна имунореактивност за IgG4. Отрицателна имунореактивност за IgG4 беше установена при 45 (90%) от контролите. Пет (10%) контроли с булозен пемфигоид показват имунореактивност за IgG4. Установява се чувствителност на метода 98%, специфичност 90%, положителна прогностична стойност 91% и отрицателна прогностична стойност 98%.

Заключение: Имунохистохимично изследване при пемфигус може да се приложи, когато липсва възможност за директно имунофлуоресцентно изследване. Предимство на метода е, че не изисква специално оборудване и препаратите са трайни.

Приложение в практиката: Имунохистохимичен метод за диагностика при пемфигус.

Научни публикации:

1. Abadjieva T, Genova S, Zhelyazkova Z. Diagnosis of pemphigus by immunohistochemistry for immunoglobulin G4 on paraffin sections.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Пневмоторакс при болни с COVID-19 – клинични и параклинични корелации, усложнения, хирургични подходи за диагностика и лечение“

Ръководител на проекта: проф. д-р Ангел Учиков, дмн^{1,7}

Водещ изследовател: д-р Любомир Паунов, дм^{1,7}

Членове на изследователския екип: д-р Атанас Баташки, дм^{1,7}; д-р Емануил Йорданов, дм^{1,7}; проф. д-р Силвия Цветкова, дм^{2,7}; д-р Боян Делев^{3,7}; гл. ас. Антония Янева, дм^{4,7}; д-р Йордан Калчев, дм^{5,7}; д-р Петър Учиков, дм^{1,7}; д-р Атанас Атанасов^{6,7}

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по специална хирургия
2. Медицински факултет, Катедра по образна диагностика
3. Медицински факултет, Катедра по клинична лаборатория
4. Факултет по обществено здраве, Катедра по медицинска информатика, биостатистика и електронно обучение
5. Медицински факултет, Катедра по медицинска микробиология и имунология „Проф. д-р Елисей Янев“
6. Медицински факултет, Катедра по инфекциозни болести, паразитология и тропическа медицина
7. УМБАЛ „Св. Георги“, гр. Пловдив

Цел: Да се анализират клиничните особености, инфламаторните маркери и усложненията на пневмоторакс при болни с COVID-19.

Материал и методи: Изследвани са 26 болни с доказан COVID-19 и пневмоторакс. При 24 е извършена торакоцентеза, а VATS с частична резекция и плевролиза – при 2. Изследвани са инфламаторни маркери – левкоцити, СУЕ, Д-димери, прокалцитонин, CRP.

Резултати: Честотата на десностранный и левостранни пневмоторакс е сходна (съответно 12 и 11 случая), а при 3 е бил билатерален. По-чест е големият пневмоторакс (> 2 см) – при 10. Почти половината пациенти (14) са били интубирани и повечето от тях (12) – обект на хирургично лечение. Само 4 са били без съпътстващи заболявания, а останалите – най-често с артериална

хипертония, ХОББ, диабет. Летален изход е настъпил при 14, а 3 са изписани с подобрение. Интубацията води до двойно по-висок риск за леталитет.

Най-висок е леталитетът при пациентите над 70 г. (68.8%). При жените честотата на леталитета е два пъти по-висока (88.9%) отколкото при мъжете (47.1%). Левкоцитите, CRP и D-димерите са значително завишени – индикатор за сериозна възпалителна реакция, която на фона на развитие на инфекцията от SARS-CoV-2 може да утежни хода на пневмоторакса.

Заключение: Пневмотораксът при COVID-19 се асоциира с повишен рисков от леталитет при деснострранна и билатерална локализация, при жени и болни над 70 г. По-често се наблюдава голям пневмоторакс като усложнение на COVID-19.

Приложение в практиката: Препоръчително да се избягват големите хирургични интервенции при пневмоторакс от COVID-19 и да се поставя торакален дрен за по-дълго време. При пациенти с интубация – повишено наблюдение.

Научни публикации:

1. Uchikov A, Paunov L, Batashki A, Yordanov E, Atliev K, Stefanov Ch, Sandeva S, Uchikov P. Surgical Treatment of Pneumothorax in Patients with COVID-19 – Results and Management. Folia Medica 2021. 63(5):663-9 (Q3)
2. Hadzhiminev V, Paunov L, Dimcheva T, Uchikov A, Novakov I. Spontaneous pneumothorax associated with COVID-19 pneumonia: a single-centre retrospective study. Monaldi Arch Chest Dis 2021, doi: 10.4081/monaldi.2021.1884 (Q3, SIR 0.404)
3. Hadzhiminev V, Halacheva, Paunov L. Pneumothorax, associated with COVID-10 – the first 3 cases. Science and youth conference at MU-Plovdiv (scientific reports), 2021.

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Лабораторен мониторинг на прогностични биомаркери при хоспитализирани пациенти с COVID-19“

Ръководител на проекта: проф. д-р Таня Денева, дм^{1,2}

Водещ изследовател: д-р Десислава Арабаджийска^{1,2}

Членове на изследователския екип: д-р Деляна Давчева, дм^{1,2};
д-р Снежана Стоенчева, дм^{1,2}; д-р Валя Маркова-Христева^{1,2}

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по клинична лаборатория

2. УМБАЛ „Св. Георги“, гр. Пловдив, Централна клинична лаборатория

Цел: Да изследваме някои лабораторни показатели при хоспитализирани пациенти със средно тежка и тежка форма на COVID-19 и оценим евентуалната им връзка със системното възпаление и тежестта на протичане на заболяването.

Материал и методи: Проучването включва 90 пациенти със средно тежка ($n = 45$) и тежка ($n = 45$) форма на COVID-19 и 45 здрави контроли. Изследвани са ПКК, ДКК, рутинни биохимични показатели, CRP, LDH, феритин, IL-6, РСТ, Д Димер, витамин Д и селен. Непрекънатите променливи са изразени като средна стойност \pm стандартно отклонение, $p < 0.05$ се счита за значима.

Резултати: Средната възраст на пациентската и контролната групи не се различава статистически (56.45 ± 7.82 г. срещу 57.95 ± 5.19 г., $p > 0.05$). Пациентите с COVID-19 показват значително повисоки стойности на левкоцити, неутрофили, по-ниски лимфоцити, еозинофили, общ белтък и албумин, по-високи CRP, LDH, феритин, IL-6, РСТ и Д Димер и по-ниски витамин Д, селен и PaO_2 в сравнение със здравите контроли ($p < 0.0001$). Според тежестта на заболяването, пациентите с тежка форма имат значително повисоки серумни концентрации за IL-6 (64.06 ± 32.97 pg/ml срещу 27.51 ± 18.15 pg/ml, $p < 0.0001$), CRP (168.21 ± 66.49 mg/l срещу 81.56 ± 43.93 mg/l, $p < 0.0001$), феритин (992.03 ± 416.82 ng/ml срещу 819.17 ± 326.29 ng/ml, $p < 0.0001$) и LDH (1392.68 ± 1066.47 U/l

срещу 887.76 ± 232.48 U/l, $p < 0.0001$) в сравнение с тези с умерена форма на болестта.

Заключение: Нашите резултати насочват към връзка между повишните лабораторни маркери за възпаление, ниските стойности на витамин D и селен и тежестта на заболяването при пациенти с COVID-19.

Приложение в практиката: Предлага се използването на панел от клинико-лабораторни изследвания, които могат да насочат към клиничното протичане, разграничаване на тежка и умерена форма и изход от болестта.

Научни публикации:

1. Deneva T, Ianakiev Y, Boykinova O. (2022). Salivary mental stress biomarkers in COVID-19 patients. Front Med 9:999215. DOI: 10.3389/fmed.2022.999215 (IF= 5.085 квартил=Q2)
2. Arabadzhiyska D, Deneva T, Boykinova O. (2023) Serum vitamin D levels and inflammatory status in COVID-19 patients, Bratisl Med J 2023, 124:6,449–453 DOI: 10.4149/BLL_2023_069 (IF=1.564, квартил=Q4)
3. Arabadzhiyska D, Deneva T. (2022). Evaluation of the prognostic role and clinical relevance of laboratory biomarkers in hospitalized patients with COVID-19, Knowledge – International Journal, Vol.55.4, pp.711-716
4. Арабаджийска Д, Денева Т, Бойкинова О, Стойчева М. Лабораторни биомаркери при пациенти с умерена и тежка форма на COVID-19. Х юбилейна национална научна конференция ХИВ и екзотични паразитни и инфекциозни болести в пост пандемичния период на COVID-19, Сборник статии 2023

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Оценка на ефективността и нивото на стрес на участници в симулационна програма за обучение по ендоскопска ретроградна холангиопанкреатография (ERCP)“

Ръководител на проекта: д-р Никола Боянов, дм¹

Водещ изследовател: д-р Десислава Димитрова²

Членове на изследователския екип: проф. д-р Таня Денева, дм³; проф. Ларс Енохсон, дм⁴; проф. Евангелос Георгиу, дм⁵; д-р Атанас Даварски, дм⁶

Базова организация: Медицински университет – Пловдив

1. Медицински симулационен тренировъчен център
2. УМБАЛ „Пълмед“, гр. Пловдив
3. Медицински факултет, Катедра по клинична лаборатория
4. UMU, Department of Surgical and Perioperative Sciences
5. National and Kapodistrian University of Athens, Greece
6. Медицински факултет, Катедра по неврохирургия

Цел: Оценка на практическата приложимост и ефективност на симулатор GI Mentor II за обучение по ендоскопска ретроградна холангиопанкреатография (ERCP), както и изследване нивата на стрес при участниците. Определяне на възможността за въвеждане на програмата в стандартното обучение на начинаещи ендоскописти с цел подобряване на цялостната им компетентност.

Материал и методи: Селектирани бяха две групи. Първата – седем опитни специалисти в областта на описаната методика. Втората – тридесет начинаещи специалисти или специализанти по гастроентерология, но с опит при извършването на ендоскопски манипулации.

Резултати: Изследва се нивото на стрес в слюнчени преби при експертите и начинаещите ендоскописти в няколко последователни етапа. Измерени бяха следните показатели: ниво на кортизол, а-амилаза, човешки хромогранин А. За оценка нивото на стреса се използва и специално подбрана за целта гривна „Емпатика“ (E4WB PPG BVP).

Заключение: GI Mentor II симулатор позволява придобиване на знания и умения на неопитни ендоскописти и запознава оптимално със същността на методиката, наречена ендоскопска ретроградна холангиопанкреатография. При изпълнението на настоящия проект се отчете повишаване на интереса от страна на обучаващите се към една от най-трудните ендоскопски процедури, познати към момента, както и значително подобряване на умениета и компетентността им.

Приложение в практиката: Обучението на валидирани ERCP симулатори може да бъде начин за подобряване на обучението на начинаещите ендоскописти, както и гарантиране на безопасността на болните в ежедневната практика.

Научни публикации:

1. Georgiou, Konstantinos MD, PhD; Boyanov, Nikola MD et al. Comparing the performance of experts and novices in a virtual reality Endoscopic Retrograde Cholangiopancreatography (ERCP) simulator. *Annals of Medicine & Surgery* 85(6):p 2924-2931, June 2023.
2. Konstantinos Georgiou¹, Nikola Boyanov² et al. Validity of a virtual reality Endoscopic Retrograde Cholangiopancreatography (ERCP) simulator: Can it distinguish experts from novices? *Frontiers in Surgery*, section Visceral Surgery, Manuscript ID: 1289197.

Оценка за изпълнение на проекта: *Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.*



Тема: „Създаване на скринингов въпросник за риск от малнутриция при деца“

Ръководител на проекта: доц. д-р Иван Янков, дм¹

Водещ изследовател: доц. д-р Иван Янков, дм¹

Членове на изследователския екип: доц. д-р Маргарита Панова, дм^{1,2}; д-р Константина Бангиева²; Василена Янкова³; д-р Ирина Владимирова²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по педиатрия и медицинска генетика „Проф. д-р Иван Андреев“
2. УМБАЛ „Свети Георги“, гр. Пловдив, Клиника по детски болести
3. Медицински факултет, студент

Цел: Цел на настоящото изследване е създаването на скринингов въпросник за откриване на деца с риск от малнутриция при хоспитализацията.

Материал и методи: Проведе се едноцентрово проспективно спрезово проучването. В него са включени деца, приети за лечение в Детска клиника на УМБАЛ „Свети Георги“ за периода януари 2022 до юни 2023 г.

Резултати: В проучването са включени 706 деца – 50,2% момчета ($n = 354$) и 49,8% момичета ($n = 352$) на възраст от 20 дни до 17 години и 10 месеца (Ме 4,6 г, SD 3,6 г). Нито един от пациентите не е получил консултация, свързана с ниско тегло, преди хоспитализацията.

Разработеният въпросник включва 5 въпроса – наличието/липсата на дисфагия (въпрос 1), загуба на тегло (въпрос 2), недостатъчен тегловния прираст на детето (въпрос 3), способността на детето да поема необходимия обем храна (въпрос 4) и време на хранене > 4 часа (въпрос 5). За наличен риск от недохранване се приема сбор ≥ 2 т. Колкото по-голям е сборът на точките, толкова по-висок е рисъкът.

Резултатите от приложението на въпросника позволяват откриване на деца с риск от малнутриция, като с най-голяма тежест са въпроси 1 и 4. Останалите въпроси са с по-малка тежест.

Заключение: Нашето проучване препоръчва рутинната употреба на предложения от нас въпросник за скрининг на риска от недохранване сред хоспитализирани деца. Неговата простота на попълване и достъпност на въпросите го правят удобен и евтин за използване инструмент.

Приложение в практиката: Използването на скрининговия въпросник е подходящ за скрининг на изложените на риск от малнутриция хоспитализирани деца.

Научни публикации:

1. Янков И, Панова М, Бангиева М, Янкова В, Владимирова И. Оценка приложимостта на скринингов въпросник за риск от недохранване при хоспитализирани деца. Педиатрия, 2024, 1(LXVI), (под печат)

Оценка за изпълнение на проекта: Проектът е приключен със значими, спрямо предвидените цел и задачи пропуски.



Тема: „Сравнително лабораторно и клинично изследване на обемни и оптични изменения на CAD/CAM 3D принтирани и конвенционални топлополимеризиращи пластмаси, използвани в снемаемото протезиране“

Ръководител на проекта: д-р Божана Чучулска, дм¹

Водещ изследовател: д-р Мария Димитрова¹

Членове на изследователския екип: проф. д-р Ангелина Влахова, дм^{1,2}; д-р Рада Казакова, дм^{1,2}

Базова организация: Медицински университет – Пловдив

1. Факултет по дентална медицина, Катедра по протетична дентална медицина
2. Научен институт, CAD/CAM Център по дентална медицина

Цел: Да се проведе сравнителен анализ и да се отчетат различните обемни и оптични изменения при два вида пластмаси, които се използват за изработка на цели снемаеми протезни конструкции, получени чрез методите на 3D принтиране и чрез конвенционалната технология.

Материал и методи: Бяха изследвани общо 180 броя опитни образци от двата вида пластмаса за снемаеми протезни конструкции, бяха приложени обективни лабораторни методи за изследване на обемните и оптични изменения през трите периода на проучването (7 дни, 14 дни и 1 месец).

Резултати: Първата задача включваща изследване на опитни образци от двете групи пластмаса, които бяха поставени в стъклени контейнери с изкуствена слюнка за три периода (7 дни, 14 дни, 1 месец). Резултатите показваха, че 3D-принтираният пластмаси демонстрират по-значителни обемни изменения през първата седмица, след което тези изменения нарастват пропорционално с времето. От получените резултати по втора задача може да се констатира, че опитните тела, изработени чрез метода на 3D-принтиране, имат по-добра оптична стабилност при оцветяване за период от 1 месец. Третата задача включваща 3D-съмбулативно изследване, което показва, че топлиннополимери-

зиращите пластмаси демонстрират по-висока устойчивост след престой от 1 месец в изкуствена слюнка. Доказа се, че и двата вида пластмаси са подходящи за изработка на снемаеми протезни конструкции със задоволителни механични качества.

Заключение: Обемната и оптична стабилност на снемаемите протезни конструкции корелира с вида на пластмасата, нейния химичен състав и метода на полимеризация.

Приложение в практиката: Проведените изследвания доказват големите възможности за приложение на новите 3D-принтирани пластмаси за целите на снемаемото протезиране в ежедневната дентална практика.

Научни публикации:

1. Dimitrova M, Corsalini M, Kazakova R, Vlahova A, Chuchulska B, Barile G, Capodiferro S, Kazakov S. Comparison between Conventional PMMA and 3D Printed Resins for Denture Bases: A Narrative Review. *J. Compos. Sci.* 2022, 6, 87. <https://doi.org/10.3390/jcs6030087> (Q2, IF = 3.3)
2. Dimitrova M, Vlahova A, Kazakova R. Preferred dental materials and techniques for removable dentures by dentists in Plovdiv and the region – a survey, 2022г., Научни трудове на Съюза на Учените – Пловдив: Серия Г, Том XXVIII, 2022г., ISSN 1311 – 9427 (Print), ISSN 2534 – 9392 (Online).
3. Dimitrova M, Vlahova A, Hristov I, Kazakova R, Chuchulska B, Gladysheva A. Color Changes of 3D Printed and Conventional Dental Resins for Removable Prosthodontics after Immersion in Different Staining Agents. *J. of IMAB.* 2023 Apr-Jun;29(2):4861-4865. DOI: 10.5272/jimab.2023292.4861. (Реферирана в Web of Science)
4. Dimitrova M, Vlahova A, Kazakova R, Chuchulska B, Urumova M. Water Sorption and Water Solubility of 3D Printed and Conventional PMMA Denture Base Polymers. *J. of IMAB.* 2023 Apr-Jun;29(2):4939-4942. DOI: 10.5272/jimab.2023292.4939. (Реферирана в Web of Science)
5. Dimitrova M, Kazakova R, Vlahova A. Evaluation of the Linear Dimensional Stability of CAD/CAM Milled, 3-D Printed, and Heat-cured Denture Base Polymers Subjected to Thermocycling and Immersion in Artificial Saliva: An In vitro study. *Int J Prosthodont Restor Dent* 2023; 13 (3):177-183. (Реферирана в Scopus)
6. Dimitrova M, Vlahova A, Kazakova R, Chuchulska B. 3D-Printed vs. Heat Cured Denture Base Materials Composition and Properties: A Review, Volume 05, Issue 04, pp: 92-95 International Journal Dental and Medical Sciences Research (IJDMSR Journal), 2023, ISSN: 2582-6018, Indexed in Indian Citation Indexed (ICI), www.ijdmsrjournal.com

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



**Тема: „Проучване на ролята на антиневроналните анти-
тела като биомаркер при пациенти с паранеопластичен
неврологичен синдром“**

Ръководители на проекта: проф. д-р Жанет Грудева-Попова, дм²;
доц. д-р Хасан Бурнусузов, дм³

Водещ изследовател: д-р Милен Христозов¹

Членове на изследователския екип: д-р Петя Гарджева¹;
доц. д-р Веселин Попов, дм²; д-р Габриела Райчева²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по медицинска микробиология и имунология „Проф. д-р Елисей Янев“
2. Медицински факултет, Катедра по клинична онкология
3. Медицински факултет, Катедра по педиатрия и медицинска генетика „Проф. д-р Иван Андреев“

Цел: Проучване на ролята на антиневроналните антитела (ANeA) при пациенти с малигнени неоплазии и с паранеопластичен неврологичен синдром (PNS).

