SECOND INTERNATIONAL MEDICAL CONGRESS

Diabetes & Complications
Cardiovascular Diseases
Healthcare Reforms & Funding

7- 10 September 2011
Nesebar, Bulgaria

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SEEMF

SOUTHEAST EUROPEAN MEDICAL FORUM

(SEEMF)

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ABSTRACTS

РЕЗЮМЕТА

DIABETES AND COMPLICATIONS

ДИАБЕТ И УСЛОЖНЕНИЯ

INNOVATIVE AND MINIMALLY INVASIVE SURGICAL TREATMENT FOR ADVANCED PROLIFERATIVE DIABETIC VITREORETINOPATHY

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Purpose: The advent of pars plana vitrectomy considerably improved the prognosis of advanced stages of diabetic retinopathy. Despite improved techniques, the surgical prognosis is lagging behind patient expectations. Our study purpose was to compare and evaluate long- term results of sparing and traditional vitreoretinal surgery (VS) for advanced proliferative diabetic retinopathy.

Methods: 74 eyes of 66 patients with proliferative diabetic vitreoretinopathy (PDVR) performed by vitrectomy from 2006 to 2010 were analyzed. We used our modified (sparing) vitreous surgical technique in 50 eyes (44 patients) and the traditional vitreous surgery technique in 24 eyes (22 patients). Patients were operated on by the same surgeon (M.M.Shishkin). During sparing VS under local anesthesia we avoided totally removing the fibrovascular membrane or proliferation tissue where it was highly adherent to the retina; in these instances we retained the rest of proliferative fibrovascular membrane in eyes. The intraoperative and postoperative complications were compared in both groups. RESULTS: Sparing VS showed a lower incidence of intraoperative and postoperative complications than traditional vitreous surgery. The mean duration of surgery was notably shorter in the sparing surgical technique than in the tradition approach, and all patients who received the sparing vitreous surgery technique reported minimal discomfort during the procedure. We have not observed any postoperative re-proliferation of pieces (islets) of proliferative tissue in the group treated with the sparing vitreous surgical technique in the long-term period (follow-up range 6 to 38 month). This procedure has demonstrated evidence of reduced trauma to retina and results in a reduced rehabilitation period.

Conclusion: Our new sparing approach offers the advantages of minimally invasive vitreoretinal surgery with less “surgical stress”, shorter duration of surgery, reduced incidence of intra- and postoperative complication in diabetic patients. Our clinical observations show that vitreoretinal traction plays a key role in the pathogenesis of PDVR.

ОСТАТЪЧЕН СЪРДЕЧНО-СЪДОВ РИСК ПРИ МЕТАБОЛИТЕН СИНДРОМ И ЗАХАРЕН ДИАБЕТ ТИП 2

Доц. д-р Владимир Христов
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Успехите в сърдечно-съдовата превенция, постигнати през последните няколко десетилетия, сега са поставени пред сериозно изпитание от влиянието на глобалната епидемия от затлъстяване, метаболитен синдром и диабет тип 2. Повишената честота на затлъстяването е ключов фактор, допринасящ за честотата на диабет тип 2, която достига до 57%. На свой ред метаболитният синдром и диабетът повишават сърдечно-съдовата заболеваемост и смъртност при възрастното население. За съжаление, текущите стандарти за медицински грижи

не успяват адекватно да повлияят този променящ се профил на рисковите фактори. Въпреки тяхната ефективност, включително постигането на целевите стойности на LDL-холестерола, артериалното налягане и гликемията, пациентите остават изложени на висок риск от макроваскуларни инциденти (миокарден инфаркт и инсулт), както и на микроваскуларни усложнения на диабета (ретино, нефро- и невропатия).

По дефиниция значителният остатъчен риск от макроваскуларни инциденти и микроваскуларни усложнения е този, който персистира при повечето пациенти с МС и ЗД тип 2, въпреки текущите медицински стандарти, включително достигането на целевите стойности на LDL-холестерола и интензивния контрол на артериалното налягане и кръвната захар.

В настоящата лекция се коментира възникването на международната инициатива за редукция на остатъчния риск (Residual Risk Reduction Initiative R^3I), структурирането на международен ръководен комитет, неговата организация и програми. Обсъждат се възможни данни за остатъчния сърдечно-съдов риск и неговото намаляване на базата на редица доказателствени проучвания и се акцентира върху възможните терапевтични подходи в това отношение.

АКТУАЛНИ ПРОБЛЕМИ НА НАДНОРМЕНОТО ТЕГЛО И ЗАТЛЪСТЯВАНЕТО В ДЕТСКАТА ВЪЗРАСТ В БЪЛГАРИЯ

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Разпространението на затлъстяването сред децата и юношите постоянно ескалира. Глобалната епидемия от наднормено тегло и затлъстяване бързо се превръща в съществен проблем на общественото здраве в много части на света. Според Световната Здравна Организация (СЗО), в края на 2010 г. около 43 милиона деца под 5-годишна възраст са с наднормено тегло. Превенцията на затлъстяването на населението ще бъде важна част от усилията да се спре тази надигаща се вълна от детското затлъстяване. Спешно са необходими стратегически усилия за въвеждане на ефективни и подходящи програми и инициативи за предотвратяване на затлъстяването в детска възраст, като със сигурност се включат уязвимите групи - например деца с увреждания. Над 22 милиона деца в ЕС са с наднормено тегло и 5 милиона страдат от затлъстяване. Според данните от европейския проект "Диогенес", България е сред първите шест страни в Европа по разпространение на детското затлъстяването. Изследване на

Националният център по опазване на общественото здраве (НЦООЗ) от 2008 г. показва, че 200 000 деца в България са с наднормено тегло, а от тях 65 000 са със затлъстяване. Същото изследване показва, че 30,6% от децата в първи клас са с наднормено тегло и 15,6% са със затлъстяване. За последните 10 години се наблюдава 7,3% увеличение на броя деца в първи клас с наднормено тегло и този брой нараства всяка година. Проучване на деца и юноши (от 6 до 18 годишна възраст) в София, демонстрира основните рискови фактори за възникване на наднормено тегло и затлъстяване - генетичната предиспозиция, нерационален хранителен режим с предпочитание към нездравословни продукти, намалена консумация на зеленчуци и плодове и хиподинамия. Според групата по детско

затлъстяване към Европейската Асоциация за изследване на затлъстяването целите на правилното хранене в детска възраст са да се постигне нормално телесно тегло и да се развият здравословни хранителни навици, които да се поддържат през целият живот на детето. Първата стъпка за успешно хранително консултиране е оценката на калорийния прием и навиците на хранене. Това трябва да включва оценка на досегашната консумация (като се акцентира върху плодовете и зеленчуците, подсладените напитки, бързите храни, размера на порциите), както и тенденциите на похапвания и основни хранения (например, честотата и качеството на храненията като закуската). Изразходването на енергия чрез физическа активност е важна част от уравнението за енергиен баланс, който определя телесното тегло. Съвременните изследователи на детското затлъстяване обръщат особено внимание на перинаталните и пренаталните проблеми.

Подчертава се, че профилактиката на затлъстяването, захарния диабет и болшинството от сърдечно-съдовите заболявания започва още от вътреутробното развитие на индивида. Децата (и възрастните), веднъж засегнати от затлъстяване, трудно губят тегло чрез физическа активност и здравословен режим на хранене.

За това предотвратяването на наддаване на тегло още от най-ранна детска възраст е признато за стратегия, която ще бъде от полза за здравето им в дългосрочен план. Опитът в някои страни показва, че успешната превенция на затлъстяване и промяна в поведението на подрастващите може да бъде постигната чрез въвеждане на комбинация от мерки, прилагани едновременно на национално и локално ниво – в зависимост от местните условия и програми прилагани в училищата и местната общност.