Материал и методи: Изследвани са serumни преби на 52 пациенти, от които 9 с диагноза малигнени неоплазии без PNS (контролна група) и 43 с диагноза PNS (таргетна група). Използвана е индиректна имунофлуоресценция (IIFA) за определяне на ANeA, асоциирани с повърхностно-клетъчни антигени и имуноблот (IB) – за ANeA, асоциирани с интрацелуларни антигени.

Резултати: Всичките девет пациенти в таргетната група са положителни за ANeA, съответно: anti-NMDAR антитела се установяват при осем пациенти, като те са с остра лимфобластна левкемия (ОЛЛ), остеосарком и anti-NMDAR енцефалит; anti-GAD65 – при пациент с ОЛЛ и anti-Zic4 – при пациент с паранеопластична церебеларна дегенерация (PCD). От пациентите в контролната група четирима са положителни (9%), тридесет и девет са отрицателни (91%). От положителните пациенти: anti-Recoverin се установяват при пациент с карцином на гърда; anti-Hu – при пациент

с карцином на гърда; anti-Ri – при пациент с карцином на яйчници; anti-SOX1 – при пациент с карцином на гърда.

Заключение: Доказа се диагностичната стойност на anti-NMDAR при ОЛЛ, остеосарком и anti-NMDAR енцефалит, като при тези заболявания се наблюдава PNS и автоантителата корелират с тежко общо състояние на пациентите. Резултатите показват anti-SOX1, anti-Recoverin и anti-Hu при карцином на гърда без PNS и anti-GAD65 при ОЛЛ. Доказа се диагностичната стойност на anti-Ri при карцином на яйчници без PNS и диагностичната стойност на anti-Zic4 при PCD и anti-NMDAR енцефалит.

Приложение в практиката: Въведени са панели от ANeA, използващи методите на IIFA и IB.

Научни публикации:

1. Hristozov M, Burnusuzov H, Raycheva G, Popov V., Gardzheva P., Grudeva-Popova Zh., Murdjeva M. Antineuronal antibodies - biomarkers associated with paraneoplastic neurological syndromes in patients with or without malignant neoplasia. Folia Medica (подготвена за подаване).

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Биомеханични проблеми при ендодонтски лекувани зъби след отстраняване на сепарирани инструменти“

Ръководител на проекта: доц. д-р Силвия Димитрова, дм¹

Водещ изследовател: д-р Виктория Димитрова¹

Членове на изследователския екип: проф. Пламен Загорчев, дб, дбн²; доц. д-р Стефан Златев, дм³; д-р Петя Каназирска, дм⁴; д-р Любомир Вангелов, дм¹; Васил Димитров⁵

Базова организация: Медицински университет – Пловдив

1. Факултет по дентална медицина, Катедра по оперативно зъболечие и ендодонтия
2. Фармацевтичен факултет, Катедра по медицинска физика и биофизика
3. Факултет по дентална медицина, Катедра по протетична дентална медицина
4. Факултет по дентална медицина, Катедра по образна диагностика, дентална алергология и физиотерапия
5. Факултет по дентална медицина, студент

Цел: Да се анализират промените в обема и дизайна на кореновия канал, след отстраняване на сепарирани ендодонтски инструменти и да се създаде минимално инвазивен клиничен протокол, предпазващ от термична и механична увреда.

Материал и методи: Проведени са 5 изследвания, от които четири *in vitro* (СВСТ анализ на промени в обема и дизайна на кореновия канал след отстраняване на сепарирани ендодонтски инструмент с и без ласо техника и с и без ендодонтски водач; термометрично изследване на ултразвуков накрайник, сепарирани ендодонтски инструмент и твърди зъбни тъкани при два работни протокола; СЕМ и EDX) и едно *in vivo* (СВСТ анализ преди и след отстраняване на сегмент с две техники на 30 пациенти).

Резултати: При отстраняване на сегмент с ласо (*in vitro* и *in vivo*) и статичен ендодонтски водач се установи статистически значимо по-малък процент отнет дентин в сравнение с ултразвуковата техника. С увеличаване на мощността на ултразвуковия

апарат статистически значимо се повишава генерираната температура. При изследвания протокол с 10-секундни работни интервали се достигат статистически значимо по-ниски температурни стойности. На СЕМ фотомикрографии се регистрира, че по-високата мощност на ултразвуковия апарат и увеличаване времето на манипулацията се асоциират с по-висока степен на увреждане на дентина и формиране на микропукнатини. Елементният анализ показва липса на значими промени в състава на дентина след приложение на ултразвуковата техника.

Заключение: Използването на ласо техниката и статичните ендодонтски водачи статистически значимо намалява загубата на дентин.

Приложение в практиката: Предлагат се алтернативни техники за отстраняване на сепариран ендодонтски инструмент, намаляващи риска от формиране на микропукнатини и загряване на твърдите зъбни тъкани.

Научни публикации:

1. Dimitrova V., Dimitrova S., Kanazirska P. Comparison of different imaging techniques for the detection of separated endodontic instruments. Supplement Journal of IMAB, 2022, Section Dental medicine, e-ISSN: 1312-773X; p. 77-80.

Оценка за изпълнение на проекта: *Проектът е приключен със значими, спрямо предвидените цел и задачи пропуски.*



Тема: „**Експресия на anti HIF1alpha, Ki 67, E-cadherin, β-cathenin, SMA в огнища с ендометриоза, при ендометриални и яйчникови карциноми**“

Ръководител на проекта: доц. д-р Елена Порязова-Маркова, дм¹

Водещ изследовател: д-р Даниел Марков¹

Членове на изследователския екип: д-р Деница Сертева, дм¹;
д-р Десислава Божкова, дм¹; Гълъбин Марков²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по обща и клинична патология

2. Медицински факултет, студент

Цел: Да се изследва имунохистохимичната експресия на HIF-1α, Ki 67, E-cadherin, β-cathenin, SMA и Fascin в огнища с ендометриоза, при ендометриални и яйчникови карциноми и да се потърси корелация с хистологични и клинико-патологични параметри.

Материал и методи: Прегледани бяха общо 296 случая от съответните групи, имунохистохимично изследвани са 50 подходящи случая с маркерите **HIF-1α, Ki 67, E-cadherin, β-cathenin, SMA и Fascin**.

Резултати: HIF-1α е основният функционален протеин на HIF-1 комплекса. Високо ниво на експресия на HIF-1α наблюдавахме при случаите с ендометриални карциноми, в инвазивния фронт на тумора и около зони с некроза. При случаи с ендометриоза експресията на HIF-1α беше свързана с дълбочината на лезията и стадия на заболяването. Наблюдавахме по-силна експресия в огнищата с аденоомиоза и ендометриоза в сравнение с нормалния ендометриум. При тип 1 ендометриален карцином експресията на HIF-1α корелира с грейдинга и FIGO стадия на тумора. При тип 2 ендометриален карцином по-силна и дифузна експресия, включително и перинекротична експресия на HIF-1α отчетяхме при всички изследвани пациентки, независимо от миометралната инвазия, инвазия в аднексите, съдовата инвазия и TNM

стадия на тумора. HIF-1 α може да помогне да се идентифицират рискови пациентки с ендометриоза, които биха изисквали по-специфично наблюдение и лечение. Ендометриозата трябва да се разглежда като заболяване с потенциал за малигненост.

Заключение: Имунохистохимичният профил на различните морфологични лезии на ендометриума и яйчниците може да се използва за анализ на прогресията на ендометриозата и туморната тъкан.

Приложение в практиката: Избраните имунохистохимични маркери са от значение за оценка на пролиферативната активност, инвазията и туморната прогресия, както и за бъдеща терапия.

Научни публикации:

1. Endometriosis and related neoplasms of the ovary and endometrium. Reporting 11 cases. Markov D.Y., Poryazova E.G., Eurasian Union of Scientists. Series: medical, biological and chemical sciences, №08 (109), Vol.1, 2023, p.3-8, ISSN: **2782-2486**, DOI: **10.31618/ 2782-2486**.
2. EXPRESSION OF p53 AND Ki67 IN TYPE 1 AND TYPE 2 ENDOMETRIAL CARCINOMAS AND IN LOW AND HIGH GRADE SEROUS OVARIAN CARCINOMAS Markov D., Serteva D., Bozhkova D., Poryazova E., Znanstvena misel journal №82/2023, p. 11-16, ISSN: **3124-1123**, DOI: **10.5281/zenodo.8369259**
3. Expression of HIF-1 α , Ki67, SMA and E-Cadherin in endometriosis, endometrial and ovarian carcinoma, Daniel Markov, Elena Poryazova, Ralitsa Raycheva, Galabin Markov Folia Medica 2023 Submitted to the Editorial Office

Оценка за изпълнение на проекта: Проектът е приключи навреме, реализиран е успешно с добра публикационна активност.



Тема: „Серумно ниво на индоксил сулфат и пара-крезол при пациенти с ХБЗ IV – V ст като биохимични маркери за чревна дисбиоза при уремия – клинично значение и възможности за терапевтичен контрол“

Ръководител на проекта: проф. д-р Емил Кумчев, дм¹

Водещ изследовател: д-р Теодор Кускунов²

Членове на изследователския екип: гл. ас. Красимир Боянов, дб³;
Калина Методиева³

Базова организация: Медицински университет – Пловдив

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Секция по нефрология
2. Медицински факултет, Катедра по пропедевтика на вътрешните
болести „Проф. д-р Антон Митов“
3. Фармацевтичен факултет, Катедра по медицинска биохимия

Цел: Да се изследва серумната концентрация на индоксил сулфат (ИС) и пара-крезил сулфат (п-КС) при пациенти на хемодиализно лечение, както и възможностите за повлияване на някои маркери за възпаление и оксидативен стрес след прием на синбиотик.

Материал и методи: Включихме 30 пациенти с краен стадий на хронично бъбречно заболяване (ХБЗ), които приемаха синбиотик в състав *Lactobacillus acidophilus* La-14 2×10^{11} (CFU)/g и пре-биотични фруктоолигозахариди. Изследвахме серумните нива на ИС, п-КС, Интерлевкин-6 (IL-6) и Малондиалдехид (МДА) в началото и след 8 седмична синбиотична суплементация.

Резултати: Базовите стойности на четирите изследвани показатели при пациентите бяха значително по-високи – п-КС (29.26 ± 58.32 pg/mL), ИС (212.89 ± 208.59 ng/mL), IL-6 (13.84 ± 2.02 pg/mL), МДА (1430.33 ± 583.42 pg/mL) в сравнение с получените резултати след 8 седмичен прием, като установихме сигнификантно понижаване на параметрите спрямо изходните – п-КС (6.40 ± 0.79 pg/mL, $p = 0.041$), ИС (47.08 ± 3.24 ng/mL, $p < 0.001$),

IL-6 (9.14 ± 1.67 pg/mL, $p < 0.001$), МДА (1003.47 ± 518.37 pg/mL, $p < 0.001$).

Заключение: Нашето проучване предполага, че подобряването и възстановяването на чревното синбиотично състояние при пациентите на хемодиализно лечение значително понижава нивото на уремични токсини, произведени от чревната микробиота. Вероятно това повлиява благоприятно някои от характерните усложнения на ХБЗ, като персистиращото нискостепенно възпаление и оксидативния стрес.

Приложение в практиката: ИС и п-КС спадат към групата на протеин-свързаните уремични токсини, поради което степента им на редукция при пациенти на хемодиализно лечение е ограничена. Синбиотичната суплементация води до понижаване на серумните им концентрации и се разглежда като нова, допълнителна възможност за повлияване на уремичното състояние при пациенти с ХБЗ.

Научни публикации:

1. Kuskunov T, Tilkiyan E, Doykov D, Boyanov K, Bivolarska A, Hristov B. The Effect of Synbiotic Supplementation on Uremic Toxins, Oxidative Stress, and Inflammation in Hemodialysis Patients-Results of an Uncontrolled Prospective Single-Arm Study. Medicina (Kaunas). 2023 Jul 28;59(8):1383.
2. Т. Кускунов, Е. Тилкиян, К. Боянов, А. Биволарска „Промяна в серумното ниво на интерлевкин-6 при пациенти, провеждащи хемодиализно лечение след прием на синбиотик.“ Научни трудове на Съюза на учените в България – Пловдив. Серия Г. Медицина, фармация и дентална медицина т.XXVIII. ISSN 1311-9427 (Print), ISSN 2534-9392 (On-line) 2022

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Фармакоаналитичен контрол на адаптогени от растителен произход – охарактеризиране на екстракт от *Rhaponticum carthamoides*“

Ръководител на проекта: доц. маг.-фарм. Калин Иванов, дф¹

Водещ изследовател: ас. маг.-фарм. Велислава Тодорова¹

Членове на изследователския екип: доц. маг.-фарм. Станислава Иванова, дф¹; ас. маг.-фарм. Ваня Кожухаров¹; ас. маг.-фарм. Станислав Дянков¹; ас. маг.-фарм. Ваня Налбантова¹; доц. маг.-фарм. Диана Карчева-Бахчеванска, дф¹; доц. маг.-фарм. Нико Бенбасат, дф¹; Иоана Димова, биолог¹

Базова организация: Медицински университет – Пловдив

1. Фармацевтичен факултет, Катедра по фармакогнозия и фармацевтична химия

Цел: Идентификация и количествено определяне на фитоекдистероиди в екстракт от *Rhaponticum carthamoides* (Willd.) Iljin. чрез високо ефективна тънкослойна хроматография (HPTLC) и високо ефективна течна хроматография (HPLC). Изследване на анти-адипогенна активност на екстракта и неговите вторични метаболити.

Материал и методи: Високо ефективна тънкослойна хроматография (HPTLC), високо ефективна течна хроматография (HPLC) и клетъчни линии – адipoцити.

Резултати: Разработен е и е валидиран нов HPTLC метод за откриване и количествено определяне на екдистерон, туркестерон и понастерон А. Методът е приложен за количествен анализ на трите фитоекдистероида в екстракт от *R. carthamoides*. Получените резултати от HPTLC, се потвърдиха чрез разработен и валидиран HPLC/UV метод. Предложените методи се характеризират с висока чувствителност, ефективност, устойчивост и възпроизвидимост. Установено е, че екстракт от *R. carthamoides*, екдистерон и туркестерон значително намаляват натрупването на липиди в човешки адipoцити, както и че екстракта и екдистерон ефективно стимулират базалната липолиза.

Заключение: Съдържанието на екдистерон, туркестерон и понастерон А са количествено определени в екстракт от *R. carthamoides*. Екстрактът и екдистеронът значително повлияват адипогенезата и адиполизата, докато туркестеронът повлиява само адипогенезата.

Приложение в практиката: Валидираните подходи за анализ, могат да бъдат успешно прилагани в научни изследвания и рутинен контрол. Резултатите получени от изследването за антиадипогенната активност, са ценни за бъдещи изследвания. Също така екстракт от *R. carthamoides*, екдистерон и туркестерон имат голям потенциал в мениджмънта на затлъстяване.

Научни публикации:

1. Todorova V, Ivanov K, Karcheva-Bahchevanska D, Ivanova S. Development and validation of high-performance liquid chromatography for identification and quantification of phytoecdysteroids ecdysterone and turkesterone in dietary supplements. *Processes*. 2023;11(6):1786.
2. Todorova V, Savova MS, Ivanova S, Ivanov K, Georgiev MI. Anti-adipogenic activity of *Rhaponticum carthamoides* and its secondary metabolites. *Nutrients*. 2023;15(13):3061.

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Функционални аспекти на човешкия клауструм при излагане на сетивни стимули от различни модалности“

Ръководител на проекта: проф. д-р Стефан Сивков, дм¹

Водещ изследовател: ас. д-р Marin Kanarev¹

Членове на изследователския екип: доц. д-р Ferihane Ahmed-Popova, дм¹; гл. ас. д-р Zdravka Harizanova-Vylcheva¹; проф. инж. Magdalena Stoeva, дм²; ас. д-р Tina Zdravkova²; ас. Надежда Петрова, дб¹; Теодор Лоловски³

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по анатомия, хистология и ембриология
2. Медицински факултет, Катедра по образна диагностика
3. Медицински факултет, студент

Цел: Целта на проучването е изследването чрез функционално невроизобразяване на морфологичната структура, активността и функционалните взаимовръзки на човешкия клауструм с други структури на нервната система при сетивни стимули от различни модалности.

Материал и методи: Изследването беше реализирано в базата на Комплекса по трансляционни невронауки при Медицински университет – Пловдив. В проучването се включиха 113 здрави доброволци на възраст 19 – 39 години при липса на неврологични заболявания. Беше проведено морфологично и функционално невроизобразяване с 3 Тесла ядрено-магнитен резонанс, еднократно в целия му обем от няколко серии /блока/. На всеки от участниците бяха представени снимки с изображения и звуци, поотделно и заедно, групирани в серии от съответстващи и несъответстващи. Получените резултати бяха обработени статистически чрез софтуерни програми (SPM и Matlab).

Резултати: Получените резултати варират в голяма степен между отделните изследвани на индивидуално ниво. Обобщено има статистически значими огнища на зрителна и слухова кора

при блоковете на съответните модалности, но на контрасти сравняващи Match срещу Mismatch сериите се получават огнища в областта на клауструма и инсулата, които достигат значимост на cluster level, но не достигат достатъчна значимост на peak level. Вероятно това е във връзка с малките размери и обем на изследваните структури.

Заключение: Клауструмът вероятно има роля в интегрирането на сетивни стимули от различни модалности, като потенцира значимите за оцеляването на индивида и играе важна роля при фиксиране на вниманието.

Приложение в практиката: Разбирането на механизмите на функциониране на клауструма при човека би помогнало при опити за клинично уточняване и повлияване на отклонения и дефицити на вниманието и възприятието на околната среда.

Научни публикации:

1. Kanarev M, Petrova N, Petrova A, Sivkov S. **Functional Aspects of the Human Claustrum – Literary Review.** Acta Morphologica et Anthropologica, Sofia. 29: 3-4, 2022.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Изследване на влиянието на фебуксостат върху нивото на IL-1, IL-2 и COX-2 при пациенти с подагра“¹

Ръководител на проекта: проф. д-р Мариела Генева-Попова, дм¹

Водещ изследовател: гл. ас. д-р Красимир Краев, дм¹

Членове на изследователския екип: д-р Станислава Попова-Белова, дм¹; д-р Величка Попова, дм¹; д-р Божидар Христов, дм²; доц. д-р Иван Шейтанов, дм³; Деспина Пупаки⁴

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по пропедевтика на вътрешните болести „Проф. д-р Антон Митов“
2. Медицински факултет, Първа катедра по вътрешни болести, Секция по гастроентерология
3. Медицински университет – София, Медицински факултет, Катедра по ревматология
4. Българска академия на науките, Секция по имунобиология на репродукцията

Цел: Да се изследва нивото на IL-1, IL-2, COX-2 при пациенти с подагра – изходно ниво и 30, 60 и 90 дни след приема на фебуксостат, както и на 20 здрави контроли

Материал и методи: Ще бъдат включени 100 пациенти, болни с подагра, на възраст между 18-80 години и контролни групи – 20 здрави индивиди. Нивата и на IL-1, IL-2, COX-2 в серума на болните ще се определят чрез ELISA-методика.

Резултати: За период от 3 месеца бяха проследени 50 пациенти с подагра, на лечение с фебуксостат, заедно с 20 здрави контроли. Строгото проследяване на нивата на интерлевкин-1 (IL-1), интерлевкин-2 (IL-2) и циклооксигеназа-2 (COX-2) разкрива значително понижение на нивата им при 42 пациенти. Използвайки статистически методи, включително корелационния коефициент на Pearson, ние установихме положителна корелация между приема на фебуксостат и намаляването на нивата на IL-1, IL-2 и COX-2. Освен това беше използван t-тест на Student за сравняване на средните нива на цитокини между здрави контроли и пациенти, потвърждавайки статистически значими разлики.

Интересно е, че при продължителна терапия се наблюдава прогресивно намаляване на нивата им. Тези констатации подчертават потенциала на фебуксостат като ефективна интервенция при подагра, предоставяйки представа за неговите противовъзпалителни свойства и предлагайки пътища за по-нататъшно изследване.

Заключение: Получените резултати разкриват потенциала на фебуксостат не само като медикамент за намаляне на пикочната киселина, но и като възможност за ефективна противовъзпалителна интервенция.

Приложение в практиката: Резултатите от проучването показват, че включването на фебуксостат в лечението на подагра би оптимизирало лечението чрез намаляване на провъзпалителните маркери, позволявайки по-персонализирани подходи и потенциално подобрявайки дългосрочните резултати.

Научни публикации:

1. Kraev, KI, Geneva-Popova MG, Hristov BK, Uchikov PA, Popova-Belova SD, Kraeva MI, Basheva-Kraeva YM, Stoyanova NS, Mitkova-Hristova VT. Celebrating Versatility: Febuxostat's Multifaceted Therapeutic Application. Life 2023, 13, 2199. <https://doi.org/10.3390/life13112199>
2. Краев К., Генева-Попова М., Попова-Белова С., Попова В., Шейтанов И. Ролята на новите медикаменти, използвани за лечение на подагра, за блокиране на цитокинов синтез и COX-2. Мединфо, 11: 45-9, 2022.

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Параметри на оралното здраве при пациенти с разстройства на храненето. Анкетни и клинични проучвания“

Ръководител на проекта: проф. д-р Георги Томов, дм¹

Водещ изследовател: д-р Маргарита Хаджиева¹

Членове на изследователския екип: Иванина Тотова²

Базова организация: Медицински университет – Пловдив

1. *Факултет по дентална медицина, Катедра по пародонтология и заболявания на оралната лигавица*
2. *Факултет по дентална медицина, студент*

Цел: Чрез анкетни и клинични проучвания да се установят основни параметри на оралното здраве при български пациенти с разстройства на храненето.

Материал и методи: Набрани са 60 пациента с разстройства на храненето, които участват доброволно в анкетно проучване. Клинични и параклинични изследвания са проведени на 14 пациента с булимия и 12 пациента с анорексия.

Резултати: Възрастовият диапазон при анкетираните е от 18 – 57 г., като 95% от тях са жени. 58,3% посещават стоматолог само при проблем. Мнозинството от респондентите не одобряват тялото и килограмите си, които се опитват да коригират с неправилно хранително поведение и навици. 87% от тях имат орално-хигиенни навици, несъобразени с хранителното разстройство. Съобщават и за редица субективни симптоми – сухота и парене в устата, неприятен дъх, както и кървене от венците. 90% от анкетираните имат изразена чувствителност на зъбите, а 43% от тях установяват настъпили промени в устната си кухина, но не са запознати с оралните изяви на хранителните разстройства. 83,3% от респондентите са заинтересовани да получат допълнителна информация и насоки от денталния лекар. При изследванията на тези пациенти се регистрираха комплекс от орални изяви и

отклонения в буфериращия капацитет, pH и количеството на слюнката.

Заключение: Установи се специфична орална патология при пациенти с разстройства на храненето, както и липса на информираност за възможните орални усложнения и правилна превенция.

Приложение в практиката: Изготвиха се информационни брошури с насоки към пациентите с разстройства на храненето относно препоръчителните орално-хигиенните мерки и профилактика на най-често срещаните оралните изяви.

Научни публикации:

1. Margarita Hadzhieva, Ivanina Totova, Georgi Tomov Oral manifestations in a patient with bulimia – case report. сборник „Наука и младост – 2023 МУ Пловдив“.2023; 1: 179 - 181

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Полипрагмазия при хронично болни в условията на COVID-19“

Ръководител на проекта: доц. Даниела Грекова-Кафалова, дф¹

Водещ изследовател: ас. Евелина Гавазова¹

Членове на изследователския екип: гл. ас. Радиана Стайнова, дф¹

Базова организация: Медицински университет – Пловдив

1. Фармацевтичен факултет, Катедра по фармацевтични науки

Цел: Цел на настоящото проучване е фармако-социално анализиране на влиянието на пандемията от COVID-19 върху лекарствената употреба при пациенти с хронични заболявания.

Материал и методи: Охарактеризиране на данни за предписането на ЛП при пациенти със съпътстващи заболявания, лекувани от COVID-19. Анализирани са 200 предписания чрез DDD методологията на СЗО. Проведено е и анкетно проучване за оценка на полипрагмазията сред възрастни пациенти.

Резултати: Изчислена е Дефинираната дневна доза (DDD) 50 лекарства, сред които са антибактериални лекарствени продукти, глюокортикоиди, бронходилататори, муколитици, нестероидни противовъзпалителни лекарства, антихистамини, лекарства, влияещи върху гастроинтестиналния тракт, лекарства за лечение на сърдечно-съдови заболявания, железни препарати и други. Бактериалните инфекции рядко са усложнения на курса на инфекция с нов коронавирус, затова повечето пациенти с COVID-19, особено при леки и умерени случаи, не се нуждаят от антибиотична терапия. Въпреки това, антибиотиците бяха идентифицирани в 74,3% от случаите. Над половината от респондентите (54%) съобщиха, че приемат от 5 до 8 лекарства на ден, следвани от тези, които приемат повече от 9 (33%).

Заключение: Анализът на предписанията по време на COVID-19 рецепти дава представа за консумацията на лекарствени продукти, както и дава възможност за идентифициране на нерационални практики на предписване.

Приложение в практиката: Идентифицираната неподходяща полипрагмазия при лечението на пациенти застрашени от двойната заплаха от тежко протичане и усложнен COVID-19 и хронични заболявания показва необходимост от вземане на мерки за ограничаване на нейните негативни въздействия. Препоръчителната стратегия за управление на полипрагмазията е подпомагане усилията на лекуващите лекари чрез въвеждане в практиката на валидиран метод за преглед на лекарствата (medication review).

Научни публикации:

1. Гавазова Е, Стайнова Р, Грекова-Кафалова Д. Фармакоикономически преглед на диагностичните и терапевтични подходи за лечение на COVID-19. Научни трудове на СУБ-Пловдив - Серия Г. Медицина, фармация и дентална медицина.
2. Gavazova E, Staynova R, Grekova- Kafalova D. Managing Polypharmacy Through Medication Review Tools – Pros and Cons. Folia medica.

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Проспективно проучване за оценка на диагностични и прогностични зависимости между клиничния изход от оствър исхемичен мозъчен инсулт при пациенти, лекувани с интравенозна тромболиза и показатели от КТ-перфузия на главен мозък“

Ръководител на проекта: проф. д-р Николета Трайкова-Джамбазова, дм¹

Водещ изследовател: д-р Ерай Халил^{2,3}

Членове на изследователския екип: д-р Костадин Чомпалов, дм^{2,3}; д-р Борислава Атанасова^{2,3}; д-р Мирослава Христова^{2,3}; д-р Нели Атанасова¹

Базова организация: Медицински университет – Пловдив

1. УМБАЛ „Св. Георги“, гр. Пловдив, Отделение по образна диагностика
2. УМБАЛ „Св. Георги“, гр. Пловдив, Клиника по нервни болести
3. Медицински факултет, Катедра по неврология

Цел: При пациенти с оствър исхемичен инсулт, да се проучи кои показатели от диагностичната КТ-перфузия на главен мозък могат да бъдат сензитивни и специфични предиктори за клиничния изход на заболяването, оценен със скали за неврологичен дефицит.

Материал и методи: Изследвани са 30 пациенти с оствър исхемичен инсулт, лекувани чрез интравенозна тромболиза след проведена КТ-перфузия

Резултати: При пациенти, постъпили със симптоми на оствър исхемичен инсулт бе проведена нативна, КТ на главен мозък, както и КТ-перфузия с изчисляване на стойностите на показателите CBV, CBF, MTT, Tmax и TTP. Пациентните бяха оценени по скалите за неврологичен дефицит NIHSS, mRS и Barthel Index и лекувани чрез интравенозна тромболиза. Амбуторно проследяване на пациентните се извърши на 3-ти месец и 1-ва година, когато се проведе и контролна КТ на главен мозък. Предварителните резултати показват висока сензитивност и

специфичност на показателите CBV и CBF относно крайния обем на некротизираната мозъчна тъкан при остръ исхемичен инсулт, както и високата специфичност и сензитивност на показателите Tmax и MTT относно обема на пенумбрата.

Заключение: намалени стойности на показателите CBV и CBF от КТ-перфузия в голям обем от мозъчна тъкан са свързани с по-тежък неврологичен дефицит на 1-ва година от съдовия инцидент. Резултатите са предварителни и могат да бъдат обект на промяна с натрупването на допълнителни данни и продължаването на анализа. Крайните заключения ще бъдат формулирани след завършване на цялостното изследване и анализ на всички събрани данни.

Приложение в практиката: Предлага се използването на показателите от КТ-перфузия на главен мозък при пациенти с остръ исхемичен инсулт като предиктори на краткосрочна и дългосрочна прогноза.

Научни публикации:

1. Halil E. CT perfusion – an up-to-date element of the contemporary multimodal diagnostic approach to acute ischemic stroke. *Folia Medica*. 2023 Aug 31;65(4):531–8.
2. Halil E., Atanassova B., Hristova M., Chompalov K., Traikova N., Atanassova P. Computed tomography perfusion as a method for selection of potential candidates for intravenous thrombolysis in acute ischemic stroke – presentation of clinical cases. *Bulgarian Neurology*, 2023 Vol.24 No. 1; 36-39.

Оценка за изпълнение на проекта: *Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.*



Тема: „Приложение на (био)принтирането в персонализираната медицина – етични, социални и правни аспекти“

Ръководител на проекта: доц. Десислава Бакова, дм¹

Водещ изследовател: д-р Добромира Шопова, дм²

Членове на изследователския екип: проф. д-р Мария Семерджиева, дм¹; проф. д-р Виктория Сарафян, дмн³; доц. д-р Стефан Златев, дм²; доц. Момчил Мавров, доктор по право¹; ст. преп. Анна Михайлова, дф¹; ст. преп. Петя Каснакова, доктор по управление на здравните грижи¹; гл. ас. Антония Янева, дм⁴; гл. ас. Мария Христозова, доктор по право¹; гл. ас. Йордан Сбирков, дб³; гл. ас. Николета Парахулева, дм⁵; Васил Будев⁶; Никол Харизанова⁷; Сали Ленен⁶

Базова организация: Медицински университет – Пловдив

1. Факултет по обществено здраве, Катедра по управление на здравните грижи
2. Факултет по дентална медицина, Катедра по протетична дентална медицина
3. Медицински факултет, Катедра по медицинска биология
4. Факултет по обществено здраве, Катедра по медицинска информатика, биостатистика и електронно обучение
5. Медицински факултет, Катедра по акушерство и гинекология
6. Факултет по дентална медицина, студент
7. Медицински факултет, студент

Цел: Да се установят етични, социални и правни норми на (био)принтирането в персонализираната медицина.

Материал и методи: Извърши се сравнителен анализ на литературата за разпространение и приложение на (био)принтирането. Бяха разработени авторски анкетни карти за проучване информироваността и нагласите на лекари, дентални лекари и фармацевти относно приложението на (био)принтирането в персонализираната медицина, както и нагласите на потенциални пациенти и обществото.

Резултати: Експертни и високоспециализирани научни изследвания за приложение на (био)принтирането се осъществяват

ефективно в областта на медицината, денталната медицина и фармацията. Установихме някои значими възможности: по-добро осигуряване процесите на трансплантирана, отпечатване на аналогични органи или тъкани, намаляване на вероятността от отхвърляне на трансплантирани органы или тъкани, преодоляване на половите различия при трансплантирана, отстраняване на вродени дефекти на различни тъкани и органи, създаване на 3D модели за хирургично обучение на млади лекари и тестване на нови хирургични методи. Промяната на парадигмата от конвенционална към персонализирана медицина, която се основава в голяма степен на (био)принтирането, се очаква да окаже значително позитивно влияние върху качеството на живот на пациентите.

Заключение: 3D (био)принтирането има потенциала да повлияе на широк спектър от здравословни проблеми. Чрез въвеждането на принтерните технологии значително ще се намалят огромните финансови здравни разходи.

Приложение в практиката: Създаването на ясни регуляторни механизми (напр. етичен стандарт; законови и подзаконови нормативни актове) ще регламентира хуманния подход и ще намали риска от възникването на значими проблеми, свързани с приложението на биопринтирането в персонализираната медицина.

Научни публикации:

1. Shopova D, Mihaylova A, Kasnakova P, Yaneva A, Hristozova M, Sbirkov Y, Sarafian V, Semerdjieva M, Bakova D. (BIO) PRINTING IN MODERN MEDICAL EDUCATION. In ICERI2022 Proceedings 2022 (pp. 7157-7161). IATED.
2. Shopova D, Yaneva A, Bakova D, Mihaylova A, Kasnakova P, Hristozova M, Sbirkov Y, Sarafian V, Semerdzhieva M. (Bio) printing in Personalized Medicine—Opportunities and Potential Benefits. Bioengineering. 2023 Feb 23;10(3):287. (**IF=4.6**)
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4. Yaneva A, Shopova D, Bakova D, Mihaylova A, Kasnakova P, Hristozova M, Semerdjieva M. The Progress in Bioprinting and Its Potential Impact on Health-Related Quality of Life. Bioengineering. 2023 Aug 1;10(8):910. (**IF=4.6**)

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6. Христозова М, Шопова Д, Михайлова А, Мавров М, Бакова Д. Законодателна рамка на ЕС за регулиране на 3D биопринтирането в медицината. Сборник доклади от научна конференция „Знание, наука, иновации, технологии”, Велико Търново, 29.09.2023.
7. Христозова М, Шопова Д, Михайлова А, Янева А, Каснакова П, Мавров М, Семерджиева М, Бакова Д. Етично и правно регулиране в здравеопазването. Издателство FASTPRINTBOOKS, Пловдив, 2023 ISBN: 978-619-236-462-5
8. Шопова Д, Михайлова А, Сбирков Й, Златев С, Реджеб М, Янева А, Каснакова П, Христозова М, Сарафян В, Семерджиева М, Бакова Д. Монография: Приложение на биопринтирането в здравеопазването. Издателство FASTPRINTBOOKS, Пловдив, 2023 ISBN: 978-619-236-463-2

Оценка за изпълнение на проекта: Проектът е приключи навреме, реализиран е успешно с добра публикационна активност.



Тема: „Информационен портал на най-честите хирургични заболявания в детската възраст“

Ръководител на проекта: проф. д-р Пенка Стефанова-Пеева, дм^{1,2}

Водещ изследовател: проф. д-р Пенка Стефанова-Пеева, дм^{1,2}

Членове на изследователския екип: ас. д-р Бисер Иванов, дм^{1,2}; ас. д-р Димитър Дачев, дм^{1,2}; д-р Стоян Лупанов, дм^{1,2}; д-р Иван Кирев²; д-р Борислав Исаков²; д-р Николай Маврев²

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по пропедевтика на хирургическите болести, Секция по детска хирургия

2. УМБАЛ „Св. Георги“, гр. Пловдив, Секция по детска хирургия

Цел: Цел на проекта е създаване на електронен сайт, информационен портал за най-честите хирургични заболявания в детската възраст като: ингвинална херния, хидроцел, ретенция на тестиса, пъпни хернии, фирмози, анални фисури във вид на снимки, филми, диплянки и достъпна за пациентите информация.

Материал и методи: Използвани са информационни, статистически, клинични и описателни методи на изследване.