ПРОБЛЕМЪТ ДИАБЕТНО ХОДИЛО

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Декларацията от Сент Винсент от 1989г. обоснова актуалността на захарния диабет и неговите сериозни усложнения като съществен здравно социален проблем за всички страни в света. Съществени заплашващи живота са гнойно - некротичните процеси на ходилото при болните със захарен диабет / Н.Н. Чур и съавт. 2003, Vinik and oth. 1992/

Важността на проблема се подчертава и от факта, че при 25% от болните с усложнения от захарния диабет имат гнойно-некротични процеси на ходилата. При това през 1996г. болните от диабет в света са наброявали около 120млн и се прогнозира, че към 2025г. техния брой ще нарасне на 250 млн. / А.Н. Косинец и А.А. Зеньков 2003г./ В доклада на Комитета на експертите по захарния диабет на СЗО диабетното ходило не се разглежда само като проява на диабетна микроангиопатия, а се определя като самостоятелен синдром с основни клинични прояви, предизвикани от микрангиопатия, вегетативна полиневропатия и остеоартропатия с присъединена към тях инфекция. Пак по определението на Експертния комитет по диабета на СЗО синдрома на диабетното ходило протича в три клинични форми:

1. Невропатична форма

2. Невроисхемична форма
3. Исхемична клинична форма

В нашите лични наблюдения, ние сме се придържали към тази квалификация.
Материали и методи:
За периода 2000г-2009г. под наше наблюдение са били 174 болни със синдром на диабетното ходило на възраст от 46г. до 87г, 101 мъже = 58,5% и 73 жени=41,3%.
По клинична форма на проява на синдрома болните са били:

a) С невропатична форма – 87 болни=50%
b) С невроисхемична форма-63 болни=36,2%
c) С изсхемична форма – 24 болни=13,7%

При всички болни с невропатична форма е имало язви по планта педис и по възглавничките на пръстите или между пръстите. От болните с невроисхемична форма 29 болни=45,5% са били с флегмон на ходилото с различна големина и фаза на развитие, а при останалите 34 болни=53,9% е имало и гангренозни процеси / суха гангрена на меките тъкани /. При болните с исхемична форма е имало тотална суха гангрена на пръстите или на части от дисталната зона на ходилото, като при 5 от тях гангрената и възпалителния процес е обхващал цялото ходило до талуса и калканеуса.
Микробологичното изследване от огнището на възпаление показва наличие на разнообразна бактериална флора:

- Стафилококус ауреус -96 болни=55,1%
- Смесена бактериална флора от Стафилококи-39,08%
- Анаеробна бактериална флора /пептострептококус, клепсиела, фражилис/ е установена при 117 болни=61,4%

При болните с исхемична форма е извършено изследване доплер сонография на ходилата и подбедриците-установено е намален кръвоток с по-богата колатерална мрежа и стеснения на артерия тибиалис постериор и артерия дорзалис педис, но не е установена пълна обструкция на тези артериални съдове. При тези болни ехографията на артерия феморалис също показва налични смущения в проходимостта, без тромбоза на артериалния съд.
При нашите болни сме се придържали към единна лечебна стратегия:

- Редовна хирургична обработка на язвите на меките тъкани
- Инцизия с последователно рутинно хирургично поведение при некрози на меките тъкани
- Инцизия с последваща редовна иригация с кислородна вода и антисептични разтвори при болните с флегмонозни процеси и абсцедирания.
- Редовен контрол на нивата на кръвната захар и корекция на отклоненията
- Антибиотична и антимикробна друга терапия при болните
- Мерки за преодоляване на интоксикацията и развита септицемия чрез активна инфузионна интравенозна терапия по назначения на реаниматор
- Ампутация на различни нива.

Починали са 6/шест/ болни от групата от развит тежък сепсис. В групата с ампутации в различен обем са починали . Леталитет в групата равен на 29,1%. При това починалите болни са били над 76 годишна възраст.
Нашите наблюдения ни позволяват да направим следните изводи:

1. Синдромът на диабетното ходило се развива при болни с по-продължително съществуване на основното заболяване /захарен диабет/
2. При всеки болен, независимо от клиничната форма на синдрома следва да се предприеме активно хирургично лечение и максимално възможна корекция на въглехидратния баланс.
3. При болните с невропатична форма трябва от рано да се предприемат мерки за щадене на ходилото при двигателен режим, съобразен с биомеханиката на съответното ходило.
4. Ефективната борба с наличната инфекция е важен способ за избягване на ампутации и други усложнения за по-дълъг период от време.
5. Развиващата се инфекция и въглехидратен дисбаланс са основни елементи за високия леталитет при подобни болни.
6. Болни със синдрома на диабетно ходило изискват стриктно диспансерно наблюдение с участие на ендокринолог, ортопед и общ хирург.

СЪДОВИЯТ ПРОБЛЕМ ПРИ ДИАБЕТНО ХОДИЛО

Василев В, Вл.Костов, А. Кехайов, Е.Лефтеров, проф. А.Атанасов
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Декларацията от Сент Винсент и програмата на Световната здравна организация по диабет/ 1992 / подчертават актуалността на диабета като медико – социален проблем. Установено е, че в Света около 120 млн. души боледуват от диабет и техният брой прогресивно нараства / С30 2006 /. Около 25 % от диабетно болните имат установен синдром на диабетното ходило / И. В. Гуръева 2001 /.

Синдромът на диабетното ходило е патологично състояние при болните с диабет, възникващо на фона на поражения на периферните нерви, кожата и меките тъкани, кости и стави, които се проявяват с възникване на остри и хронични язви, костни – ставни поражения и гнойно – некротични процеси / А. М. Светухин съавтор 2008 /.

В патогенезата на синдрома на диабетното стъпало лежат множество процеси като полиневропатия, ангиопатия, остроартропатия и присъединяващата се към тях инфекция. При болни с полинерропатия е висок рискът от развитие на синдром на диабетното ходило / Н. Н. Чур съавтор 2003 /.

Микроциркулация в долните крайници, предимно в кожата и подкожието се регулира от периферната нервна система по два основни механизма:

1. Прекапилярите се намират под неврогенен контрол и при нарушението на този контрол се развиват стенози с нарушение на хидростатичното налягане и филтрацията между пред и посткапилярното пространство.
2. Автономната нервна система, която регулира съдовия тонус отговаря за състоянието на артериоло-венуларните шънтове. Настъпва нарушение на тонуса им и паралитично разширение на тези шънтове, с патологичен внос на артериална кръв във венозните разклонения. Възниква феноменът на „откradване на капилярна кръв в микроциркулаторното русло"

Според приетата от Световната здравна организация клинична класификация при синдрома на диабетното ходило се различават три клинични форми:

а) невропатична;

б) невроисхемична;

в) исхемична.

Синдромът още може да бъде разглеждан като асептичен стадии на развит и инфициран / късен стадии / на развитие, при който се развиват гнойно – некротични процеси на ходилото, влажна гангрена, абцеси и флегноми.

За развитие на диабетна ангиопатия от значение е и вида на диабета. При инсулино-независим диабет – II тип, диабетно ходило се наблюдава значително по – често.

За диабетната ангиопатия при синдрома на диабетното ходило няма единни мнения. Болшинството автори приемат, че трябва да се разбира специфично поражение на малките съдове на ходилото / капиляри, артериоли и венули/ , а поражението на големите съдове не се различава от типичното поражение на тези съдове при атеросклероза / В. Л. Богданович 1998 /. Атеросклеротичните съдови изменения настъпват обикновенно в напреднала старческа възраст, докато диабетната ангиопатия се наблюдава при 5 – 10 годишно наличие на захарен диабет при отделните пациенти, независимо от възрастта.

Диабетната ангиопатия по класификацията на А. С. Ефимов 1989 по форма бива микроангиопатия и макроангиопатия, а по стадии на развитие бива:

а) до клинична: метаболитен стадии: съдовите нарушения се отбелязват само чрез специални методи на изследване;

б) функционален стадии – / хипертонус на съдовете, хипотонус, спастичноатомична форма /, със субективни и обективни клинични симптоми;

в) органичен стадии – с необратими изменения в съдовото русло;

г) язвено – некротичен, гангренозен стадии – дълбоки трофични промени и развитие на язви и гангрени.