Резултати: Постигната е поставената цел на проекта да се създаде електронен сайт, като информационен портал за най-честите хирургични заболявания в детската възраст. Включени са заболявания като: ингвинална херния, хидроцеле, ретенция на тестиса, пъпна херния, фирмоза, анална фисура във вид на снимки и кратки информативни данни.

Заключение: Дигитализацията в здравеопазването води до подобряване на информативността на обществото, в случая родителите, при наличие на здравословен проблем. По този начин се подобрява качеството на оказваната медицинска помощ на децата с най-честите хирургични заболявания.

Приложение в практиката: Добрата и пълна информативност относно най-честите хирургически заболявания в детската възраст е сигурна основа във взаимоотношенията лекар-родител-

пациент и създава силна връзка на довери помежду им, което по-добрява качеството на предлаганата медицинска помощ.

Научни публикации: –

Оценка за изпълнение на проекта: Проектът е приключен с известни пропуски спрямо предвидените цел и задачи.



Тема: „Прилагане и изследване на концепцията за microlearning в обучението по „Ортопедия и травматология“

Ръководител на проекта: проф. д-р Владимир Ставрев, дмн¹

Водещ изследовател: ас. д-р Петър Молчовски¹

Членове на изследователския екип: д-р Валентин Петров¹;
д-р Румен Минчев¹; Татяна Зафирова¹

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по ортопедия и травматология

Цел: В настоящото проучване е представена концепцията за въвеждане на допълнителен модул за обучение по ортопедия и травматология чрез мобилни устройства и се мотивира нуждата от развитието и прилагането на тази и подобни технологии за подобряване на резултатите от практическата и теоретична подготовка на студентите по медицина.

Материал и методи: Проучването е извършено през зимен семестър на учебната 2022/2023 г. в Катедра по ортопедия и травматология на Медицински университет – Пловдив. Включени са всички студенти от два потока, с обучение на български и английски език.

Създаден е допълнителен модул за обучение на мобилни устройства. Материалите се състоят от малка по обем концентрирана важна информация по темите от програмата по ортопедия и травматология.

За доставяне на микро-лекциите към студентите е използван Moodle LMS с нейното мобилно приложение (Moodle mobile application). Обучението на студентите е извършено по предварително подгответена схема и контролирано с входящ, междинен и изходящ тест.

Резултати: Резултатите от междинния тест показват по-добро представяне и по-високи резултати при студентите, обучавани с комбинация от конвенционален и допълнителен мобилен метод.

В края на семестъра се наблюдава изравняване на резултатите, като все още лек превес се установява при групата, обучавана с комбинацията от двета метода за целия срок.

Заключение: Допълнителното обучение на дигитални устройства е икономичен, иновативен и надежден метод, който може да бъде включен в програмата по ортопедия и травматология.

Приложение в практиката: Новият „смесен“ метод на преподаване е част от новите образователни стратегии.

Научни публикации:

1. Molchovski, P., Petrov, V., Zafirova, T., Stavrev, V. and Tokmakova, K.: Additional Module for Teaching in Orthopedics and Traumatology Through Mobile Devices. THE JOURNAL OF THE BULGARIAN ORTHOPAEDICS AND TRAUMA ASSOCIATION. 60, 01 (Jul. 2023), 55–59. DOI:<https://doi.org/10.58542/jbota.v60i01.79>

Оценка за изпълнение на проекта: Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.



Тема: „Влияние на COVID-19 инфекцията при пациенти с ревматични заболявания и нуждата от отдалечен достъп до медицински грижи по време на пандемията“

Ръководител на проекта: проф. д-р Анастас Баталов, дм¹; доц. д-р Росица Димова, дм²

Водещ изследовател: ас. Александар Маринков¹

Членове на изследователския екип: доц. д-р Росица Каракилова, дмн¹; гл. ас. Пламен Тодоров, дм¹; гл. ас. Величка Попова, дм¹; гл. ас. Згуро Баталов, дм¹; инж. Татяна Боева, дми³; Цветелин Колев⁴; Константин Баталов⁴

Базова организация: Медицински университет – Пловдив

1. Медицински факултет, Катедра по пропедевтика на вътрешните болести „Проф. д-р Антон Митов“
2. Факултет по общество здраве, Катедра по здравен мениджмънт и икономика на здравеопазването
3. Отдел „Учебна и научна документация“
4. Медицински факултет, студент

Цел: Оценка на риска пациентите с ревматични заболявания (РЗ) да се заразят с COVID-19, тежестта на протичането и въздействието на имуносупресивна терапия чрез електронна платформа, онлайн проучване и клинично наблюдение.

Материал и методи: Чрез обсервационно, крос-секционно онлайн проучване събрахме данни от 1288 пациенти с РЗ, използвайки специално разработена уеб-базирана платформа. От участниците 81,6% са жени със средна възраст 47,03 години. IBM SPSS Statistics v. 25.0 беше използвана за анализ, използвайки описателна статистика, логистична регресия и метод на дървото на решенията (CRT) при ниво на значимост $P < 0,05$.

Резултати: Сред пациентите с РЗ 28,80% са преболедували COVID-19, като 85,60% са на домашно лечение, а 1,20% са на интензивно лечение. Обичайните лечения на РЗ включват JAK инхибитори ($n = 537$) и кортикоステроиди ($n = 345$). Повечето пациенти (81%) са имали лек/умерен COVID-19, 13,50% тежко и 3,50% много тежко. Комуникацията с ревматолозите значително повлия

на удовлетворението, като комуникацията на място го увеличи с 452,8% в сравнение с тези, които не можаха да се свържат със своя ревматолог. Запазването/увеличаването на посещенията повишава удовлетвореността с 43,3%/94,6%. Проблемите с получаването на лекарства намаляват удовлетворението с 67,5%, а съществуващите заболявания го намаляват с 47,0%.

Заключение: Проучването подчертава развиващия се пейзаж на ревматологичните грижи по време на пандемията COVID-19, подчертавайки необходимостта от оптимизиране на отдалечения достъп и разработване на специфични алгоритми за индивидуална грижа за пациентите.

Приложение в практиката: Оптимизирането на дистанционното медицинско обслужване за пациенти с РЗ, като се застъпва за персонализирани алгоритми за справяне с индивидуалните нужди на пациентите, осигурявайки навременна и адекватна медицинска помощ по време и след пандемията.

Научни публикации:

1. Marinkov A, Dimova R, Karalilova R, Keskinova D, Bahariev D, Batalov K, Popova V, Batalov Z, Batalov A. THE COVID-19 PANDEMIC'S IMPACT ON RHEUMATIC DISEASE PATIENTS' SATISFACTION WITH ACCESS TO MEDICAL SERVICES; RHEI-D-23-00835R1. *Rheumatology International* (IF 4.0). ISSN 0172-8172

Оценка за изпълнение на проекта: *Проектът е приключил навреме, реализиран е успешно с добра публикационна активност.*



Project title: “Rapid microbiological diagnosis of genital infections in women and men – a comparative analysis”

Project director: Eli Hristozova¹

Leading scientist: Zoya Rachkovska¹

Research team: Prof. Marianna Murdzheva¹; Prof. Ekaterina Uchikova²; Assoc. Prof. Tihomir Derendziev¹; Tsonka Miteva-Katrandzieva³; Vida Georgieva⁴; Tsvetomir Pavlov⁵

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Medical Microbiology and Immunology "Prof. Dr. Elissay Yanev"
2. Faculty of Medicine, Department of Obstetrics and Gynecology
3. Faculty of Public Health, Department of Social Medicine and Public Health
4. University Hospital "St. George", Plovdiv, Laboratory of Microbiology
5. University Hospital "Pulmed", Plovdiv, Laboratory of Microbiology

Aim: Complex analysis of the genital microflora in men and women, diagnosis of dysbiosis and sexually transmitted infections and evaluation of the benefits of the simultaneous application of molecular biological and classical microbiological methods.

Materials and methods: 121 materials were examined – 72 vaginal and 49 urethral secretions with routine tests and Femoflor Screen and Androflor Screen. Separately, 51 vaginal and cervical secretions were tested for HPV (6,11,16,18) with HPV Quant-4.

Results: Two studies were performed by RT-PCR Femoflor Screen. In the first screening of genital infections in symptomatic non-pregnant women, it showed that 2/3 of women up to 30 years of age had severe dysbiosis from *G. vaginalis* (57.1%), and vaginal candidiasis was predominant in normocenosis women. The second study found that the most common cause of candidiasis was *C. albicans* (n = 13, 76%).

Anandroflor Screen showed that in men the predominant opportunistic myctoflora were staphylococci (n = -31.63%), and the most common pathogen was *C. trachomatis* (n = 6, 12%). Mixed infection or increased levels of transient flora were found in men with *G. vaginalis*.

In the human papillomavirus test, HPV-16 was the dominant variant with a morbidity of 9.8%.

Conclusion: Classic and modern pCR methods for screening genital infections should complement each other due to the need for a complex approach in diagnosis and interpretation.

Practical applications: Routine implementation of the slips in pre-hospital/hospital care. It is proposed that the combined study become part of a clinical path to the clinics of Urology and Obstetrics and Gynecology at the “St. George” University General Hospital.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Research area: Biomedical
Contract: Project № NO-08/2020

Project title: “Microbiota and pathophysiology of depression with comorbid alcohol use disorder”

Project director: Prof. Stefan Popov¹

Leading scientist: Andriana Kakanakova¹

Research team: Mladen Mantarkov¹; Ivo Mitrev¹; Assoc. Prof. Sevdalina Kandilarova¹; Prof. Drozdstoy Stoyanov¹; Prof. Nikolay Sirakov²; Prof. Nonka Mateva³; Maria Ivanovska⁴

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Psychiatry and Medical Psychology
2. Faculty of Medicine, Department of Diagnostic Imaging
3. Faculty of Public Health, Department of Medical Informatics, Biostatistics and E-learning
4. Faculty of Medicine, Department of Medical Microbiology and Immunology
“Prof. Dr. Elissay Yanev”

Aim: To research the differential diagnostic value of neuroimmuno-logical and neuroimaging markers in depression and alcohol use disorder.

Material and methods: 3 patients diagnosed with depression and comorbid alcohol use disorder and 10 patients diagnosed with depression were evaluated.

Results: Depression, and in particular Major Depressive Disorder (MDD), is among the diseases of the highest social importance and is one of the leading causes of psychiatric consultation in outpatient practice. There is a serious comorbidity between MDD and alcohol use disorder reaching 28%. Recruiting patients from a population group with comorbid Alcohol Use Disorder and Major Depressive Disorder has proved extremely difficult which resulting in an inability to meet the intended patient numbers. The implementation of the second part of the study: immunological research is impossible to be carried out in Bulgaria, within the framework of MU of Plovdiv or another institution, as of the time of holding the project.

Conclusion: The preliminary data from the conducted study repeat the relations observed in other studies between biochemical

processes in the central nervous system (registered by spectroscopy) and pathophysiological processes (registered by functional MRI), as well as with the peripheral immune response (through biological tests in peripheral blood).

Practical applications: Neuroimmunological and neuroimaging markers can be used in the evaluation in depression and alcohol-related disorder.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Research area: Biomedical / Therapeutic
Contract: Project № NO-11/2020

Project title: “Diagnostic and prognostic genetic markers in acute myeloid leukemia”

Project director: Prof. Veselina Goranova-Marinova^{1,4}

Leading scientist: Ivan Zhelyazkov^{2,5}

Research team: Katya Sapunarova^{1,4}; Vasko Graklanov^{1,4}; Hristina Ivanova^{1,4}; Hristo Ivanov^{2,5}; Alexander Linev^{2,5}; Prof. Vili Stoyanova^{2,5}; Prof. Zhanet Grudeva-Popova^{1,3}

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, First Department of Internal Medicine, Section of Hematology
2. Faculty of Medicine, Department of Paediatrics and Medical Genetics "Prof. Dr. Ivan Andreev"
3. Faculty of Medicine, Department of Clinical Oncology, Section of Medical Oncology
4. University Hospital "St. George", Plovdiv, Clinic of Hematology
5. University Hospital "St. George", Plovdiv, Department of Medical Genetics

Aim: To study the frequency of the most common genetic mutations in newly diagnosed acute myeloid leukemia (AML) patients detected by digital droplet PCR and to analyze their prognostic significance.

Patients and methods: Between April 2020 and April 2023, a cohort of 83 patients diagnosed with Acute Myeloid Leukemia (AML) was studied. Of these, 38 (45.8%) were male and 45 (54.2%) were female, with an average age of 59.4 ± 16.3 years. Genetic mutations identified within the cohort were as follows: AML1-ETO (RUNX1-RUNX1T1) – in 8 (9.7%); PML-RAR α – 2 (2.4%), BCR-ABL1 – 1 (1.2%), SET-CAN – 1 (1.2%), MLL – 6 (7.5%), FLT-3 – ITD – 8 (9.7%), FLT-3 – TKD – 4 (4.8%), NPM – 7 (8.4%). Patients with established genetic abnormalities were compared with those without mutations in terms of demographic characteristics, AML subvariant (de novo/secondary), clinical and laboratory parameters, type of treatment, therapeutic response and overall survival.

Results: No statistically significant difference was found by demographic characteristics. MLL+, FLT-3+, and NPM+ mutations were

predominantly found in de novo AML. The highest frequency of therapeutic response was found in patients with AML-M3, PML-RAR a+ (2/2), AML1-ETO in 6/8 and NPM+ in 5/6. Patients with FLT-3+ and MLL+ have the worst prognosis: MS of 7 months and 2 months, respectively. Three-year overall survival in NPM+ was 64% and AML1-ETO was 48%.

Conclusion: Data from the analysis confirm the favorable prognostic value of NPM+, which is associated with a high frequency of therapeutic response and long survival. We confirmed the most unfavorable prognosis in patients with MLL+ mutations, as well as in FLT-3+, despite the possibility of targeted therapy.

Project performance evaluation: The project is completed.



Project title: “Targeted genomic profiling for diagnosis and behavior in colorectal carcinoma”

Project director: Prof. Vili Stoyanova^{1,2}

Leading scientist: Dimitar Dimitrov¹

Research team: Prof. Zhanet Grudeva-Popova^{3,4}; Hristo Ivanov^{1,2}; Gabriela Raycheva^{3,4}; Neli Miteva-Marcheva^{1,2}; Aleksandar Linev²; Ivan Zheliaskov²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Paediatrics and Medical Genetics "Prof. Dr. Ivan Andreev"
2. University Hospital "St. George", Plovdiv, Department of Medical Genetics,
3. Faculty of Medicine, Department of Clinical Oncology
4. University Hospital "St. George", Plovdiv, Clinic Medical Oncology

Aim: Identification of the individual tumor genetic profile in colorectal carcinoma patients and monitoring the concentration of patient-specific prognostic genetic markers in circulating free tumor DNA (cfctDNA) before and during therapy.

Materials and methods: Sequencing of cfDNA samples isolated from 48 CRC patients. Design and synthesis of primers and probes followed by digital droplet PCR for quantification of the initiating mutation was performed.

Results: Optimization and validation of a protocol for isolation of cfDNA from peripheral blood was performed. Somatic and germline variants significant for the development, progression and treatment of colorectal carcinoma were found. Somatic mutations associated with the development and progression of CRC: ARID1A/c.3999_4001delGCA found in 95% of patients, with mutation allele frequency between 2.13%–4.02%; PARP4/c.3509C>T in 72% of patients, mutation allele frequency between 6.11%–21.26%; CBL/c.1380_1382delTGA in 95% of patients, frequency between 1.96%–3.54%; IRS2/c.2102_2104delCCG in 59% of patients, frequency 2.3%–4.69%; GATA6/c.996_998delCCA was found in 32% of patients with a frequency between 4.4%–5.26%. Germline variants carrying an increased risk of malignancies:

TP53/c.215C>G with frequency of 75% in the sequenced samples; AURKA/c.169A>G – 74% Germline variants associated with adverse drug reactions from chemotherapeutics: DPYD/c.85C>T with frequency of sequenced samples 94%; SLC22A2/c.808T>G – 85%.

Conclusion: Performing a liquid biopsy with subsequent sequencing enables establishment of somatic and germline variants.

Practical applications: Liquid biopsy has great potential for application in diagnostics, monitoring the effect of therapy and the evolution of oncological diseases.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Project title: "Preconception care for more healthy families"

Project director: Prof. Rumen Stefanov¹

Leading scientist: Eleonora Hristova-Atanasova¹

Research team: Assoc. Prof. Georgi Iskrov¹; Assoc. Prof. Ralitsa Raycheva¹; Viktoriya Mandova¹

Organization unit: Medical University of Plovdiv

1. Faculty of Public Health, Department of Social Medicine and Public Health

Aim: Improving the health culture and knowledge of family planning and preconception care among modern Bulgarian families.

Materials and methods: A qualitative study conducted among 20 women aged 18 to 49 years was performed between May and July 2022. Two focus groups were used with mixed samples of nulligravida, pregnant, and postpartum women.

Results: The participants thought that the Internet and their obstetrician-gynecologist were the only places where they could learn about getting pregnant. Only two of them discussed their PC plans with their physicians. Women pointed out that general practitioners (GPs) need to be more proactive in promoting PC. All respondents outlined the need for a web-based educational platform that could serve as a primary source of health information for future families.

Conclusion: The role and functions of GPs in the continuum of PC should be reconsidered. We recommend targeted educational measures for all stakeholders, including women and GPs. In this regard, an easily accessible, knowledge-based web platform could enhance Bulgarian women's awareness and perceptions of PC.

Practical applications: A web-based educational platform was created with the goal of enhancing the health of reproductive-age women, considering the requirements of the intended audience. A domain name and 10-year hosting package were obtained (<https://iskamdete.eu/>).

Project performance evaluation: *The project was duly completed and realized successfully with good publication activity.*



Project title: “Fetal morphology. Fetal brain development. Physiology and pathology of the nervous system”

Project director: Prof. Tanja Kitova¹

Leading scientist: Prof. Tanja Kitova¹

Research team: Prof. Ekaterina Uchikova²; Prof. Kichka Velkova³; Prof. Magdalena Stoeva³; Assoc. Prof. Kristina Kilova⁴; Angel Tenev⁵; Nader Ahmad⁵; Atanas Davarski⁶; Donka Popova³; Maria Godwin-Kingsley⁵

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Anatomy, Histology and Embryology
2. Faculty of Medicine, Department of Obstetrics and Gynecology
3. Complex of Translational Neuroscience
4. Faculty of Public Health, Department of Medical Informatics, Biostatistics and E-learning
5. Faculty of Medicine
6. Faculty of Medicine, Department of Neurosurgery

Aim: Using functional magnetic resonance tomography (FMRI) on pregnant women to evaluate fetal development by examining fetal brain structures, skull and internal organs.

Results: All diagnoses are the result of the multidisciplinary approach in proving brain malformations, malformative syndromes. The application of functional nuclear magnetic resonance enabled the diagnosis of CNS anomalies – 26%, such as hydrocephalus and neural tube defects in the fetus. Abnormalities of the placenta concerning the presentation and morphology were diagnosed in 52% of the studies, 22% of those studied with malformative syndromes of the fetus. Material for future scientific research was collected and research methodology was improved, which in principle is hampered by the movement of the fetus and the size of the fetus in the different gestational weeks of research.

Conclusion: Despite the small size of the study group, the results support the use of FMRI in suspected fetal central nervous system pathology detected using prenatal ultrasonography. Confirming additional malformations helps parents make a definitive decision on the

pregnancy's outcome, the results form an important stage in the multidisciplinary diagnosis of congenital abnormalities such as neural tube defects, chromosomal, cardiac abnormalities and rare syndromes.

Practical application: The results obtained are of applied and theoretical importance as they may be helpful in prenatal diagnosis, embryology, and embryonic organogenesis.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Project title: “Mutational and expression profile of protein-coding genes in children with specific language impairment”

Project director: Prof. Ivan Ivanov¹

Leading scientist: Iglika Sotkova²

Research team: Hristo Ivanov^{1,3}; Prof. Vili Stoyanova^{1,3}; Prof. Iliyana Pacheva^{1,2}; Dimitar Dimitrov¹; Neli Miteva-Marcheva^{1,3}; Elena Timova²; Alexander Linev³; Ivan Zhelyazkov³; Yurka Doneva

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Pediatrics and Medical Genetics “Prof. Dr. Ivan Andreev”
2. University Hospital “St. George”, Plovdiv, Department Pediatrics and Genetic Diseases
3. University Hospital “St. George”, Plovdiv, Department of Medical Genetics

Specific language impairment (SLI) is a neurodevelopment disorder affecting 7% of pre-school children, characterized by delayed speech development despite normal non-verbal intelligence. The disorder's genetic etiology is complex, involving multiple genetic and environmental risk factors.

Aim: This project aims to characterize the mutational and expression profile of protein-coding genes in children with SLI.

Material and methods: The study involved 40 children with SLI and 24 healthy controls. RNA sequencing analysis and whole exome sequencing were performed.

Results: 61 genes with differential expression were identified in children with SLI, mainly related to immunity and cellular regulation. GINS2 showed the greatest difference in expression. About 330 variants with a global frequency in gnomAD below 0.01% were identified in the SLI group.

Conclusion: Significant abnormalities in gene expression were found in children with SLI compared to healthy controls. Altered expression of GINS2 and dysregulated immune-related pathways were identified. A significant proportion of the variants identified by exome

sequencing associated with language deficits in our patients are implicated in pathways related to the sensory processing of sound. Variants in these genes may subtly interfere with the normal development and functioning of neural networks in areas related to language skills, resulting in impaired language abilities. Further functional studies are needed to fully understand the relationship between these mutations and SLI.

Practical applications: A protocol for RNA isolation from peripheral blood and a ddPCR gene expression analysis protocol were implemented.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Project title: "Traumatic brain injury – alternatives for quick and reliable diagnosis"

Project director: Assoc. Prof. Svetlozar Spasov¹

Leading scientist: Stela Yancheva^{1,5}

Research team: Assoc. Prof. Maria Kazakova²; Assoc. Prof. Georgi Pavlov³; Assoc. Prof. Iliya Bivolarski⁴; Ivan Tsranchev^{1,5}; Valentin Dichev²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Forensic Medicine and Deontology
2. Faculty of Medicine, Department of Medical Biology
3. Faculty of Medicine, Department of Anesthesiology, Emergency and Intensive Care Medicine
4. Faculty of Medicine, Department of General and Clinical Pathology
5. University Hospital "St. George", Plovdiv, Department of Forensic Medicine

Aim: To investigate the diagnostic value of the markers p-Tau and NF-L by examining their concentration in cerebrospinal fluid and plasma, in parallel with β -APP in patients and deaths with traumatic brain injury (TBI).

Materials and methods: Plasma and cerebrospinal fluid (CSF) from 20 cases of patients with isolated TBI and brain tissue from 12 TBI deaths were studied, and 11 cases of non-traumatic deaths were employed as a control group.

Results: Plasma pTau levels are higher in TBI patients. Examination of NF-L levels in CSF and plasma revealed higher levels of NF-L in the control group compared to TBI patients. When evaluating the significance of high levels of NF-L and p-Tau in CSF and plasma in the studied group of patients with an unfavorable outcome in the first 6 months after TBI, no statistically significant correlation was observed. Immunohistochemical examination of 4 brain sections from TBI survivors revealed significantly higher β -APP expression with greater injury severity.

Conclusion: Elevated plasma pTau levels are indicative of an existing TBI within the first 24 hours. NF-L levels in plasma and

cerebrospinal fluid cannot be used to diagnose TBI in the first 24 hours. Immunohistochemical study of β-APP expression in brain tissue correlates with the severity of trauma.

Practical applications: Investigation of p-Tau concentration in plasma can serve for early diagnosis of TBI in patients. Investigation of p-Tau plasma levels and β-APP can serve to solve forensic cases of particular complexity.

Project performance evaluation: The project is completed successfully with significant insufficiency regarding the aim and tasks set in the project.



Project title: "Morphofunctional aspects of testicular spermato- and steroidogenesis in melatonin deficiency conditions"

Project director: Prof. Yvetta Koeva¹

Leading scientist: Darina Barbutska¹

Research team: Prof. Katerina Georgieva²; Prof. Yana Tchekalarova³; Aneliya Petrova¹; Delyana Davcheva⁴; Georgi Nanov⁵

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Anatomy, Histology and Embryology
2. Faculty of Medicine, Department of Physiology
3. Bulgarian Academy of Sciences, Institute of Neurobiology
4. Faculty of Medicine, Department of Clinical Laboratory
5. Faculty of Medicine, student

Aim: To investigate the role of melatonin in testicular spermato- and steroidogenesis in a melatonin deficiency model in rats of different ages.

Material and methods: Testicular fragments from 5-, 16-, and 20-month-old male rats divided into two groups: post-pinealecstasy and SHAM were used. The morphological changes were investigated by staining with Hematoxylin and Eosin and Heidenhain's Azan. The expression of Cyclin D1, Bcl6, BDNF/TrkB, SubstanceP, NeurokininB, tACE was studied by immunohistochemistry. The serum concentration of testosterone, LH and FSH was monitored by ELISA method.

Results: The routine histological technique revealed age-related changes in the testis at 5, 16 and 20 months, with no difference between the two groups. A statistically significant increase in the immunoexpression of Cyclin D1 was found in the Leydig cells /LC/ of 20-month-old pinealectomised animals. A more pronounced expression of BDNF/TrkB was demonstrated in LCs of animals with removed pineal glands in the three age groups. Increased immunoexpression for NeurokininB and SubstanceP was found in the testis of 20- and 16-month old rat after pinealecstasy. A statistically significant increase in tACE immunoreactivity was found in the LCs of 5- and 16-month-old

rats from the control group. There was no statistically significant difference in the serum levels of testosterone, LH and FSH between the pinealecotmised animals and the controls.

Conclusion: The obtained results confirm the role of melatonin in testicular morphology and function.

Practical applications: Proposing of more effective approaches to influence the aging processes and to improve the quality of life of the elderly population.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: “Biochemical markers for assessment of osseointegration of titanium implants”

Project director: Prof. Tatyana Vlaykova^{1,3}

Leading scientist: Teodora Stankova¹

Research team: Ivan Nachkov²; Nikola Stamenov²; Chief Assist. Prof. Iliyan Dimitrov¹; Assist. Prof. Katya Stefanova¹; Tanya Tacheva³; Tsvetelina Atanasova⁴; Georgi Georgiev⁵; Radka Cholakova²

Organization unit: Medical University of Plovdiv

1. Faculty of Pharmacy, Department of Medical Biochemistry
2. Faculty of Dental Medicine, Department of Periodontology and Oral Mucosa Diseases
3. Trakia University, Stara Zagora, Faculty of Medicine, Department of Medical Chemistry and Biochemistry
4. Faculty of Dental Medicine, student
5. Faculty of Medicine, student

Aim: To investigate the possible role of key molecules of bone metabolism as serum biomarkers for biochemical assessment of the degree of osseointegration following titanium dental implants placement.

Results: Our study included 100 patients who received titanium implants and were followed up at 1, 3/4, and 6 months through radiograph testing and measurement of primary and secondary stability. Accordingly, the patients were classified into three groups: those who successfully accepted the implants, with peri-implantitis, and with implant failure. Serum levels of indicators of bone metabolism, mineral homeostasis and lipid profile were determined. Patients who rejected the implants had statistically significantly higher serum concentrations of undercarboxylated osteocalcin (UcOC) while lower levels of osteoprotegerin and magnesium compared to those who accepted the implants and those who developed peri-implantitis. Significant positive correlations were established between the levels of osteoprotegerin and magnesium as well as between RANKL and UcOC in the entire study cohort. A higher RANKL/osteoprotegerin index and LDL-cholesterol levels were found in patients who rejected implants compared to those who accepted them. Both groups with post-implant

complications showed higher concentrations of MMP-8. No statistically significant differences were observed among the three compared groups regarding serum levels of 25-hydroxyvitamin D, osteocalcin, fetuin-A, HDL-cholesterol, and calcium.

Conclusion: The established differences in the serum levels of osteoprotegerin, RANKL, UcOC, MMP-8, and their correlations with parameters of bone and mineral metabolism underscore their potential role in the process of osseointegration after dental implant placement.

Practical applications: Our results could help in patient selection and in prediction of the response to implantological treatment.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Analysis and optimisation of protocols for tissue differentiation of human adipose-derived stromal cells into cartilage tissue for the needs of tissue engineering, regenerative medicine and surgery”

Project director: Regina Hatar¹

Leading scientist: Parvan Voinov²

Research team: Chief Assist. Prof. Yordan Sbirkov³; Prof. Victoria Sarafian³

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Propedeutics of Surgical Diseases
2. Unihospital, Panagyurishte, Bulgaria
3. Faculty of Medicine, Department of Medical Biology

Aim: To analyse and optimise protocols for differentiation of adipose-derived human mesenchymal stem cells (MSCs) into chondrocytes for the needs of tissue engineering, regenerative medicine and surgery.

Materials and methods: Established MSC cell lines; adipose tissue from donors who have undergone aesthetic procedures at the Department of Plastic and Reconstructive Surgery; isolation of adipose-derived SVF (stromal vascular fraction) cells including MSCs; cell culture; cyto/histochemical analyses of induction of chondrogenesis by staining for glycosaminoglycans with Alcian blue and Safranin O; RT-qPCR analysis of chondrocyte markers.

Results: New methods/laboratory protocols for the university and the country were developed and validated for: 1) the isolation and 2) the *in vitro* cell culturing of adipose-derived SVF cells; 3) induction of chondrocyte differentiation; 4) cyto/histochemical and morphological validation of chondrocyte differentiation; 5) optimisation of protocols for expansion of differentiated chondrocytes. After induction of chondrocyte differentiation for 3 weeks, intense alcian blue staining and increased gene expression of the chondrocyte markers Aggrecan and Sox9 were observed. In addition, the project provided the

opportunity for pilot studies in a potential second stage of the project – 3D bioprinting of SVF cells.

Conclusion: The potential for *in vitro* differentiation of chondrocytes from autologous adipose tissue is demonstrated. This provides the opportunity to grow sufficient number of chondrocytes for subsequent 3D bioprinting.

Practical applications: This is a pilot study, thanks to which a number of protocols with practical applications in laboratory experimental work have been developed. This lays the foundation of subsequent projects in the field of tissue engineering.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Effect of biomimetic self-assembling peptides, fluorides and caries infiltration on initial lesions on smooth surfaces in children”

Project director: Prof. Ani Belcheva¹

Leading scientist: Assist. Prof. Irina Uzunova-Raycheva¹

Research team: Elitsa Veneva¹; Tanya Nihtyanova-Grafalska¹; Svetla Petrova-Buchkova¹; Plamena Sapunarova¹; Kostadin Georgiev²; Assoc. Prof. Ralitsa Raycheva³; Iliyan Dobrev⁴; Prof. Dancho Danalev⁵

Organization unit: Medical University of Plovdiv

1. Faculty of Dental Medicine, Department of Pediatric Dentistry
2. Faculty of Dental Medicine, Department of Operative Dentistry and Endodontics
3. Faculty of Public Health, Department of Social Medicine and Public Health
4. University of Food Technologies – Plovdiv, Department of Microbiology
5. Chemical Technology and Metallurgical University – Sofia, Department of Biotechnology

Aim: To study the effect of application of contemporary methods and means for non-operative treatment of initial caries on smooth surfaces, based on experimental and clinical studies.

Material and methods: For the experimental tasks, 96 samples of orthodontically extracted premolars were prepared, randomly divided into four groups: Gr-P₁₁-4, Gr-CPP-ACFP, Gr-Icon, Gr-control. Artificial carious lesions were evaluated before and after demineralization and on the twenty-first day of application of a pH-cycling model in a biofilm reactor, by microhardness testing, SEM-analysis, and confocal microscopy. The clinical task included 44 patients with 176 initial lesions, treated and followed for 12 months. ANOVA test or non-parametric alternatives are used for statistical analysis.

Results: Experimental data obtained using the newly developed protocol showed that all tested materials have the ability to improve the condition of artificial enamel lesions. The SAP P₁₁-4 group showed a better effect compared to CPP-ACFP, caries infiltration and the control group, but with no statistically significant difference between them

($p > 0.05$). The preliminary results of the conducted clinical study showed that all three agents improve the condition of the lesions in combination with oral hygiene instructions.

Conclusion: SAP P₁₁₋₄, CPP-ACFP and the carious infiltration method are effective means of prevention and non-operative treatment of initial carious lesions on smooth surfaces in children.

Practical applications: The comparison between traditional remineralization, biomimetic regeneration, and resin infiltration as forms of non-invasive preventive treatment allows to choose the best clinical approach in treating the initial carious lesions and managing the carious process in children.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Project title: “Influence of selective androgen receptor modulators (SARMs) on the physical working capacity and their side effects in experimental rats”

Project director: Prof. Nikolay Boyadjiev¹

Leading scientist: Veselin Vasilev¹

Research team: Prof. Katerina Georgieva¹; Prof. Slavi Delchev²; Prof. Pepa Atanasova²; Chief Assist. Prof. Fanka Gerginska²; Prof. Tanya Deneva³; Desislava Arabadzhiyska³; Zaki Abdi⁴

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Physiology

2. Faculty of Medicine, Department of Human Anatomy, Histology and Embryology

3. Faculty of Medicine, Department of Clinical Laboratory

4. Faculty of Medicine, student

Aim: To examine the effects of SARMs in combination with endurance training and establish some of their side effects in rats.

Results: Following eight weeks of administration of ostarine or ligandrol, combined with endurance training, we found that they decreased the submaximal endurance of rats, but this effect was only present in training animals. Regarding maximal oxygen consumption, ostarine had no effect and ligandrol significantly decreased $\text{VO}_{2\text{max}}$. The effect of ligandrol was evident in the non-training rats, and was neutralized by exercise in the training rats. The two active substances did not affect maximal time to exhaustion and maximal sprinting speed. Ligandrol increased grip strength, while ostarine had no effect. Our results also showed that ostarine increased myostatin myogenic gene expression in m. gastrocnemius, and ligandrol decreased VEGF-A myogenic gene expression in the same muscle. Ostarine and ligandrol did not affect the oxygen-carrying capacity of the blood or the number of blood cells. Both substances caused adverse changes in the lipid profile, as ostarine increased the concentration of total cholesterol, while ligandrol also increased the concentration of triglycerides. The two non-steroidal representatives of SARMs lowered fasting

serum glucose concentration. Within the experimental period of 8 weeks, ostarine did not change the serum concentrations of gonadotropic hormones and testosterone. Ligandrol showed an adverse effect, significantly lowering the concentration of FSH and caused a pronounced tendency to decrease the concentration of testosterone.

Practical applications: The obtained results will enrich the information about SARMs as candidate therapeutics in various socially significant diseases.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: "Investigation of NGAL in urine as a marker of kidney damage in children with cancer undergoing chemotherapy"

Project director: Prof. Marya Spassova¹

Leading scientist: Petya Markova¹

Research team: Neofit Spasov¹; Prof. Tanya Deneva²; Zeyra Halil¹; Antonia Yaneva³

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Pediatrics and Medical Genetics "Prof. Dr. Ivan Andreev"

2. Faculty of Medicine, Department of Clinical Laboratory

3. Faculty of Public Health, Department of Medical Informatics, Biostatistics, and E-learning

Aim: To elucidate the role of urinary NGAL as an early marker of acute kidney injury in children with cancer undergoing chemotherapy

Material and methods: 40 children, a total of 116 chemotherapy cycles, were studied, with urinary NGAL levels measured before and 12 hours following the end of therapy. FEFi was also studied as a marker for the occurrence of tubular damage resulting from nephrotoxicity, as well as 30 children who finished their treatment more than a year ago, for chronic kidney disease.

Results: A statistically significant difference was observed in NGAL levels before and at the 12th hour following a chemotherapy cycle in patients who have completed or undergone their second ($Z = -2.908$, $p = 0.004$) and third cycle ($Z = -2.737$, $p = 0.006$), as well as in those with more than 4 chemotherapy cycles completed ($Z = -2.678$, $p = 0.007$). However, NGAL levels remained within their reference ranges. A statistically significant increase in the fractional excretion of phosphates at the 12th hour was also found, both after a single cycle and after more than one chemotherapy cycle. In the children who finished their chemotherapy more than one year ago, the stage of by the generally accepted criteria of KDIGO – was found in

11 of 30 children (36%), while elevated NGAL values in only two of them (6.6%).

Conclusion: NGAL, as a marker of nephrotoxicity, is nonspecific and unreliable. FEFi is highly specific for acute kidney injury, caused by nephrotoxic drug therapy.