Материал и методи: За периода от 2001г. до 2010 г. ние проверихме съдовите промени при 69 болни със синдром на диабетно ходило на възраст 44 – 69 години с давност на диабет от 6 до 11 години средно 8 год. и 7 мес., 45 мъже (65.20%) и 24 жени (34.70%). Първи тип диабет, инсулино зависим е отбелязан при 15 болни (21.70%) и при Втори тип диабет / инсулино независим / е отбелязан при 54 болни (78.20%). По клинична форма на синдрома на диабетното ходило болните са разпределени:

- Невропатична форма – 42 болни = 60.90 %
- Невроисхемична форма – 27 болни = 39.10 %

При всички болни за изследване на микроциркулация с прилагане главно физикални методи на изследване:

- Характеристика на периферния пулс – на а.феморалис, на а.поплитея на а.ретромалеоларис и а.дорзалис педис.
- Оценка на пулсово кръвоснабдяване на пръстите чрез компреси и бързо отпускане, доплер – сонография на бедро, подбедрица, ходило.
- Артеография при избрани болни.

Изледване на същите показатели при контролна група от 12 болни на възраст 65 – 67 години.

Резултати:

При всички болни е установена повишена кръвна захар 100 % , нарушена липидна обмяна – повишение на общи масти – при 21 болни с невропатична форма на диабетно ходило – 50 %и при всички 27 болни – 100 % при болните с невроисхемична форма. Нивото на триглицеридите е било повишено при всички 69 наблюдавани болни – 100 %. Периферен пулс е установен, както е показано на таблица № 1.

Таблица №1

Палпация на периферен пулс с уставен пулс	***Болни в %***	***Клинична форма на СДХ***	
		Невропатична	***Невроисхемична***
a.corotis	***100.00%***	***42***	***27***
a.poplitea	***100.00%***	***42***	***27***
a.retromaleolaris	***92.80%***	***35***	***4***
a.dorsalis pedis	***26.10%***	***11***	***0***

Ехографията на ходилото показва данни за нарушена микроциркулация на меките тъкани при всички болни – 100 %.

Рентгенографията на ходилото показва начални нарушения на костния скелет при 14 болни с невропатична форма – 33,30 % и при 21 болни – 77.70 %, със невроисхемична форма. Някои данни от Доплер сонографията са показани на таблица №2

Таблица №2

Данни от Доплер сонография	***Изследвани групи***		
	Здрави с херниотомия N – 12	***Невропатична форма N – 42***	***Невроисхемична форма N – 27***
Систолично – диастоличн индекс – SD – index	***52.4 +- 12.8***	***9.3 +- 0.6***	***6.4 +- 0.59***
Пулсаторен индекс – PI	***14.1 +- 1.2***	***0.95 +- 20.1***	***0.88 +- 19.0***

P < - 0.05

Данните са средно аритметично със стандартно отклонение.

Заключение: Показаните резултати за изследването на ангиопатичните нарушения при синдром на диабетното ходило, както и други наши клинични наблюдения за диагностика и лечение на общо 296 болни със синдром на диабетно ходило ясно позволяват да се присъединим към общото заключение на водещи клинични школи в Западна Европа и Русия, че синдромът диабетно ходило е самостоятелен синдром, с мултифакторна етиопатогенеза и многостранна симптоматика, и не може да се третира като усложнения на

диабета. Ангиопатията е важно звено в развитие на синдрома, още в неговите начални форми, за което следва да се предприемат енергични профилактични мерки:

- Нормализиране на нарушения метаболитен баланс
- Постоянна оценка и максимално възможна корекция на биомеханиката на ходилото.
- Своевременно и адекватно лечение, симптоматично и каузално, при постоянно променящата се клинична симптоматика на синдрома
- Ефикасни мерки за профилактика, лечение на развиващата се ангиопатия, тъй като ангиопатията е основен елемент на синдрома на диабетното ходило.

КАНДИДА ИНФЕКЦИИ ПРИ ПАЦИЕНТИ С DIABETES MELLITUS В НАШАТА ПРАКТИКА

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Кандидиазата е възпалителна болест с различна локализация , клинична картина, с акутно или хронично протичане предизвикана от гъби-дрожди , най-често от Candida albicans която изцяло е зависима от живия организъм който със своя защитен механизъм се защитава от тяхната инвазия.

Целта на труда е да се покаже наличието на кандида инфекции при пациенти с Diabetes mellitus или при пациенти, които поради микотични инфекции са били насочени за лабораторно изследване което е потвърдило самото заболяване.

Материал и методи. Анализиран е период от пет години (2006 – 2010) в който са регистрирани 425 пациенти от които 270 мъже и 155 жени на възраст от 20-70 годинини с потвърдена кандида инфекция на кожа и лигавици. 52 от тях са с новооткрит Diabetes mellitus.

Резултати. При изследваните пациенти са регистрирани 175 с Balanitis Balanoposthitis, 60 с Vulvovaginitis, 32 с Angulus infectiosus oris, 10 с Candidosis mucosae oris, 62 с Intertrigo candidomycetica, 38 с Onyxis et perionyxis canidomycetica и 48 с Erosio interdigitalis. Най-чести кандида инфекции в нащата практика са Balananitis и Balanoposthititis candidomycetica - 41%.

Заключение. Кандида инфекциите при пациенти с Diabetes mellitus не са редки в дерматологичната практика даже често са пръвите признаци, които насочват към диабет. Добрата глюкорегулация и антимикотичната терапия подобряват качеството на живот на пациентите.

DIABETES MELLITUS TYPE 2 AND ERECTILE DYSFUNCTION

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Introduction: Erectile dysfunction is the inability to achieve and maintain an erection long enough to have a couple of pleasant sexual intercourse.
Diabetes mellitus is one of the most common reasons for erectile dysfunction disorder nerve stimulation and changes in the microcirculation. 30-50% of men with diabetes have problems with erectile dysfunction.

Objective: The influence of type 2 diabetes on the development of erectile dysfunction.

Material and methods: The study included 86 men with type 2 diabetes aged 40 to 65 years with different disease duration. We analyzed the following parameters: HbA1c, serum lipid levels, testosterone levels, smoking and alcohol consummation.
We investigated the influence of the mentioned parameters on the occurrence of erectile dysfunction in men with diabetes mellitus type-2.

Conclusion: The level of HbA1c, lipid disorders, the level of testosterone, alcohol consumption, smoking and encourage early development of erectile dysfunction in diabetes mellitus typ 2.

Keywords: erectile dysfunction, diabetes mellitus type 2, HbA1c, serum lipid levels, smoking.

DIABETES MELLITUS T1 ADOLESCENTS - COMPUTER TECHNOLOGY IN THE SERVICE OF PREVENTION COMPLICATIONS - SOFTWER QUANTIFICATION SELF TREATMENT QUALITY

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Introduction: Pediatric diabetology team put the metabolic control (optimum level HbA1c) as a main target in therapy with the aim to prevent diabetic microvascular complications. Actual therapeutic instruments which involved whole family members in home treatment DMT1 include quantification of self treatment(grafic visualization of BG level and metabolic control) using softwer and computer technology.

The aim: One year follow up evaluated computer softver quantification self measurement BG with SPix (smart-pix) instrument PC connected.

Methodology:We compared questionary evaluated patients and family adherence for PC technology, and graphics picture of DM management (number of visit, number of checking, HbA1C level).

Results: Sample collected of 27 pediatric patients (14 boys and 13 girls), from 9 to 17 years old,(med 15,3) with duration of DMT1 min 2 years (med 5,7), with correct personal and family education for self - management treatment. Data find cooperation higher in girls (total number of visit f 52/ m 42), adherence for therapy regimen higher in younger family patients. Number of BG checking/ month (25-256, med 71) more frequent at first four years of DM duration, neg. correlate with HbA1c level. Influence

of using SPix reflect on HbA1c correction more in girls – improvement correlate with number of visit. Adolescents are less worried of their parents, about metabolic control category (non stabile, stabile , predominate high or low) but had more adherence for objective graphic measurement.

Conclusion: Using PS technology in pediatric diabetology is effective and reflects on patients adherence to therapy teem. Adolescents patients are curious and cooperate with self conclusion it therapy interventions.

OBESITY AND OTHER COMORBIDITIES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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More than 220 million people worldwide have diabetes. Over time, diabetes can damage the heart, blood vessels, eyes, kidneys, and nerves. About 90% of patients who develop type 2 diabetes mellitus are obese.