Practical applications: It is suggested that FEFi be included in the routine follow-up of all patients undergoing chemotherapy with nephrotoxic drugs.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: “Investigating the capabilities of electro-impedance tomography as a clinical method for monitoring of the dynamics of pulmonary contusion in mechanically ventilated patients with thoracic trauma”

Project director: Prof. Chavdar Stefanov¹

Leading scientist: Ivaylo Minev¹

Research team: Prof. Nikoleta Traykova²; Teodora Gogova²; Emral Kyosebekirov¹

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Anesthesiology, Emergency and Intensive Care
2. University Hospital “St. George”, Plovdiv, Department of Image Diagnostics

Aim: To propose a methodology for real-time monitoring of the evolution of pulmonary contusion.

Materials and methods: The investigation includes computer tomography (CT) and electro-impedance tomography (EIT) data of 10 mechanically ventilated patients with pulmonary contusion, admitted to the Department of Anesthesiology and Intensive care, University General hospital “St. George” (Plovdiv, Bulgaria).

Results: Protocolized approach to the individual patient was created. Following CT scan analysis, a **level of interest** and reference points for electrodes positioning were defined. The raw EIT data was reconstructed in the individualized contour of the patient’s thorax. The spatial morphological sensitivity of the EIT to pulmonary contusion disposition was determined by comparative analysis between the lung areas on the CT image and the reconstructed EIT image taken at the corresponding level (conformity index > 0.82). The limitations for placing the EIT electrodes at levels different, than initially recommended by the producer are surmounted and indications for potential clinical application of EIT in conditions characterized by heterogeneously disseminated or solitary lesions occur.

Conclusion: The personalized approach reveals EIT potential to provide sufficient spatial resolution of pulmonary contusion, enhance real-time monitoring of lung function and morphology and support the optimization of mechanical ventilation, especially in case of heterogeneously disseminated or solitary lesions.

Practical applications: Protocol for personalized clinical application of EIT increasing the informational value of the method and supporting the optimization of the protective mechanical ventilation.

Hybrid method for image diagnostics and monitoring of the pathophysiological changes in ventilation and perfusion in pulmonary contusion.

Project performance evaluation: *The project is completed successfully with significant insufficiency regarding the aim and tasks set in the project.*



Project title: "Biological Activity Study of DIQ [1-(2-chlorophenyl)-6,7-dimethoxy-3-methyl-3,4-dihydroisoquinoline] Synthesized from Natural Amino Acids as a Derivative of Papaverine"

Project director: Assoc. Prof. Iliyana Stefanova¹

Leading scientist: Assist. Prof. Vera Nikolaeva Gledacheva¹

Research team: Chief Assist. Prof. Valeri Slavchev¹; Chief Assist. Prof. Mina Pencheva¹; Assoc. Prof. Stoyanka Nikolova²; Assoc. Prof. Darinka Dimitrova³; Chief Assist. Prof. Kremena Saracheva⁴

Organization unit: Medical University of Plovdiv

1. Faculty of Pharmacy, Department of Medical Physics and Biophysics
2. University of Plovdiv, Faculty of Chemistry, Department of Organic Chemistry
3. Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology
4. Faculty of Pharmacy, Department of Pharmacology and Drug Toxicology

Aim: To investigate the potential biological activity of DIQ[1-(2-chlorophenyl)-6,7-dimethoxy-3-methyl-3,4-dihydroisoquinoline] by influencing the bioelectrogenesis and mechanical activity of isolated gastric smooth muscles and effect on the cognitive and motor abilities of rats, compared to the reference papaverine molecule.

Material and methods: Following approval from the Bulgarian Food Safety Agency (BFSA) and the Ethics Committee, albino ICR mice and Wistar rats were utilized in the following methodologies: Grunewald's synthesis, "Isometric registration of contraction activity of isolated tissues", "Shuttle-Box Active Avoidance", and "Step-Down Passive Avoidance".

Results: DIQ was synthesized as a papaverine derivative of natural amino acids. Muscle relaxant activity and low toxicity of the newly synthesized isoquinoline were suggested by the in silico calculations. Ex vivo applied DIQ relaxes smooth muscle preparations from the corpus part of the rat stomach in the $10^{-7}\div 10^{-4}$ M range. Under conditions of 42 mM KCl-depolarization and submaximal concentration, DIQ

($5 \cdot 10^{-5}$ M) reduced the tone of spontaneous muscle contractions by 41.04%, as opposed to papaverine which caused an 18.79% reduction. The newly synthesized molecule demonstrated its biologically active potential in *in vivo* learning and memory tests. Significant improvements in cognitive function were observed in rats at 5 mg/kg compared to 10 mg/kg for papaverine isoquinoline.

Conclusion: The demonstrated direct antispasmodic effect and low toxicity of DIQ make it a potential drug agent and are essential for its applicability in rational drug design.

Practical applications: The results presented show the potential of the created isoquinoline molecule to exhibit antispasmodic properties and to serve as a model for creating new generations of biologically active isoquinolines with pharmacologically important properties.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: "Epigenetic and neurofunctional profile of insomnia phenotypes"

Project director: Assoc. Prof. Kiril Terziyski¹

Leading scientist: Todor Georgiev²

Research team: Assoc. Prof. Sevdalina Kandilarova²; Assoc. Prof. Nikolay Mehterov³; Aneliya Draganova¹; Prof. Dora Zlatareva⁴; Rositsa Paunova²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Pathophysiology

2. Faculty of Medicine, Complex for Translational Neuroscience

3. Faculty of Medicine, Department of Medical Biology

4. Medical University – Sofia, Department of Diagnostic Imaging

Aim: To establish an epigenetic and neurofunctional profile of insomnia phenotypes, including those with normal and reduced sleep duration.

Materials and methods: Thirty-five patients with chronic insomnia disorder (CID) and 14 healthy controls (ongoing) were studied. Each underwent a polysomnographic sleep assessment (PSG), miRNA expression levels were examined, and functional magnetic resonance imaging (fMRI) was performed.

Results: After measuring the expression of 10 miRNAs in insomnia patients and healthy controls, and performing fMRI on them, we found decreased expression of let-7 in white blood cells and of miR-125b in plasma in patients suffering from chronic insomnia compared to healthy controls. Interpretation of these results in the light of mediators regulating the sleep-wake cycle is indicative of a disturbance in the post-transcriptional effects of the neurotransmitter orexin, whose activity is potentially altered in patients with insomnia. In addition, fMRI revealed aberrant connections in patient neuronal networks – inhibitory from the dorsomedial prefrontal cortex to the posterior cingulate gyrus and from the medial prefrontal cortex to the left insula. These data support the hypothesis of an inability to suppress

neuronal networks in a resting state in patients suffering from chronic insomnia.

Conclusion: Alterations in the expression of micro RNA let-7 may play a role in the post-transcriptional regulation of orexin, leading to increased levels of wakefulness in patients with insomnia. fMRI data confirm the inability of the CNS to achieve a resting state in insomniacs.

Practical applications: An alternative theory examining the cause of chronic insomnia is proposed.

Project performance evaluation: The project is completed successfully with significant insufficiency regarding the aim and tasks set in the project.



Project title: “Electroimpedance analysis for assessment of perioperative total body water and body fluids distribution in major surgeries”

Project director: Prof. Chavdar Stefanov^{1,2}

Leading scientist: Emral Kyosebekirov^{1,2}

Research team: Ivaylo Minev^{1,2}

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Anesthesiology and Intensive Care Medicine

2. University Hospital “St. George”, Plovdiv, Department of Anesthesiology and Intensive Care Medicine

Aim: To assess the feasibility of bioimpedance analysis (BIA) in monitoring fluid status and the effect of fluid therapy in major surgeries.

Materials and methods: An observational, prospective study was conducted with the financial support of the Medical University Plovdiv, Bulgaria (Project number 12/2021), from April 2021 to November 2022 among patients hospitalized for elective major surgical interventions at St. George University General Hospital, Plovdiv, Bulgaria. BIA measurements were taken 1 hour before and after general anesthesia administration. Standard intraoperative monitoring was implemented, and net fluid balance was calculated. BodyStat Multiscan 5000 equipment along with the manufacturer's electrodes were utilized. Parameters analyzed included overhydration (OHY), total body water (TBW), extracellular water (ECW), and intracellular water (ICW).

Results: Forty patients (19 female and 21 male), with a mean age of 59.15 ± 9.68 years and a mean BMI of 27.1 ± 4.3 kg/cm², participated in the study. The mean operation time was 189.75 ± 87.63 minutes, comprising 18 laparotomies, 15 thoracotomies, and 7 craniotomies. The calculated mean net fluid balance was 1344.64 ± 533.02 ml. Total body water (TBW), extracellular water (ECW), intracellular water (ICW), and overhydration (OHY) increased from initial values of 44.84 ± 10.38 l, 15.08 ± 3.35 l, 29.66 ± 7.29 l, and -0.77 ± 0.84 to final

values of 46.38 ± 10.57 l, 16.62 ± 3.52 l, 29.76 ± 7.3 l, and 1.28 ± 0.75 , respectively. A correlation was observed between net balance and the increase in TBW ($r = 0.41$, $p < 0.05$), ECW ($r = 0.47$, $p < 0.05$), and OHY ($r = 0.33$, $p < 0.05$), while the increase in ICW was not statistically significant ($p = 0.24$).

Conclusion: BIA gives promising results in the evaluation of TBW and body fluid distribution in the perioperative period and could be a useful tool in the complex fluid therapy management. Although relatively old, the method is gaining increasing popularity and wider application amongst patients.

Practical applications: the application of bioimpedance analysis as a tool for objective assessment of fluid status and body fluids distribution.

Project performance evaluation: *The project is completed successfully with significant insufficiency regarding the aim and tasks set in the project.*



Project title: “Evaluation of the capabilities of multiparametric MRI for the detection of prostate cancer”

Project director: Prof. Silviya Tsvetkova-Trichkova¹

Leading scientist: Lyubomir Chervenkov¹

Research team: Assoc. Prof. Katya Doykova¹; Aleksander Georgiev¹; Assoc. Prof. Mladen Doykov²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Diagnostic Imaging

2. Faculty of Medicine, Department of Urology and General Medicine

Aim: Evaluation of the capabilities of multiparametric MRI for the detection of prostate cancer.

Materials and methods: Fifty-three patients, aged 44 to 82 years, were evaluated for clinically significant prostatic carcinoma. Assessment methods included GE Discovery 3T MRI, prostate-specific antigen (PSA) serum levels, transrectal ultrasonography (TRUS), and 12-core TRUS biopsy.

Results: mp-MRI showed 83.20% concordance with TRUS biopsy: sensitivity of 91.43% (76.90–98.20), specificity of 75.00% (34.90–96.80), positive predictive values 94.10% (82.80–98.20) and negative predictive values 66.70% (38.70–86.40). Of the patients classified in prostate imaging-reporting and data system (PI-RADS) scores 4 and 5, 94.12% had positive TRUS biopsy, as well as 44.40% of PI-RADS had score 3. Irrespective of the patients' age and PSA, PI-RADS was found to be a significant predictor of a positive TRUS biopsy ($p = 0.009$).

Conclusion: According to our findings, mp-MRI and TRUS biopsy have a high level of concordance for the initial detection of prostatic carcinoma. The incorporation of mp-MRI into the diagnostic pathway for prostatic carcinoma can significantly reduce the number of incorrect diagnoses based on PSA serum levels and/or suspicious physical and digital examinations.

Practical applications: The significance of multiparametric magnetic resonance scanning in the diagnostic algorithm of prostate carcinoma detection is demonstrated, as well as the need for a standardized description of findings according to the PI-RADS system.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Low-carbohydrate (ketogenic) diet in children with obesity”

Project director: Prof. Ivan Ivanov¹

Leading scientist: Ivanka Paskaleva¹

Research team: Assoc. Prof. Narcis Kaleva¹; Valya Markova²; Lyubov Chochkova¹; Petya Markova¹; Tsvetelina Tsvetanova¹; Dimitar Iliev³; Bozhidar Bukov⁴

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Pediatrics and Medical Genetics “Prof. Dr. Ivan Andreev”
2. Faculty of Medicine, Department of Clinical Laboratory
3. Faculty of Medicine, Department of Endocrinology
4. Faculty of Medicine, student

Aim: To determine the effect of “well-formulated ketogenic diet” in children with obesity, metabolic syndrome, and insulin resistance.

Material and methods: 100 children aged 7–18 years underwent clinical, anthropometric, laboratory, and ultrasound examinations and were placed on a ketogenic diet for 16 weeks.

Results: 58 patients who successfully completed the 16-weeks on-diet period underwent control examinations. There was a significant decrease in all tracked anthropometric indicators – weight, BMI, waist-to-height ratio. Insulin sensitivity was improved (decreased average levels of insulin and HOMA-IR index, increased QUICKI and adiponectin). The number of patients with arterial hypertension, hepatic steatosis, and metabolic syndrome decreased. All 8 girls with polycystic ovarian syndrome experienced return to spontaneous menstruation with decreased testosterone. Lipid profile was improved (decreased average levels of triglycerides, triglycerides/HDL, apoB, atherogenic index of plasma, carotid intima-media thickness). Patients with good and moderate diet compliance showed significantly more improvement of the examined indicators. Diet side effects were mild and did not necessitate discontinuation.

Conclusion: The “well-formulated ketogenic diet” is proven effective for weight loss and visceral fat reduction in children. It leads to improved insulin sensitivity, regression of metabolic syndrome, reduced cardiovascular risk, and affects positively arterial hypertension, hepatic steatosis, and polycystic ovary syndrome, with good tolerance and mild side effects.

Practical applications: the adoption of a low-carbohydrate (ketogenic) diet is proposed as one of the possible dietary options for children with obesity, insulin resistance, metabolic syndrome, and accompanying comorbidities.

Project performance evaluation: *The project was duly completed and realized successfully with good publication activity.*



Project title: “Diagnosis of pemphigus by immunohistochemistry for immunoglobulin G4 on paraffin sections”

Project director: Assoc. Prof. Tsvetana Abadjieva^{1,3}

Leading scientist: Zhaneta Zhelyazkova^{1,3}

Research team: Prof. Vesselin Belovezh dov^{2,4}

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Dermatology and Venereology
2. Faculty of Medicine, Department of General and Clinical Pathology
3. Department of Dermatology and Venereology
4. University Hospital “St. George”, Plovdiv, Department of General and Clinical Pathology

Aim: To evaluate the usefulness of immunohistochemistry for immunoglobulin G4 on paraffin sections as a diagnostic test for pemphigus.

Materials and method: Fifty formalin-fixed paraffin-embedded specimens of patients with pemphigus were selected according to order of admission. The specimens were from the histopathology archives of the Clinic. Patients were previously diagnosed by direct immunofluorescent assay and histopathological examination. Fifty formalin-fixed paraffin-embedded blocks of tissue from patients with bullous diseases other than pemphigus were used as controls. Immunohistochemistry for immunoglobulin G4 (IgG4) was performed on 4 µm-thick paraffin sections with an anti-IgG4 antibody. Positivity was defined as distinctive, concentrated, uninterrupted immunoreactivity localized to the intercellular junctions of keratinocytes. A finding that did not meet these criteria was defined as negative.

Results: Forty-three (86.0%) of the examined patients had pemphigus vulgaris and seven (14%) had pemphigus foliaceus. Forty-nine (98.0%) specimens of pemphigus patients were immunoreactive for IgG4, one (2%) upper back biopsy from patient with oral pemphigus showed negative immunoreactivity. Negative immunoreactivity was found in 45 (90%) controls. Five (10%) controls with bullous pemphigoid showed immunoreactivity for IgG4. Sensitivity of the method was

established to be 98%, specificity 90%, positive predictive value 91%, and negative predictive value 98%.

Conclusion: Immunohistochemical examination in pemphigus can be applied when direct immunofluorescence examination is unavailable. The advantage of this method is that it does not require special equipment and the preparations are permanent.

Practical applications: Immunohistochemical method for diagnosis of pemphigus.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: “Pneumothorax in COVID-19 patients – clinical and paraclinical correlations, complications, surgical approaches for diagnostics and treatment”

Project director: Prof. Angel Uchikov^{1,7}

Leading scientist: Lyubomir Paunov^{1,7}

Research team: Atanas Batashki^{1,7}; Emanuil Yordanov^{1,7}; Prof. Sylvia Tzevtkova^{2,7}; Boyan Pavlov^{3,7}; Antonia Yaneva⁴; Yordan Kalchev^{5,7}; Petar Uchikov^{1,7}; Atanas Atanassov^{6,7}

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Special Surgery
2. Faculty of Medicine, Department of Diagnostic Imaging
3. Faculty of Medicine, Department of Clinical Laboratory
4. Faculty of Public Health, Department of Medical Informatics, Biostatistics and E-learning
5. Faculty of Medicine, Department of Medical Microbiology and Immunology "Prof. Dr. Elissay Yanev"
6. Faculty of Medicine, Department of Infectious Diseases, Parasitology and Tropical Medicine
7. University Hospital "St. George", Plovdiv

Aim: To analyze the clinical features, inflammatory markers and complications of pneumothorax in patients with COVID-19.

Material and methods: 26 patients were examined with proven COVID-19 and pneumothorax. Thoracocentesis was performed in 24, and VATS with partial resection and pleurodesis – in 2. Inflammatory markers – leukocytes, ESR, D-dimers, procalcitonin, CRP, were examined.

Results: The frequency of right- and left-sided pneumothorax was similar (12 and 11 cases, resp.); it was bilateral in 3 cases. Large pneumothorax (> 2 cm) was more common – in 10 cases. Almost half of the patients (14) were intubated and most of them (12) underwent surgical treatment. Only 4 had no concomitant diseases, and the rest – most frequently had arterial hypertension, COPD, diabetes. Lethal outcome occurred in 14; only 3 were discharged with improvement. Intubation doubled the risk of death.

The highest mortality (68.8%) was found in patients > 70 years. Mortality rate was twice higher in women (88.9%) than in men (47.1%). Leukocytes, CRP and D-dimers were significantly elevated – indicators of serious inflammatory reaction which against the background of the developing SARS-CoV-2 infection aggravates the course of pneumothorax.

Conclusion: Pneumothorax in COVID-19 is associated with increased risk of mortality in right-sided and bilateral localization, in women and patients > 70 years. Larger pneumothorax is more commonly observed as complication of COVID-19.

Practical applications: It is advisable to avoid large-scale surgical interventions and to place a thoracic drain for a longer period of time. In intubated patients increased monitoring is advised because of the two-fold higher mortality.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Research area: Biomedical
Contract: Project № COV-04/2021

Project title: “Laboratory monitoring of prognostic biomarkers in hospitalized patients with COVID-19”

Project director: Prof. Tanya Deneva^{1,2}

Leading scientist: Desislava Arabadzhiyska^{1,2}

Research team: Delyana Davcheva^{1,2}; Snezhana Stoencheva^{1,2}; Valya Markova-Hristeva^{1,2}

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Clinical Laboratory

2. University Hospital “St. George”, Plovdiv, Central Clinical Laboratory

Aim: To investigate some laboratory parameters in hospitalized patients with moderate and severe form of COVID-19 and evaluate their possible relationship with systemic inflammation and the severity of the course of the disease.

Material and methods: The study included 90 patients with moderate ($n = 45$) and severe ($n = 45$) form of COVID-19 and 45 healthy controls. CBC, DBC, routine biochemical parameters, CRP, LDH, ferritin, IL-6, PCT, D Dimer, vitamin D and selenium were measured. Continuous variables are expressed as mean \pm standard deviation, $p < 0.05$ was considered significant.

Results: The mean age of the patient and control groups did not differ statistically (56.45 ± 7.82 years vs. 57.95 ± 5.19 years, $p > 0.05$). Patient with COVID-19 showed significantly higher values of leukocytes, neutrophils, lower lymphocytes, eosinophils, serum total protein and albumin, higher CRP, LDH, ferritin, IL-6, PCT and D Dimer and lower vitamin D, selenium and PaO_2 compared to healthy controls ($p < 0.0001$).

According to the severity of the disease, patients with severe form had significantly higher serum concentrations of IL-6 (64.06 ± 32.97 pg/ml vs. 27.51 ± 18.15 pg/ml, $p < 0.0001$), CRP (168.21 ± 66.49 mg/l vs 81.56 ± 43.93 mg/l, $p < 0.0001$), ferritin (992.03 ± 416.82 ng/ml vs 819.17 ± 326.29 ng/ml, $p < 0.0001$) and LDH (1392.68 ± 1066.47 U/l

vs 887.76 ± 232.48 U/l, $p < 0.0001$) compared to those with moderate form.

Conclusion: The presented data provide a relationship between increased inflammatory laboratory markers, low serum vitamin D and selenium levels and disease severity in COVID-19 patients.

Practical applications: We propose a panel of laboratory tests that can guide the clinical course, distinguish between severe and moderate form and outcome of the disease.

Project performance evaluation: *The project was duly completed and realized successfully with good publication activity.*



Project title: “Evaluation of the effectiveness and stress level of participants in endoscopic retrograde cholangiopancreatography (ERCP) simulation training program”

Project director: Nikola Boyanov¹

Leading scientist: Desislava Dimitrova²

Research team: Prof. Tanya Deneva³; Prof. Lars Enochsson⁴;
Prof. Evangelos Georgiou⁵; Atanas Davarski⁶

Organization unit: Medical University of Plovdiv

1. *Medical Simulation Training Center*
2. *University Hospital “Pulmed”, Plovdiv*
3. *Faculty of Medicine, Department of Clinical Laboratory*
4. *UMU, Department of Surgical and Perioperative Sciences*
5. *National and Kapodistrian University of Athens, Greece*
6. *Faculty of Medicine, Department of Neurosurgery*

Aim: Evaluation of the effectiveness and practical implementation of a GI Mentor II simulator for endoscopic retrograde cholangiopancreatography (ERCP) training, measuring the stress levels of the participants. Another aim is determining the possibility of including this training as a part of the GI residents’ program in order to improve their overall competence.

Results: Two groups were selected. The first – seven experienced endoscopists in the field of the described methodology. The second – thirty novice specialists or specialists in gastroenterology, but with experience in performing endoscopic manipulations.

The stress levels were measured in saliva samples. They were obtained from the experts and novice endoscopists in several stages. The following indicators were measured: cortisol level, α -amylase, human chromogranin A. To assess the stress level, a specially selected “Empathika” bracelet (E4WB PPG BVP) was also used.

Conclusion: GI Mentor II simulator allows acquisition of knowledge and skills of inexperienced endoscopists. It represents optimally the essence of the methodology. In the end of the present project, there was an increase in the interest of the beginners in one of

the most difficult endoscopic procedures, as well as a significant improvement of their skills and competence.

Practical applications: ERCP simulators can be a way to improve the training of novice endoscopists as well ensuring patient safety in daily practice.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Development of a screening questionnaire for risk of malnutrition in children”

Project director: Assoc. Prof. Ivan Yankov^{1,2}

Leading scientist: Assoc. Prof. Ivan Yankov^{1,2}

Research team: Assoc. Prof. Margarita Panova^{1,2}; Konstantina Bangieva²; Vasilena Yankova³; Irina Vladimirova²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Paediatrics and Medical Genetics
“Prof. Dr. Ivan Andreev”

2. University Hospital “St. George”, Plovdiv, Department of Pediatrics

3. Faculty of Medicine, student

Aim: The aim of the present study is to create a screening questionnaire to detect children at risk of malnutrition during hospitalization.

Materials and methods: A single-center prospective cross-sectional study was conducted. It includes children admitted at the Department of Pediatrics in University General Hospital “St. George” from January 2022 to June 2023.

Results: The study enrolled 706 children, comprising 50.2% boys (n = 354) and 49.8% girls (n = 352), with ages ranging from 20 days to 17 years and 10 months (median 4.6 years, standard deviation 3.6 years). None of the patients received counseling regarding low weight before hospitalization.

The questionnaire application results enable the identification of children at risk of malnutrition, with questions 1 and 4 carrying the most significant weight. The remaining questions hold comparatively less weight.

Conclusion: Our study recommends the routine use of our proposed questionnaire for screening the risk of malnutrition among hospitalized children. Its ease of completion and accessibility of the questions make it a convenient and inexpensive tool to use.

Practical applications: The use of the screening questionnaire is suitable for screening hospitalized children at risk of malnutrition.

Project performance evaluation: *The project is completed successfully with significant insufficiency regarding the aim and tasks set in the project.*



Project title: “Comparative laboratory and clinical study of volumetric and optical changes of CAD/CAM 3D printed and conventional heat-cured dental resins used in removable prosthodontics”

Project director: Bozhana Chuchulska¹

Leading scientist: Mariya Dimitrova¹

Research team: Prof. Angelina Vlahova^{1,2}; Rada Kazakova^{1,2}

Organization unit: Medical University of Plovdiv

1. Faculty of Dental Medicine, Department of Prosthetic Dentistry

2. Research Institute, CAD/CAM Center of Dental Medicine

Aim: to conduct a comparative analysis and report on the differing volumetric and optical changes in two types of dental resin utilized for the fabrication of complete removable dentures obtained by 3D printing and conventional technology.

Material and methods: A total of 180 experimental samples of both types of plastic for removable dentures were examined, and objective laboratory methods were applied to study the volumetric and optical changes during three study periods (7 days, 14 days, and 1 month).

Results: The first task involved testing experimental samples from both groups of dental resin, which were placed in glass containers with artificial saliva for three periods (7 days, 14 days, and 1 month). The results indicated that the 3D-printed resins exhibited more significant volumetric changes during the first week. For the second task, it can be concluded that the 3D-printed experimental bodies demonstrated better optical stability when stained for 1 month. The third task involved a 3D simulation study, which revealed that thermosetting plastics exhibited higher resistance after 1 month in artificial saliva. It has been demonstrated that both types of resin are suitable for fabricating removable dentures with satisfactory mechanical properties.

Conclusion: The volumetric and optical stability of removable dentures correlates with the type of dental resin, its chemical composition, and the method of polymerization.

Application in practice: The conducted studies prove the great possibilities of the application of the new 3D-printed dental resin for the manufacturing of removable dentures in daily dental practice.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Exploring the role of antineuronal antibodies as a biomarker in patients with paraneoplastic neurological syndrome”

Project directors: Prof. Zhanet Grudeva-Popova²; Assoc. Prof. Hasan Burnusuzov³

Leading scientist: Milen Hristozov¹

Research team: Petya Gardjeva¹; Assoc. Prof. Veselin Popov²; Gabriela Raycheva²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Medical Microbiology and Immunology
“Prof. Dr. Elissay Yanev”
2. Faculty of Medicine, Department of Clinical Oncology
3. Faculty of Medicine, Department of Paediatrics and Medical Genetics
“Prof. Dr. Ivan Andreev”

Aim: To study the role of antineuronal antibodies (ANeA) in patients with malignant neoplasia and patients with paraneoplastic neurological syndrome (PNS).

Material and methods: Serum samples of 52 patients were studied, of which 9 with malignant neoplasia without PNS (control group) and 43 with PNS (target group). Indirect immunofluorescent assay (IIFA) was employed to determine ANeA associated with cell surface antigens and immunoblot (IB) – for ANeA associated with intracellular antigens.

Results: All nine patients in the target group were positive for ANeA, respectively: anti-NMDAR antibodies were detected in eight patients with acute lymphoblastic leukemia (ALL), osteosarcoma, and anti-NMDAR encephalitis; anti-GAD65 – in a patient with ALL and anti-Zic4 – in a patient with paraneoplastic cerebellar degeneration (PCD). Of the patients in the control group, four were positive (9%), thirty-nine were negative (91%). Of the positive patients: anti-Recoverin was found in a breast carcinoma patient; anti-Hu – in a breast carcinoma patient; anti-Ri – in an ovarian carcinoma patient; anti-SOX1 – in a breast carcinoma patient.

Conclusion: The diagnostic value of anti-NMDAR in ALL, osteosarcoma and anti-NMDAR encephalitis was proven and in these diseases PNS is observed and autoantibodies correlate with severe general condition of the patients. The results showed anti-SOX1, anti-Recoverin and anti-Hu in non-PNS breast carcinoma and also anti-GAD65 in ALL. The diagnostic value of anti-Ri in ovarian carcinoma without PNS and the diagnostic value of anti-Zic4 in PCD and anti-NMDAR encephalitis was demonstrated.

Practical applications: ANeA panels using IIFA and IB have been introduced.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: “Biomechanical problems in endodontically treated teeth after separated instruments removal”

Project director: Assoc. Prof. Silvia Dimitrova¹

Leading scientist: Viktoria Dimitrova¹

Research team: Prof. Plamen Zagorchev²; Assoc. Prof. Stefan Zlatev³; Petya Kanazirska⁴; Lubomir Vangelov¹; Vasil Dimitrov⁵

Organization unit: Medical University of Plovdiv

1. Faculty of Dental Medicine, Department of Operative Dentistry and Endodontics
2. Faculty of Pharmacy, Department of Medical Physics and Biophysics
3. Faculty of Dental Medicine, Department of Prosthetic Dentistry
4. Faculty of Dental Medicine, Department of Diagnostic Imaging, Dental Allergology and Physiotherapy
5. Faculty of Dental Medicine, student

Aim: To analyze changes in root canal volume and design after separated endodontic instruments removal and to create a minimally invasive clinical protocol protecting against thermal and mechanical damage.

Material and methods: Five studies were conducted, of which four in vitro (CBCT analysis of root canal volume and design after segment removal with or without lasso and with or without an endodontic guide; thermometric examination of an ultrasound tip, separated endodontic instrument and hard dental tissues in two working protocols; SEM and EDX) and one in vivo (CBCT analysis before and after removal of a segment with two techniques of 30 patients).

Results: The segment retrieval with lasso technique (both in vitro and in vivo) and static endodontic guide demonstrated a statistically significantly lower percentage of dentin removed compared to the ultrasound technique. Additionally, as the power of the ultrasound device increased, there was a statistically significant increase in generated temperature. However, the protocol involving 10-second work intervals reached a statistically significantly lower temperature. Scanning electron microscopy (SEM) analysis revealed that higher power

of the ultrasound apparatus and longer manipulation times were associated with a greater degree of dentine damage and the formation of microcracks. Furthermore, elemental analysis showed no significant changes in the composition of dentin after application of the ultrasound technique.

Conclusion: The use of the lasso technique and static endodontic guide statistically significantly reduces dentin loss.

Practical applications: Alternative techniques for removing a separated endodontic instrument are offered, reducing the risk of microcrack formation and heating of hard dental tissues.

Project performance evaluation: The project is completed successfully with significant insufficiency regarding the aim and tasks set in the project.



Project title: “Expression of anti HIF1alpha, Ki 67, E-cadherin, β-catenin, SMA in endometriosis foci, in endometrial and ovarian carcinomas”

Project director: Assoc. Prof. Elena Poryazova¹

Leading scientist: Daniel Markov¹

Research team: Denitsa Serteva¹; Desislava Bojkova¹; Galabin Markov²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of General and Clinical Pathology

2. Faculty of Medicine, student

Aim: To investigate the immunohistochemical expression of HIF-1α, Ki 67, E-cadherin, β-catenin, SMA and Fascin in endometriosis foci, in endometrial and ovarian carcinomas and to seek correlation with histological and clinicopathological parameters.

Material and methods: A total of 296 cases from the respective groups were reviewed, 50 relevant cases were immunohistochemically examined with the HIF-1α, Ki 67, E-cadherin, β-catenin, SMA and Fascin markers.

Results: HIF-1α is the main functional protein of the HIF-1 complex. We observed a high level of HIF-1α expression in endometrial carcinoma cases, at the invasive front of the tumor and around areas with necrosis. In cases with endometriosis, HIF-1α expression was correlated with lesion depth and disease stage. We observed stronger expression in adenomyosis and endometriosis foci compared to normal endometrium. In type 1 endometrial carcinoma, HIF-1α expression correlates with tumor grading and FIGO stage. In type 2 endometrial carcinoma, stronger and diffuse expression, including perinecrotic expression of HIF-1α was observed in all examined patients, regardless of myometrial invasion, adnexal invasion, vascular invasion and TNM stage of the tumor. HIF-1α may help identify at-risk endometriosis patients who would require more specific monitoring and treatment. Endometriosis should be considered as a disease with the potential for malignancy.

Conclusion: The immunohistochemical profile of the different morphological lesions of the endometrium and ovaries can be used to analyze the progression of endometriosis and tumor tissue.

Practical applications: The selected immunohistochemical markers are relevant for the assessment of proliferative activity, invasion and tumor progression, as well as for future therapy.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: "Serum level of indoxyl sulfate and para cresol in patients with CKD IV-V stage as biochemical markers for gut dysbiosis in uremia – clinical significance and possibilities for therapeutic control"

Project director: Prof. Emil Kumchev¹

Leading scientist: Teodor Kuskunov²

Research team: Chief Assist. Prof. Krasimir Boyanov³; Kalina Metodieva³

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Second Department of Internal Diseases
2. Faculty of Medicine, Department of Propaedeutics of Internal Diseases "Prof. Dr. Anton Mitov"
3. Faculty of Pharmacy, Department of Medical Biochemistry

Aim: To research the serum concentration of Indoxyl sulfate (IS) and p-Cresyl sulfate in end-stage renal disease (ESRD) patients undergoing hemodialysis, as well as to study the possibilities of influencing some markers of inflammation and oxidative stress after taking a symbiotic.

Materials and methods: We included 30 patients undergoing hemodialysis treatment who were taking a symbiotic in the form of *Lactobacillus acidophilus* La-14 2×10^{11} (CFU)/g and prebiotic fructooligosaccharides. Serum levels of total IS, total p-CS, Interleukin-6 (IL-6) and Malondialdehyde (MDA) were measured at baseline and after 8 weeks of symbiotic supplementation.

Results: The baseline values of the four investigated indicators in the patients were significantly higher – p-CS (29.26 ± 58.32 pg/mL), IS (212.89 ± 208.59 ng/mL), IL-6 (13.84 ± 2.02 pg /mL), MDA (1430.33 ± 583.42 pg/mL) compared to the results obtained after 8 weeks of supplementation – p-CS (6.40 ± 0.79 pg/mL, $p = 0.041$), IS (47.08 ± 3.24 ng/mL, $p < 0.001$), IL-6 (9.14 ± 1.67 pg/mL, $p < 0.001$), MDA (1003.47 ± 518.37 pg/mL, $p < 0.001$).

Conclusion: The current study found that the restoration of the intestinal microbiota in patients with ESRD significantly decreases the

level of certain uremic toxins. It is likely that this favorably affects certain aspects of CKD, such as persistent low-grade inflammation and oxidative stress.

Practical applications: IS and p-CS belong to the group of protein-bound uremic toxins, which is why their degree of reduction in hemodialysis patients is limited. Synbiotic supplementation leads to a decrease in their serum concentrations and is considered as a new, additional possibility to influence the normal state in patients with CKD.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “**Pharmacoanalytical control of plant adaptogens – characterization of *Rhaponticum carthamoides* extract**”

Project director: Assoc. Prof. Kalin Ivanov¹

Leading scientist: Assist. Prof. Velislava Todorova¹

Research team: Assoc. Prof. Stanislava Ivanova¹; Assist. Prof. Vanya Kozhuharov¹; Assist. Prof. Stanislav Dyankov¹; Assist. Prof. Vanya Nalbantova¹; Assoc. Prof. Diana Karcheva-Bahchevanska¹; Assoc. Prof. Niko Benbassat¹; Yoana Dimova¹

Organization unit: Medical University of Plovdiv

1. Faculty of Pharmacy, Department of Pharmacognosy and Pharmaceutical Chemistry

Aim: Identification and quantification of phytoecdysteroids in *Rhaponticum carthamoides* (Willd.) Iljin. roots and rhizomes extract utilizing high-performance liquid chromatography (HPTLC) and high-performance thin layer chromatography (HPLC). Subsequently, the extract and its secondary metabolites were investigated for their anti-adipogenic activity.

Results: A novel HPTLC method for detection and quantification of ecdysterone, turkesterone and ponasterone A has been developed and validated. It was utilized for determining the quantity of the phytoecdysteroids in *R. carthamoides* extract. The HPTLC results were affirmed by HPLC/UV analysis using a newly developed and validated method. The proposed methods are characterized by simplicity, high sensitivity, efficiency, robustness, and reproducibility. It was determined that *R. carthamoides* extract, ecdysterone, and turkesterone significantly reduced lipid accumulation in human adipocytes. Additionally, the extract and ecdysterone effectively stimulate basal lipolysis, whereas no effect was observed with ponasterone A and turkesterone application.