We conducted a cross-sectional study and analysed 1800 patients. We found 85 patients with type 2 diabetes mellitus (4.72%). We analysed data form the medical hystories of 45 patients with type 2 diabetes mellitus and compared them with data from 45 patient, randomly chosen, who did not have diabetes mellitus, matched by age and sex.

We found that there were significantly higher body mass index (BMI) and the level od triglycerids in patients with diabetes mellitus, compared to those who did not have diabetes mellitus. Patients who had diabetes mellitus and Methabolic syndrome X had a significantly higher BMI compared to those who did not have Methabolic syndrome X, but there were no significantly differences in the level of cholesterol and triglycerids. The most prevalent comorbid state were hypertension, followed by ischaemic coronary disease, vascular diseases and diabetic microvascular complications.

The overall risk of dying among people with diabetes is at least double the risk of their peers without diabetes. Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use can prevent or delay the onset of type 2 diabetes.

DICUMAROL AND DIABETES MELLITUS:CONSEQUNS OR COICIDENS ?

Djurovic Mladenovic Slavica, *Health Centre vranje, Serbia*

Pacients with thrombosis of the vein and oder hipercoagulabilitys tatus (especially those after heart oteracions, implatatio valvulae, Bay pass, infarctus myocardii, sistemic lupus eritemathodes, pulmonal embolism, cerebral embolism,

pectoral amgina and thrombosis atrii) have been subject to anticoagulant therapu for many years.

We have examined 540 patients bay per oral anticoagulant therapy (ACT). They have all been on anticoagulant therapy for more then years. Aport from biochemical parametres forexaminacion of liver function : transaminase, urhea in blood, electrolyts level in blood, protein level – albumin, we have also been looking for the glucose level im blood. Glicemia has been measured Glucometar GX made Ames – USA, in mmol/l, and the results werw tabularly presented accerding to thei sex, age, diagnoses by which they hove been subject to ACT.

Twelve of them hadregulateddiabetes mellitus before staring the ACT and there fore they were not controled. Fotry pacients have shown the glukose level I blood higher thouaverage : 18 had 9 mmol / l and 22 had 7,4 mmol/l. They were approximately 40-50 years of age ere 31 women and 9 men. ; 12 pacients of 540 have shown the signs of lovering the glucose level in blood , but they lhave also had some other parametres that showed the reduction of lever function. One pacient has been alopecia areata diagnosed in dermatological department.

We are presentet and disscused incidence of diabetes mellitus in pacients who have ACT many years. Cosequence or coincidence we been in new investigation ?

SCREENING FOR UNDETECTED DIABETES IN PRIMARY HEALTH CARE

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Introduction: Diabetes mellitus is one of the most common non-communicable diseases globally. The proportion of undiagnosed diabetes ranges from 30-90 %. Preliminary findings from the diabetes screening literature support the notion that early detection and treatment might be worthwhile.
Objective: To estimate the frequency of undiagnosed diabetes mellitus type 2, pre-diabetes and related risk factors using the FINDRISK questionnaire as a simple screening tool.

Material and methods: Screening was conducted at the Primary Health Care in Banjaluka (Bosnia and Herzegovina). The study involved 433 examines of both gender, aged 25-75 years with no diagnosed diabetes who visited their family physicians for any reasons in period from October 2007 to May 2008 year. Anamnestic data trough diabetes risk score, antropometric measures and relevant blood glucose test were collected. Diabetes mellitus and intermediate hyperglycemia were defined according to WHO/IDF criteria.

Results: The prevalence of undiagnosed diabetes was 4,15% and pre-diabetes (impaired fasting glycaemia/impaired glucose tolerance) 5,54%. According to FINDRISK score, the most frequent risk factor was central obesity 76,67% examines. The most frequent presence of two risk factors were central obesity and high body mass index (BMI) value 66,51%, and most frequent presence of three risk factors were: high

blood pressure, abdominal obesity and high BMI value in 36,03% of examines. Age, overweight, obesity, central obesity, physical inactivity were associated with high prevalence of hyperglycemia.

Conclusion: These results show high prevalence of new diagnosed diabetes and pre-diabetes and the strong association with related risk factors. Since most of these risk factors are modificable, screening for diabetes is justified and necessary.

CONTEMPORARY TREATMENT AND REVIEW OF PATIENT WITH TYPE 2 DIABETES IN REGION OF STIP

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Background: Diabetes type 2 is the basic problem in the diabetic science due to several reasons, such as the unexplained etiology and pathogenesis of the disease and therapy. The most important problem in treating the disease, remains the insulin resistance, possibly, due the inability to be explained, it will remain a long time in the realm of speculation and in the area of trials and efforts of the pharmaceutical industries in order to find the right therapy. The main aim of the project is the definition of the main reason for increasing the number of suffering from diabetes mellitus as well as determining the type of the most commonly used therapeutic techniques in Shtip (R. of Macedonia) diabetes center between 2005 and 2009th.

Methods: In this researcher is included 100 patients whith type 2 diabetes in region of Stip, R.of Macedonia.

Results: The number of registered cases of type 2 diabetes mellitus in the center of diabetes in. Clinical Hospital Stip from 2005 – 2009 is greater than before; an excess of them are womens (52%). Most of them used metformin with a proper diet and exercise program. Metformin controlling high blood sugar helps prevent kidney damage, blindness, nerve problems, loss of limbs, and sexual function problems. It works by helping to restore body's proper response to the insulin naturally produce.

Conclusion: In this researches is used a descriptive method for collecting and processing the results. 61% of all patients with diabetes mellitus type 2 treated in Shtip diabetic center are taking an insulin therapy at the same time with metformin, in which only 93% is achieved a normglycaemia condition.

REPRESENTATION OF DIABETES IN CHILDREN AND ADOLESCENTS IN EASTERN MACEDONIA

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Introduction-Two more children under five years Europe will be infected by type 1 diabetes from 2005 to 2020*.In diabetes type 1 beta stations gradual collapse of the thyroid gland that produce insulin to complete loss of insulin.

Objective: Type 1 diabetes often appears in contrast to type 2 and a rate of seven to 10 percent in all cases of diabetes. In children, they scale conflict in a larger

number drzhavi.Nauchnitsite found that the total number of sufferers grows by 3.9 percent per year. The study does not explain the trend of growth, but scientists believe that too an increasing number of sufferers can be prescribed to genetic factors. They focus on the role of obesity and more caesarean section.Number of sick children from type 1 diabetes in this age postijano and grew rapidly primarily as a result of genetic предиспозиција.Инсулинската treatment should regulate parents.

Results: In the period of 2009. In my municipality were registered suffering from diabetes and this: From 3-6 years. 35 children infected of whom 15 women and 20 children 6-11, the male children..Od. Infected 47 children of whom 35 women and 12 children 12-18, the male children.Od. 50 children infected of whom 27 women and 23 male children. Period of 2010. In my municipality were registered suffering from diabetes and this: From 3-6 years. Infected 42 children of whom 20 women and 22 children guys. 6-11 god.Ill patients 50 children, of which 35 female and 15 male children 12-18 .Sufferers 58 children, 38 women children and 20 boys.Conclusion: The display may be noted that the number of sick children and adolescents with diabetes each year have experienced steady growth.

Key words: diabetes, insulin therapy, insulin

PATIENTS WITH TYPE 2 DIABETES - OBESITY AND CONTROL OF HYPEGLYCAEMIA

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Background: Obesity is due to the development of insulin resistance, one of the causes of type 2 diabetes (T2D). Excessive weight maintenance or even its increase are an indicator of the quality of treatment of T2D.

The aim: To determine the percentage of obese patients in the group of patients with T2D in primary care medicine and the distribution by sex. To determine the correlation between body mass index (BMI) and waist- hip circumference ratio (WHR) with the control of glycemia, determined by measuring the value glycosylated hemoglobin (HbA1c) in the observed group of patients.

Material and methods: Statistical data from the medical records of 75 patients with T2D, measurement of height (H) and weight (W), circumference of waist (WC) and hips (HC) , then calculation of BMI and WHR, and HbA1c determination in the hospital laboratory. Data were analyzed using student T test.

Results: In the group of 75 patients with T2D, of which 12 were on insulin treatment , and 63 use oral hypoglycemic drugs , average age 70.3 years (SD = 11.1), there were 29 men and 46 women.

The observed group of patients had a mean BMI 26.24 kg/m2, and HbA1c 6.99%. Men had a mean BMI 26.08 kg/m2, WC= 90.31 cm, WHR= 0.98 and HbA1c was 7.13%, and women had a mean BMI 26.34 kg/m2, WC= 86.0 cm, WHR= 0.91 and HbA1c =6, 91%.BMI <25 kg/m2 with 30 patients or 40%, and BMI> 25 kg/m2 has 45 patients or 60%, with no statistically significant differences between gender (BMI <25 kg/m2 has 38% of men and 42% of women).

There is a significant difference in the average HbA1c among both, men and women, with BMI <25 and those with values above 25 kg/m2. In men, the ratio of

HbA1c is 6.41% vs. 7.59% and among women is 6.49% vs. 7.21% ($t_1 = 9.077$, $t_2 = 6.976$, $p < 0.001$).

There is a statistically significant difference in HbA1c among both gender in relation to waist circumference (WC). Among men with WC <94 cm average HbA1c was 6.73%, among men with the WC= 95-102 cm HbA1c was 7.67, and among those with WC> 102 cm HbA1c was 8.21% (t_1=5.846, t_2=4.174, $p < 0.001$). Among women with WC <80 cm and WC= 80-88 cm was no statistically significant differences between value of HbA1c (6.62% vs. 6.65%), while among women with WC > 88 cm HbA1c was 7.34% ($t = 6.685$, $p <0.01$).

Looking at the waist-hip ratio (WHR) we see that 82% of women and 41.4% of men with T2D have an “apple body shape”. Statistically significant difference was not observed in HbA1c among women with low or moderate risk and women with high risk of illness or death from cardiovascular disease. HbA1c was 6.78% vs. 6.94% ($t = 1.162$, $p> 0.01$). Among men, there was a statistically significant difference in value of HbA1c between the groups with low (WHR <0.95, HbA1c = 6.31%), moderate (WHR= 0.95 to 1.0, HbA1c = 7.28%) and high risk (WHR > 1.0, HbA1c = 8.18%). ($t_1 = 7.462$, $t_2 = 6.154$, $p <0.01$).

Conclusions: Most patients with T2D is moderately to considerably overweight, and women has the "apple body shape" more often than men. HbA1c values in obese patients with T2D were significantly higher than in patients with normal weight. BMI, waist circumference and WHR give the determination of significant difference in HbA1c in patients with T2D , except by WHR among women, probably because we observed a very homogenized population.

Key words: body mass index (BMI), waist-up- hips ratio (WHR), glycosylated hemoglobin (HbA1c)

COMPLICATIONS OF DIABETES MELLITUS

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Background. The fundamental complications of diabetes mellitus are result of damages of the blood vessels and nerves.The damages of big blood vessels lead to damage the heart, the accumulated damage to the small blood vessels lead to nephropathy and rethinopathy.

The aim of the investigation was to present the long-term complications of diabetic patients over 10 years.

Methods.We examinated 134 diabetics in age og 20 to 70 years old, 80 were females and 54 were males. All the patients were submitted to the following analysis: glycaemia and cholesterol color enzymatic,glycated hemoglobin, blood pressure,eye inspection, urine analysis and albuminuria.Results.The results were: serum glucose 9,2 mmol/L +/- 2,2; cholesterol 6,9 mmol/L +/- 1,5; HbA1c 9,5% +/- 2,2. The following complications were found: 52,3% diabetics have HTA, in 64,8% hyperholesterolemia, 9,4% developed rethinopathy and severe visual impairments, 13,3% nephropathy and 67,2% neuropathy.

Conclusion: Diabetes has been a major global public health problem.The complications caused of diabetes impose significant medical problem on individuals,

families, health systems and country.The prevention and early detection of diabetes are imperative for control the disease and its long-term complications.

SKOPRYL PLUS MEDICINE OF CHOISE IN THE THERAPY FOR HYPERTENSION

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Background: Arterial hypertension is one of the most usual cardiovascular illness. Use of Skopryl plus in monotherapy with fix combination of Lisinopryl 20 mg and Hidrahlorthiazzid 12,5 mg.

Material and methods: 40 patients diagnosed with arterial hypertension, in the cource of three mounths from Oktomber to December 2010) all of the patients were put on mono therapy with fixed combination of Skopryl plus.

Results and discussion: Out of 40 patients, in the age limit between of 50 and 70.Their systolic blood pressure ranged with the limits of 160to 140, while the diastolic ranged from 100 to 90 mm. In the course of three mounts all the patients took skopryl plus once per day. This resulted in decrease in blood preasure.The systolic pressure was decreased within the limits from 140 to 130 while diastolic within the limits of 80 to 75 mercury. In addition to the Skopryl plus therapy, twelve of the patient were treated with verapamil 240 mg pills once per day. The therapy was extended for the duration of the survey as well.

Conclusion: Skopryl plus is a medicine of choice for patients with increased blood pressure. The fix combination provides comfort in taking the medicine while the efficiency is evident.

FREQUENCY ANALYSIS OF DIABETIC RETINOPATHY IN PATIENTS WITH DIABETES AT PRIJEDOR HEALTH CENTER

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Introduction: Diabetic retinopathy represents a chronic evolutive microvascular complication in an eye of the patients with diabetes mellitus type 1 and 2 and is considered to be the primary cause of blindness in modern world.

Aims: To analyze the frequency and clinical classification of diabetic retinopathy and determine its relation to the type and duration of diabetes, age, parameters of the metabolic control of diabetes and blood pressure values.

Methodology: The research was carried out in eight Family Medicine departments of the Prijedor Health Center in the period from 15. 12. 2010 to 15. 01. 2011. The criteria for inclusion are patients of both sexes with diabetes mellitus type 1 and 2 for more than 5 years. The data were collected by means of a questionnaire.

Results: The research included n=200 patients; diabetic retinopathy is present in 15.13% of them. Proliferative retinopathy is represented with 16.8% and non-proliferative retinopathy with 83.2%. We found diabetic retinopathy in 21 patients with type 1 diabetes aged between 41 and 64 years and with its duration of more than 10

years (81.3%), and 9 patients with type 2 diabetes who are older than 64 and with five-year duration of the illness. All the diabetic retinopathy patients have parameters of the metabolic control of diabetes and blood pressure values above those recommended.

Conclusion: Diabetic retinopathy is more frequent in patients with type 1 diabetes mellitus whose illness lasted for more than 10 years. The non-proliferative form of diabetic retinopathy is the most frequent. A positive correlation exists between diabetic retinopathy and the type and duration of diabetes, age, parameters of the metabolic control of diabetes and blood pressure values. Metabolic control of diabetes is a main prerequisite for the prevention of this illness as well as the progression of present damage and regular checkups are the imperative for both patients and doctors.

Keywords: diabetic retinopathy, diabetes mellitus, metabolic control

DISCOVERING OF RISK FOR THE DIABETES MELLITUS AMONG HEALTHY POPULATION

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Diabetes mellitus takes on a modern epidemic proportions. Before the moment of discovery, it was undiscovered in a decade. In order to minimize the number of new patients of diabetes mellitus, and early and late complications of this disease (which is a major health and economic problem of the country), Ministry of Health has prepared a national program for early detection of diabetes mellitus.

The aim of the work: Discovering the degree of risk of diabetes mellitus among the healthy population, whether there is a difference between sexes.

Methods: The study was conducted at the Health Center Krusevac. We used a questionnaire for assessment of the risk for diabetes mellitus, which has made Republican panel of experts, the project of the Ministry of Health. All data were statistically analyzed and tested (average values, SD, t-test, X2 test).