Conclusion: The quantity of ecdysterone, turkesterone and ponasterone A in *R. carthamoides* extract was determined. It was

established that the extract and ecdysterone affect adipogenesis and adipolysis, whereas turkesterone only affects adipogenesis.

Practical applications: The validated chromatographic methods could be successfully applied in routine quality control and research programs. The results obtained from anti-adipogenic activity are fundamental for further investigations in this field. Moreover, the extract of *R. carthamoides*, ecdysterone, and turkesterone possess a great potential in obesity management.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Functional aspects of the human claustrum during exposition to sensory stimuli of different modalities”

Project director: Prof. Stefan Sivkov¹

Leading scientist: Assist. Prof. Marin Kanarev¹

Research team: Assoc. Prof. Ferihan Popova¹; Chief Assist. Prof. Zdravka Harizanova¹; Prof. Magdalena Stoeva²; Assist. Prof. Tina Zdravkova²; Assist. Prof. Nadezda Petrova¹; Teodor Lolovski³

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Anatomy, Histology and Embryology

2. Faculty of Medicine, Department of Imaging Diagnostics

3. Faculty of Medicine, student

Aim: The aim of the study is to investigate through functional imaging the morphological structure, activity and functional connectivity of the human claustrum with other structures of the nervous system during sensory stimuli of different modalities.

Materials and methods: The study was conducted in the Center for Translational Neuroscience at the Medical University of Plovdiv. The participants were 113 healthy volunteers, aged 19–39 without a history for neurological diseases. A morphological and functional neuroimaging assay was conducted with 3 Tesla MRI in its full volume of several series. To every tested subject images and sounds were presented, separately and combined, grouped in series of matching and mismatching. The results were statistically analyzed with SPM and MatLab software.

Results: The acquired results vary amongst different subjects on an individual level. In summary there are statistically relevant clusters in the visual and auditory cortices in the series with respective modalities, but in contrasts comparing match and mismatch series there are also clusters in the claustrum-insula region that reach statistical relevance on cluster level but fail on peak level. Probably this is due to the small size and volume of the investigated structures.

Conclusion: The claustrum probably has a role in the integration of sensory stimuli from different modalities by potentiating valiant stimuli for the survival of the individual and plays an important role in fixating attention.

Practical applications: Understanding the mechanisms of functioning of the claustrum in humans would aid in attempts for clinical treatment of alterations and deficits of attention and perception of the environment.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: “Study of the influence of febuxostat on the level of IL-1, IL-2 and COX-2 in patients with gout”

Project director: Prof. Mariela Geneva-Popova¹

Leading scientist: Chief Assist. Prof. Krasimir Kraev¹

Research team: Stanislava Popova-Belova¹; Velichka Popova¹; Bozhidar Hristov²; Prof. Ivan Sheitanov³; Despina Pupaki⁴

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Propedeutics of Internal Diseases "Prof. Dr. Anton Mitov"
2. Faculty of Medicine, First Department of Internal Medicine, Section of Gastroenterology
3. Medical University – Sofia, Faculty of Medicine, Department of Rheumatology
4. Bulgarian Academy of Sciences, Section of Immunobiology of Reproduction

Aim: To examine the level of IL-1, IL-2, COX-2 in patients with gout at baseline and 30, 60 and 90 days after taking febuxostat, as well as in 20 healthy controls

Materials and methods: The study included 100 gout patients aged 18-80 years and control groups – 20 healthy individuals. The levels of IL-1, IL-2, COX-2 in the serum of the patients were determined using the ELISA method.

Results: In this 3-month clinical study, 50 patients with gout were administered febuxostat treatment, alongside 20 healthy controls. Rigorous monitoring of Interleukin-1 (IL-1), Interleukin-2 (IL-2), and Cyclooxygenase-2 (COX-2) levels revealed a substantial decrease in cytokine levels in 42 patients. Employing statistical methods including the Pearson Correlation Coefficient, we established a positive correlation between febuxostat intake and reductions in IL-1, IL-2, and COX-2 levels. Additionally, Student's t-test was employed to compare the means of cytokine levels between healthy controls and patients, confirming statistically significant differences. Intriguingly, a progressive decline in cytokine levels was observed with continued therapy. These findings underscore the potential of febuxostat as an effective

intervention for gout, providing insights into its anti-inflammatory properties and suggesting avenues for further exploration.

Conclusion: The obtained results reveal the potential of febuxostat not only as a medication to reduce uric acid, but also as a new possibility for an effective anti-inflammatory intervention.

Practical applications: Study results indicate that the inclusion of febuxostat in the treatment of gout may optimize treatment by reducing pro-inflammatory markers, allowing for more personalized approaches and potentially improving long-term outcomes.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Oral health parameters in patients with eating disorders. A survey and a clinical study”

Project director: Prof. Georgi Tomov¹

Leading scientist: Margarita Hadjieva²

Research team: Ivanina Totova³

Organization unit: Medical University of Plovdiv

1. Faculty of Dental Medicine, Department of Periodontology and Oral Mucosa Diseases

2. Faculty of Dental Medicine, student

Aim: Through survey and clinical studies, to establish basic parameters of oral health in Bulgarian patients with eating disorders

Material and methods: 60 patients with eating disorders who volunteered to participate in a questionnaire survey were recruited. Clinical and paraclinical studies were conducted on 14 patients with bulimia and 12 patients with anorexia.

Results: The age range of the respondents is from 18 to 57 years, and 95% of them were women. 58.3% of them visited a dentist only in case of a problem. A majority of the respondents expressed dissatisfaction with their body and weight, attempting to address it through unhealthy eating behaviors and habits. 87% of them had oral hygiene habits that were not aligned with the eating disorder. They reported a number of subjective symptoms. 90% of the respondents had pronounced tooth sensitivity, and 43% of them found changes in their oral cavity but were not familiar with the oral manifestations of eating disorders. 83.3% of the respondents were interested in receiving additional information and guidance from the dentist. During the examinations of these patients, a complex of oral manifestations and deviations in the buffering capacity, pH and amount of saliva were registered.

Conclusion: A specific oral pathology was found in patients with eating disorders, as well as a lack of awareness of possible oral complications and proper prevention.

Practical applications: Information brochures were prepared with guidelines for patients with eating disorders regarding recommended oral hygiene measures and prevention of the most common oral manifestations.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Project title: “Polypharmacy among patients suffering chronic conditions and COVID-19”

Project director: Assoc. Prof. Daniela Grekova-Kafalova¹

Leading scientist: Assist. Prof. Evelina Gavazova¹

Research team: Chief Assit. Prof. Radiana Staynova¹

Organization unit: Medical University of Plovdiv

1. Faculty of Pharmacy, Department of Pharmaceutical Sciences

Aim: The aim of the current study is to conduct a pharmaco-social analysis of the impact of the COVID-19 pandemic on medication usage among patients with chronic diseases.

Material and methods: Characterization of prescription data for medication used by patients with accompanying conditions, treated for COVID-19. Analysis was conducted on 200 prescriptions using the World Health Organization's Defined Daily Dose (DDD) methodology. A survey was also carried out to assess polypharmacy among adult patients.

Results: The Defined Daily Dose (DDD) was calculated for 50 medications, including antibacterial products, glucocorticoids, bronchodilators, mucolytics, nonsteroidal anti-inflammatory drugs, antihistamines, drugs affecting the gastrointestinal tract, medications for cardiovascular diseases, iron supplements, and others. Bacterial infections are rarely complications of the course of a new coronavirus infection, so most patients with COVID-19, especially in mild and moderate cases, do not require antibiotic therapy. However, antibiotics were identified in 74.3% of cases. Over half of the respondents (54%) reported taking 5 to 8 medications per day, followed by those taking more than 9 (33%).

Conclusion: Analyzing prescriptions during COVID-19 provides insights into medication consumption and the opportunity to identify irrational prescribing practices.

Practical applications: The identified inappropriate polypharmacy in the treatment of patients at risk of the dual threat of severe COVID-

19 and chronic diseases highlights the need to take measures to limit its negative impacts. The recommended strategy for managing polypharmacy involves supporting healthcare efforts by introducing a validated method for medication review into practice.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Project title: "A prospective study for assessing diagnostic and prognostic correlations between the clinical outcome of acute ischemic stroke in patients treated with intravenous thrombolysis and indicators from CT perfusion of the brain"

Project director: Prof. Nikoleta Traykova¹

Leading scientist: Eray Halil^{2,3}

Research team: Kostadin Chompalov^{2,3}; Borislava Atanassova^{2,3}; Miroslava Hristova^{2,3}; Neli Atanassova¹

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Radiology

2. Faculty of Medicine, Department of Neurology

3. University Hospital "St. George", Plovdiv, Clinic of Nervous Diseases

Aim: To investigate which diagnostic CT perfusion indicators of the brain can be sensitive and specific predictors for the clinical outcome of the disease, assessed by scales for neurological deficit, in patients with acute ischemic stroke.

Results: In patients admitted with symptoms of acute ischemic stroke, plain brain CT and CT perfusion were conducted to calculate the values of the indicators CBV, CBF, MTT, Tmax, and TTP. The patients were assessed by the scales for neurological deficit NIHSS, mRS, and Barthel Index and treated with intravenous thrombolysis. Outpatient follow-up of the patients was conducted at the 3rd month and 1st year, during which a control brain CT was also performed. Preliminary results demonstrate the high sensitivity and specificity of the CBV and CBF indicators regarding the final volume of necrotized brain tissue in acute ischemic stroke, as well as the high specificity and sensitivity of the Tmax and MTT indicators regarding the volume of the penumbra.

Conclusion: Reduced values of the CBV and CBF indicators from CT perfusion in a large volume of brain tissue are associated with a more severe neurological deficit in the first year after the vascular

incident. The results are preliminary and may be subject to change with the accumulation of additional data and the continuation of the analysis. Final conclusions will be formulated after the completion of the entire study and analysis of all collected data.

Practical applications: The use of indicators from CT perfusion of the brain in patients with acute ischemic stroke is proposed as predictors of short-term and long-term prognosis.

Project performance evaluation: The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.



Research area: Public health

Contract: Project № PMD-01/2022

Project title: “Application of (bio)printing in personalized medicine – ethical, social and legal aspects”

Project director: Assoc. Prof. Desislava Bakova¹

Leading scientist: Dobromira Shopova²

Research team: Prof. Maria Semerdzhieva¹; Prof. Victoria Sarafian³; Assoc. Prof. Stefan Zlatev²; Assoc. Prof. Momchil Mavrov¹; Senior Assist. Prof. Anna Mihailova¹; Senior Assist. Prof. Petya Kasnakova¹; Senior Assist. Prof. Antonia Yaneva⁴; Senior Assist. Prof. Maria Hristozova¹; Senior Assist. Prof. Yordan Sbirkov³; Senior Assist. Prof. Nikieta Parahuleva⁵; Vasil Budev⁶; Nikol Harizanova⁷; Sally Lenen⁶

Organization unit: Medical University of Plovdiv

1. Faculty of Public Health, Department of Healthcare Management
2. Faculty of Dental Medicine, Department of Prosthetic Dental Medicine
3. Faculty of Medicine, Department of Medical Biology
4. Faculty of Public Health, Department of Medical Informatics, Biostatistics and E-learning
5. Faculty of Medicine, Department of Obstetrics and Gynaecology
6. Faculty of Dental Medicine, student
7. Faculty of Medicine, student

Aim: To establish ethical, social and legal norms of (bio)printing in personalized medicine.

Material and methods: A comparative analysis of the literature on the distribution and application of (bio)printing was performed. Author questionnaires were created to explore the awareness and attitudes of doctors, dentists, and pharmacists regarding the use of (bio)printing in personalized medicine, along with the attitudes of potential patients and the general public.

Results: Expert and highly specialized scientific research for the application of (bio)printing was carried out effectively in the fields of medicine, dentistry and pharmacy. We have identified some significant opportunities: better securing the transplantation processes, printing analogous organs or tissues, reducing the probability of rejection of the transplanted organs or tissues, overcoming the gender disparity in transplantation, correcting birth defects of different tissues

and organs, creating 3D models for surgical training of young doctors and testing of new surgical methods. The paradigm shift from conventional to personalized medicine, which is largely based on (bio)printing, is expected to have a significant positive impact on patients' quality of life.

Conclusion: 3D (bio)printing has the potential to impact a wide range of health issues. Through the introduction of printer technologies, huge financial health costs will be significantly reduced.

Practical applications: Establishing clear regulatory mechanisms (e.g. ethical standard; laws and regulations) will regulate the humane approach and reduce the risk of significant problems arising related to the application of bioprinting in personalized medicine.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: “Information portal on the most common surgical diseases in children”

Project director: Prof. Penka Stefanova-Peeva^{1,2}

Leading scientist: Prof. Penka Stefanova-Peeva^{1,2}

Research team: Biser Ivanov^{1,2}; Dimitar Dachev^{1,2}; Stoyan Lupanov^{1,2}; Ivan Kirev²; Borislav Isakov²; Nikolay Mavrev²

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Propaedeutics of Surgical Diseases,
Section of Paediatric Surgery

2. University Hospital “St. George”, Plovdiv, Section of Paediatric Surgery

Aim: The aim of the project is to create an electronic website as an information portal for the most common surgical diseases in children such as: inguinal hernia, hydrocele, testicular retention, umbilical hernia, phimosis, anal fissure including pictures, films, leaflets and information accessible to patients.

Material and methods: Informative, statistical, clinical and descriptive research methods were used.

Results: The stated goal of the project to create an electronic site as an information portal for the most common surgical diseases in children has been achieved. Diseases such as inguinal hernia, hydrocele, undescended testicles, umbilical hernia, phimosis, and anal fissure are included in the form of pictures and brief informative data.

Conclusion: Digitalization in healthcare leads to an improvement in the informativeness of society, in this case parents, in the presence of a health problem. In this way, the quality of the medical care provided to children with the most common surgical diseases is improved.

Practical applications: Comprehensive and accurate information on the most common surgical diseases in children forms a reliable foundation in the doctor-parent-patient relationship, fostering a strong bond of trust between them. This, in turn, enhances the quality of medical care provided.

Project performance evaluation: *The project is completed successfully with partial insufficiency regarding the aim and tasks set in the project.*



Project title: “Applying and exploring the concept of micro-learning in teaching orthopaedics and traumatology”

Project director: Prof. Vladimir Stavrev¹

Leading scientist: Assist. Prof. Petar Molchovski¹

Research team: Assist. Prof. Valentin Petrov¹; Assist. Prof. Rumen Minchev¹; Tatyana Zafirova¹

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Orthopaedics and Traumatology

Aim: The present study introduces the concept of incorporating an additional module for orthopedics and traumatology training via mobile devices. It emphasizes the necessity of developing and implementing such technologies to enhance the efficacy of both practical and theoretical training for medical students.

Material and methods: The study took place during the winter semester of the 2022/2023 academic year at the Department of Orthopedics and Traumatology of the Medical University of Plovdiv. It included all students from two streams, studying in both Bulgarian and English.

An additional mobile training module has been created. The materials consist of a small volume of concentrated essential information on the topics from the orthopedics and traumatology curriculum.

Micro-lectures were delivered to the students using Moodle LMS. Student training followed a pre-prepared schedule and was monitored through entrance, mid-term, and exit tests.

Results: The midterm test results demonstrated improved performance and higher scores among students instructed using a combination of traditional methods and additional mobile techniques. By the end of the semester, the results leveled out, with a slight advantage observed for the group trained with the combined methods throughout the entire term.

Conclusion: Additional training on digital devices is an economical, innovative and reliable method that can be included in the program of orthopedics and traumatology.

Practical applications: The new hybrid method of teaching is part of the new educational strategies.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.



Project title: "Impact of COVID-19 infection in patients with rheumatic diseases and the need for remote access to medical care during the pandemic"

Project director: Prof. Anastas Batalov¹; Assoc. Prof. Rositsa Dimova²

Leading scientist: Assist. Prof. Aleksandar Marinkov¹

Research team: Assoc. Prof. Rositsa Karaillova¹; Chief Assist. Prof. Plamen Todorov¹; Chief Assist. Prof. Velichka Popova¹; Chief Assist. Prof. Zguro Batalov¹; eng. Tatyana Boeva³; Tsvetelin Kolev⁴; Konstantin Batalov⁴

Organization unit: Medical University of Plovdiv

1. Faculty of Medicine, Department of Propedeutics of Internal Diseases "Prof. Dr. Anton Mitov"
2. Faculty of Public Health, Department of Health Management and Healthcare Economics
3. Department of Educational and Scientific Documentation
4. Faculty of Medicine, student

Aim: This study aims to assess the risk of Rheumatic Diseases (RD) patients contracting COVID-19, the severity of the course, and the impact of ongoing immunosuppressive therapy through an e-platform, online survey, and clinical monitoring.

Materials and methods: An observational, cross-sectional online survey gathered data from 1288 RD patients using a specially developed web-based platform. Of the participants, 81.6% were women, with an average age of 47.03 years. IBM SPSS Statistics v. 25.0 was employed for analysis, utilizing descriptive statistics, logistic regression, and Decision Tree (CRT) method at a significance level of $P < 0.05$.

Results: Among RD patients, 28.80% contracted COVID-19, with 85.60% treated at home and 1.20% in intensive care. Common RD treatments included biologics with JAK inhibitors ($n = 537$) and corticosteroids ($n = 345$). Most patients (81%) experienced mild/moderate COVID-19, 13.50% severe, and 3.50% very severe. Communication with rheumatologists significantly impacted satisfaction, with on-site

communication increasing it by 452.8% compared to those who couldn't contact their rheumatologist. Maintaining/increasing visits boosted satisfaction by 43.3%/94.6%. Problems obtaining medications during the pandemic decreased satisfaction by 67.5%, and co-morbidities reduced it by 47.0%.

Conclusion: The study highlights the evolving landscape of rheumatological care during the COVID-19 pandemic, emphasizing the necessity to optimize remote access and develop disease-specific algorithms for tailored patient care by rheumatologists.

Application in practice: The study underscores the importance of optimizing remote medical care for RD patients, advocating for tailored algorithms to address individual patient needs, ensuring timely and adequate medical care during and post-pandemic.

Project performance evaluation: The project was duly completed and realized successfully with good publication activity.