Work results: The study included 553 patients, average age 45.53±12.46 years: 90 men (48.98±14.37 years) and 463 women (46.02±11.9 years). Half of the women (54%) had normal BMI, 29.37% had excessive body weight, and 3.24% were obese. Among men, 45.5% of the normally fed, 40% of excessive body weight, and 14.44% were obese. The difference between sexes for BMI (men 25.14±4.73 kg/m2, women 24.36±5.38 kg/m2) was not statistically significant ($t = 0.607, p < 0.1$). Desired waist (men <94cm, women <80 cm) had 55.5% women and 63.33% males, while high-risk waist (men> 104cm, women> 88cm) had 23.32% women and 16 67% men. Physically active is 78.62% female and 78.89% men. This difference was not statistically significant ($\chi 2 = 0.0069$). Average Systolic blood pressure among women was 123±23.12 mmHg, and among men, 131.47±17.67 mmHg. The difference is highly statistically significant: $t = 2.98$, $p > 0.01$). Diastolic blood pressure among women was 79.19±10.11 mmHg, and for men 81.94±10.52 mmHg. The difference between sexes was highly statistically significant ($t = 2.39$, $p > 0.01$). The average value of blood glucose among women was 4.12±0.49 mmol/l and among men, 4.48±0.75 mmol/l. The difference between genders is very highly statistically significant. Based on the answers from the questionnaires made up almost the occurrence of diabetes mellitus, total score lower than 7 and a low risk had

61.3% of respondents (62.2% women and 56.67% men). Easy elevated risk score (7-11) had 27.67% of the respondents (26.99% women and 31.11% men). Moderate risk score (12-14) had a 7.41% of the respondents (7.34% of women and 7.78% of men). High risk of developing the disease and score 15-20, had 1.63% of the respondents (1.94% of women, 0% of men). Very high risk score, greater than 20, had 1.99% of the respondents (1.51% of women and 4.44% of men). Average risk of disease among women was 6.2 ± 3.64, and among men was 6.68 ± 4.29. This difference between genders was not statistically significant: $t = 1.297$, $p < 0.1$.

Conclusion: following risk factors that have had our respondents, their risk of diabetes mellitus is low. Although in the individual risk factors there is a statistically significant, the difference between sexes in score was not statistically significant. These data are encouraging, considering the huge socio-medical importance of having Diabetes Mellitus.

Key words: Diabetes mellitus, risk assessment, score.

RECOGNIZING POLYNEUROPATHY IN PATIENTS WITH DIABETES MELLITUS NON-INSULIN DEPENDENT IN THE GENERAL PRACTITION

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Background: In view of the global pandemia of Diabetes mellitus non-insulin dependent (DM type II), you may say that in Serbia there are 400 000 people with diagnose, and as many who have a high level of glucose in their blood. Distal sensorimotor polyneuropathy is one of the most common chronic complications which leads to trauma lesions, ulcers, gangrene and amputations in both groups. In our research we want to define the frequency of polyneuropathy in our patients with DM type II although as risk factors for its appearance.

Methods: We analyzed 50 patients with DM type II. All patients passed through clinical protocol which includes: clinical examination, neurological examination, determination of Body Mass Index(BMI), laboratory analysis (preprandial glucose, glycosylated hemoglobin). Patients are divided in two groups: with and without polyneuropathy, based on neurological examination and/ or EMNG examination, and then are statistically analyzed by: demographic characteristics(age, gender), genetic predisposition, duration of diabetes (shorter or longer then 5 years), the regulation of diabetes (poorly regulated is defined when serum glucose leve l is over 7 mmol/L, and glycosylated hemoglobin is over 7,5%) and presence of obesity (BMI over 27).

Results: Based on analyzing the whole group it is determined that there are 34 men (68%) and 16 women (32%) and 46 (92%) aged over 50. With 45 (90%) people the disease lasted longer then 5 years and 15 (30%) patients had information about diabetes in family. BMI is larger than 27 with 28 patients (56%), 35 (70%) had preprandial level of blood glucose higher than 7 mmol/L and 31(62%) had glycosylated hemoglobin higher than 7,5%. Medical history of sensory disturbances had 42 (84%) patients and with 35 (70%) the existence of polyneuropathy was confirmed. Comparing the two groups showed that the group with confirmed polyneuropathy were older (older

than 50 years 100% vs 73,3%), disease lasted longer than 5 years (90% vs 10%), obesity was significantly more frequent (49% vs 6,7%),and had poore diabetes control (65,7% vs 53%). Micro trauma were more frequent in the group with polyneuropathy (75% vs 25%).

Conclusion: Among our patients who have DM type II 70% had polyneuropathy. Higher risk of appearance of polyneuropathy have people older than 50 years ($p<0.05$), obese ($p<0,001$), with poorly controlled diabetes ($p<0,05$) and those whose disease lasted longer than 5 years (p,0,001) so it is necessary to regularly check these patients and do education. Special attention should be payed on the foot micro trauma which occurred more frequently ($p<0,001$) in this group.

Key words: diabetes mellitus, polyneuropathy, general practice, glycosylated hemoglobin

INFECTIOUS AND CHRONIC NOIN-INFECTIOUS DISEASES

ИНФЕКЦИОЗНИ И ХРОНИЧНИ НЕИНФЕКЦИОЗНИ БОЛЕСТИ

БАЛАНСОВ ПОДХОД В КЛИНИЧНАТА НЕФРОЛОГИЯ: КАК КЛАСИЧЕСКИ ПОКАЗАТЕЛИ МОГАТ ДА СТАНАТ ОТНОВО АКТУАЛНИ?

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Бъбреците играят централна роля в хомеостазата чрез балансирането на: вода, електролити, алкално-киселинно състояние, метаболитни продукти, медикаменти, токсини и др. В лекцията ще бъде представена и анализирана една интересна и практически значима закономерност, отнасяща се до еволюцията в годините на класическите нефрологични показатели като урея, креатинин, пикочна киселина и натрий. Става въпрос за следния **алгоритъм: първоначален клиничен ентусиазъм ⇨ ограничение на интереса ⇨ отново нарастваща актуалност.**

Обяснението за този своеобразен „ренесанс" на горните показатели през последните 10-15 години се корени в прилагането на балансов подход /внос, натрупване, елиминация/, вместо базирането единствено на серумното ниво/натрупване/.

Уреята е органично вещество, което се синтезира от CO_2 и NH_3 в черния дроб чрез урейния цикъл. Целта е неутрализиране на токсичния NH_3 , идващ от белтъчния катаболизъм. Любопитно е това, че водните животни не произвеждат урея - NH_3 се екскретира през кожата, чрез контакта с водата.

Уреята е най-старият маркер в нефрологията. H. Rouelle през 1773 г. открива уреята в урината, а през 1828 г. F. Voehler я синтезира. През първата половина на 20-ти век кръвната урея е господстващ показател за оценка на бъбречната функция /урея и уремия – общ корен/. След въвеждане на понятието „клирънс" /1929 г./ и попадайки „ в сянката" на креатинина, уреята загубва своето значение за оценка на гломерулната филтрация /ГФ/ по две причини:

- Голяма зависимост от белтъчния внос/катаболизъм,
- 40-70% от ГФ поради тубулна реабсорбция.

Чрез балансовия подход споменатите недостатъци се превръщат в предимства, което възражда значимостта на уреята в клиничната практика:

Креатининът има водещо значение в годините и понастоящем за оценка на бъбречната функция и ГФ. Той се получава от неензимното дехидрогениране на креатин и креатинфосфат, които от своя страна са продукт на енергийната обмяна на мускулите. Креатининът е малка молекула 113D, белтъчно несвързана, която се филтрира много добре през гломерулите. Едновременно с това неговото ендогенно производство G_{CR} е относително постоянно, корелиращо с мускулната маса на индивида. Тези характеристики правят ендогенния креатининов клирънс /C_{CR} /24 ч/ 3 ч/ – обем урина/ удобен за практиката маркер за ГФ.

С течение на времето обаче се натрупаха факти, които опровергават хипотезата C_{CR} да бъде близък до „идеалния" показател за ГФ:

- Доказана 20 % тубулна секреция на креатинин ⇨ надценяване на ГФ, може да се блокира от редица медикаменти.
- Променливост на G_{CR} при отделния индивид, внос на повече месо ⇨⇧ 15 %; физическа активност; неточно измерване на обема урина; неправилно

съхраняване на събраната урина /t°⇧ Ph⇩/ увеличава с 20% креатин ⇨ креатинин; ⇧ екстраренално разграждане при бъбречна недостатъчност.

- Нежелание на болните да събират често 24 часова урина в домашни условия.

Търсенето на „иделния" тест за ГФ продължава и до днес, тъй като такъв не е намерен. Става въпрос за инфузии с инулин, изотопни клирънси йоталамат – J 125, Cr 51, технеций С 99, рентгенконтрастни средства – йохексол, гадолин, цистацин С и др. Наред със специфичните недостатъци на всеки един от тези тестове, важен момент е и високата цена - трудно многократно приложение при хронично болни. Предстои създаването на метод за определяне на ГФ, който да стане „златен стандарт – 24 карата"/Nankivel/.

От 1998 г. насам набира инерция, т.н. изчислен ГФ /eGFR-estimated/ на базата на формули, включващи основно S_{CR}, пол, възраст, т. тегло/височина, S_{UR} и др. Първата формула на Cockroft и Gault (CG), датира от 1976 /Nephron/, но дълго време остава малко популярна. Днес са публикувани голям брой формули за GFR, които от една страна корелират добре с ГФ, а от друга – са многократно приложими за скринингови проучвания, ранна диагностика на хронични бъбречни заболявания /ХБЗ/, оценка прогресията на бъбречната функция и пр. Ще спомена някои от тях: MDRD / 3 варианта/, Mayo, Nankivel, Salazar, CG и др.

От казаното до тук става ясно, че се очертава тенденция към нов възход на креатинина като масов лабораторен показател, сравним с кръвната захар, хорестерола и др. Едновременно нарастват и изискванията към неговата аналитична прецизност – усъвършенстване колориметричната проба на Jaffe с алкален ликрат, въвеждане на ензимно определяне.

Преди повече от 40 години научните изследвания върху обмяната на пурините и **пикочната киселина** /след откриване на ДНК кода/ са вълнуващи и плодотворни. На Elion и Hitchings е присъдена Нобелова награда заради синтез и въвеждане в терапията на пуриновите аналози – Azathioprin – имуносупресор, Allopurinol – понижаващ пикочната киселина.

Пикочната киселина с м.т. 168D е краен продукт на веригата – пуриннуклеотид ⇨ хипоксантин ⇨ ксантин под влияние на ксантин-оксидазата /черен дроб, тънки черва/. В кисела среда тя е слабо разтворима и кристализира. В тъканите се формират мононатриеви хидрати. В началото се възприемаше кристалзависимата токсичност на пикочната киселина за обяснение на подагрозния артрит и хроничната подагрозна нефропатия:
кристали ⇨ микротофи ⇨ възпаление ⇨ фиброза

След 70–те години на миналия век се налага мнението, че въпросите, свързани с пикочната киселина са изчерпани и интересът намалява, нещо повече – ревматолозите не винаги установяват корелация урекемия - пристъпи на подагрозен артрит. Наличието на подагрозна нефропатия се оспорва основателно. Много често изолираната хиперурикемия неправилно се свързва с белтъчно-пуринно прехранване без да е направена балансова оценка.

И при пикочната киселина се очертава вторичен пик на научен и клиничен интерес. Той е свързан с натрупаните през последните 10-15 години данни, че урекемията /извън кристалозависимата/ може да бъде маркер или увреждащ /рисков/ фактор при различни заболявания. От бъбречната физиология и еволюция могат да се получат аргументи, потвърждаващи значимостта на

балансирането на пикочната киселина за организма. След ГФ, в S_1 сегмента на проксималните тубули пикочната киселина се реабсорбира, а в сегменти S_2 и S_3 се осъществява секреция и постсекреторна реабсорбция. Този активен тубулен обмен не е случаен и цели недопускането на много високи /токсични/ урекемии. Затова и референтните граници на C_{UA} са твърде широки 5-18 ml/min. N. Bricker включва пикочната киселина в системата на „пълна регулация" заедно с Na, H_2O и К. У птиците и млекопитаещите е наличен ензимът уриказа, който превръща пикочната киселина в много добре разтворимия и напълно безвреден алантоин. У човек, поради мутация в Миоцена, уриказа липсва ⇨ компенсаторно усложнена регулация.

Ролята на бъбреците за поддържане на АН и съответно генериране на артериална хипертония /АХ/ се отнася главно до обема на кръвния ток – чрез **регулация на Na/H_2O** и регулация на еритропоезата /еритропоетин/.

Предполага се, че първобитният човек през палеолита – преди 40 000 години е внасял оскъдни количества сол с храната~30 mmol/d и съответно бъбреците са били настроени да спестяват натрия.

След масивното въвеждане на готварската сол като консервант и овкусител с т.н. Western diet през 21 век се внасят ~ 200 mmol/d. Това налага бъбреците да се нагодят да отстранят натрия.

Ако теоретично се внесат 200 mmol/d натрий и той не може да се елиминира /анурични болни на диализа/ екстрацелуларния обем /т. тегло/ ще нарастне с 18%.

Пресорната натриуреза /покачено системно и вътрегломерулно налягане/ е основният бъбречен механизъм за за отстраняване на натрия. През 1972 г. – Guyton въведе понятието „солрезистентност" и „солчувствитителност". При солрезистентните пациенти-внесеното количество сол се отстранява ефективно, с леко /в референтни граници/ покачване на артериалното и вътрекапилярно налягане. При солчувствителните пациенти това става с цената на артериална хипертония и гломерулна хиперфилтрация.

Weinberger, 1996, въведе теста за „солчувствителност" – спрямо внос 30 mmol/d натрий, внасянето на 300 mmol/d покачва с повече от 10 mmHg – средното артериално налягане.

В заключение би могло да се твърди, че чрез балансовия подход класическите нефрологични показатели – урея, креатинин, пикочна киселина могат да получат нови измерения на информативност, осъвременявайки диагностиката и лечението. Чрез балансиране на солевия внос може да се подобри контролируемостта на АХ.

СЪВРЕМЕННИ АСПЕКТИ НА ПАТОГЕНЕЗАТА И ЛЕЧЕНИЕТО НА РЕВМАТОИДНИЯ АРТРИТ

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Ревматоидният артрит е автоимунно, възпалително ставно заболяване с хронично прогресиращ ход, което засяга много или всички стави, и води до инвалидизиране, в случай че не се лекува, или с лекува неадекватно. Може да са

налице системни прояви от страна на очите, кожата, белите дробове, сърцето, съдовете, бъбреците. Честотата при възрастното население е 1 – 1.5%.

Съотношението жени:мъже е 3:1. Началото на заболяването е между 30 и 50 години.

Патогенезата е сложна и недостатъчно ясна. Роля играят нарушение на имунитета (автоимунитет), генетични и инфекциозни фактори. В здравата става тънка синовиална мембрана състояща се от два вида клетки "тапицира" вътрешната повърхност на ставната капсула. Най-характерен признак в патогенезата е абнормното активиране на имунната система с преминаване на имуно-компетентни клетки в синовиалната мембрана. Натрупаните в ставите имуно-компетентни клетки (Т и В-лимфоцити, фибробласти, макрофаги, дендритни клетки) продуцират цитокини (IL-1, IL-6, TNF-α, IL-17, IL-23) и антитела, които предизвикват ерозии и деструкция на ставните повърхности.. При ревматоидния артрит (РА), синовиална мембрана става хиперпластична. С времето се развива 'панус,' който мигрира върху ставния хрущял и подлежащата кост и образува ерозии. От генетичните фактори основна роля играят HLA клас II антигените. HLA DR4 е наличен в 70% от болните с РА. Ролята му е представяне на антигените на CD4 Т-хелперните лимфоцити.От инфекциозните фактори оля играят: Mycoplasma (суперантигени), Pravovirus B19, ретровируси (директна синовиална инфекция) и ентеробактерии, Mycobacteria и Epstein-Barr вирус (молекулярна мимикрия). Напоследък се допуска етиологичната роля на Porphyromonas gingivalis и цитрулинираната α – енолаза при болните с РА и периодонтит.

Лечението е комплексно и патогенетично, поради неясната етиология. Съвременното лечение включва нестероидни противовъзпалителни средства (НСПВС) – неселективни и селективни , които повлияват болката при ставното възпаление, но не променят хода на болестта, синтетични болест-променящи антиревматични средства (сБПАРС) и биологични болест-променящи антиревматични средства (бБПАРС). От сБПАРС основно приложение намират Methotrexate, Leflunomide (Arava), Sulfasalazine, златни соли, а от бБПАРС – антатагонисти на TNF-α (Infliximab, Adalimumab, Etanercept, Golimumab, Certolizumab), антагонисти на IL-6 (Tocilizumab), анти-CD20 антитителa (Rituximab). Лечението се започва с едно от горе упоменатите сБПАРС и ако липсва ефект върху хода на заболяването след 3 месеца, или има нежелани странични реакции, се включва бБПАРС. При някои случаи с бързо прогресиращ, тежък РА, може да се включи бБПАРС като средство на първа линия. Обикновено комбинацията от сБПАРС и бБПАРС е по-ефективна, отколкото самостоятелното прилагане на един от двата вида лечение. Последни проучвания показват, че анти-IL-6 антагониста (Tocilizumab) може да се използва като средство на първа линия вместо Methotrexate, или в комбинация с него още от самото начало на лечение на артрита. Напоследък се прилагат и т.нар. киназни инхибитори на JAK-киназата, която играе роля при синтезата на цитокини.

Често РА се обостря от вметнати инфекци, които се лекуват с адекватни антибактериално лечение, успоредно с основното.

Успоредно с медикаментозното лечение се провежда адекватна физиотерапия, и механотерапия, както и хирургическо лечение (частично или тотално протезиране и др.)

RARE AND "SUPER-RARE" DISEASES: MACEDONIAN INSIGHT

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Introduction: Rare diseases (RD) are becoming increasingly important as possible targets of new forms of treatment, as a valuable source of a novel insight in fundamental lows of biology, and in the specific mechanisms of many diseases. Molecular methods have created a better diagnosis and oftentimes treatment. RDs pose significant problem for the patients, since their problems are often not recognized by the medical community and shunned by the health insurance. The cumulative costs of diagnosis and treatment of RDs is significant for any society, oftentimes bearably acceptable developing countries.

Definitions: In Europe RD is the one which affects less than one citizen in 2000 (1, 2), in the USA - one in 1250 (3), while in Japan RD is the one that affects fewer than 50,000 patients (4). It should be stressed that many patients suffer from even rarer diseases, affecting 1 person in 100 000 or more (super RDs). Those differences stem, at least partly, from the fact that RDs have variable prevalence in different populations.
The term "orphan diseases" further adds complexity, since it is often used as a synonym for RDs (4). Originally, orphan disease was a term used for a disease for which the pharmaceutical industry has little financial incentive to produce medications. The European Organization for Rare Diseases (EURORDIS) classifies both rare diseases and neglected diseases as orphan diseases (5).

A large fraction of RDs affect children (75%). It is a striking fact that as much as 30% die before their fifth birthday (2). As many RDs end in early death, the true incidence and prevalence of many RDs are unclear. EURORDIS estimates that ~80% of RDs have genetic origins (5). Some infections, allergies, degenerative diseases, as well malignant diseases in children are RDs.

It is of note that almost all children attending a subspecialty clinic in paediatrics are suffering from a rare disease. Some 700-800 metabolic diseases diagnosed in children are RDs. There are about 250 different types of immune deficiencies which all fulfil the criteria of rare disease.

In paediatric endocrinology most disease are RDs. In paediatric nephrology there are only two types of diseases are frequent: urinary tract infections and enuresis. The nephrotic syndrome, acute or chronic renal failure, tubulopathies may be caused by hundreds of underlying kidney disorders which all fit the definition of RDs.

The society, actions taken and actions needed : EU estimates that 5-8000 distinct rare diseases affect 6-8% of the population (5). The impact of RDs in the health systems is impressive: at least 3 million patients in the UK, 4 million in Germany, and between 27 and 36 million EU citizens.
RDs have significant consequences for the individuals, their families and the societies (5-8):

1. RDs impact on the families of the affected children making many parents full-time carers.
2. Patients with RDs often need a team approach and treatment.
3. RDs are a major public health problem because of their cumulative frequency.

RDs create a particular set of challenges:

1. An epidemiological challenge: there is lack of registries on the epidemiology.
2. A pharmacological challenge: there is a lack of multicentre controlled therapeutic studies.
3. An organisational challenge: there is a lack of standardised referral of patients with RDs in Europe.
4. A legal challenge: there is a lack of legal basis for cross border genetic diagnostics.
5. An ethical challenge: there are different priorities in different European countries.

Those challenges are also the goals of EU in regard of the RDs. A Committee of experts on rare diseases (EUCERD) was created in 2009. The aim of the Committee is the assist the European Commission in creating the up guidelines for implementing EU policies for RDs. The Committee recommended the institution national plans for RDs before the end of 2013 (9 June 2009). In order to raise awareness on RDs a Rare Disease Day was created (9). The day was first held in Europe and Canada in February 2008.

Support groups: For some of the well-known RDs, such as Down syndrome, cystic fibrosis, haemophilia, there are support networks at national and international levels (10, 11).

Web resources are also important. Orphanet (a database of rare diseases and orphan drugs) quotes more than 4600 resources for more than 1500 RDs. This database contains an on-line

encyclopaedia and a directory of services for patients and professionals.

Macedonia: What is the present situation with RDs in Macedonia? First, there are no official registries at the national level. Therefore the full picture and the consequences for the society are not known. Articles on metabolic, nephrologic, tumor, haematologic, genetic and dysmorphologic diseases and syndromes were found published by Macedonian professionals on Pubmed (12).

Those articles give only a very narrow insight into the frequency, diagnosis and treatment of RDs. It is obvious that this is an iceberg situation: one sees only the tip of it.

However, the sheer number of published articles indicates that a number of physicians are educated to diagnose RDs, and oftentimes find new insight in some of their particularities. Some patients are treated (Hunter's syndrome), some other children and adults not (Gaucher's disease in children and adults). The country also lacks a significant screening for multiple diseases: Macedonia screens only hypothyroidism, while some European countries screen ~30 diseases. Nevertheless, and education program directed towards the RDs should be created, along with a national registries and an increased assistance of the state in diagnosing and treating those diseases.

Key words: rare diseases, definitions, social impact, Macedonia.

ГРИП А1 (H1N1) С АСОЦИИРАНИ ПНЕВМОНИИ-ИМУНОЛОГИЧНА АРГУМЕНТАЦИЯ ЗА КОМПЛЕМЕНТАРНО ХОМЕОПАТИЧНО ЛЕЧЕНИЕ

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Авторът представя резултатите от клиничното протичане и имунологичните изследвания при 8 болни с грип А1 (H1N1) асоциирани пневмонии .

Изследвани са нивата на антифосфолипидните антитела,и интерлевкини:IL1, IL6,IL10,TNFa .

Потвърждава се фактът, че тежко протичащите пневмонии при грип А1 (H1N1) не се дължат само на директна агресия на грипните вируси и вторичните бактериални инфекции.

Развитието им е резултат от несъразмерно силен отговор на имунната система – експресия на проинфламаторни интерлевкини - IL1, IL6, TNFa - „интерлевкинова буря", водеща до увреждане на алвеоларния епител и последващо „алвеоларно запълване"

Това нарушение на имунният отговор аргументира мястото и на хомеопатич –
ното лечение като метод за повлияване на индивидуалната реактивност.

Представени са клинични случаи с проведено комплементарно хомеопатично лечение (Phosphorus, Bryonia, Cuprum metalicum) потвърждаващи възможностите на хомеопатичния метод.

INADEQUATE NUTRITION DISEASES(IND) AND ITS INFLUENCE ON FREEQUENCY AND SEVERITY OF LOW RESPIRATORY TRACT INFECTIONS(LRTI) IN SMALL CHILDREN

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Inadequate nutrition disorders(IND) have the same genesis, but synergistically together, they have unwilling influence on children's health because of its association and mutually supporting. Malnutrition, GER(with or without aspiration syndrome), chronic diarrhea etc.are frequently associated with rachitis, decreased immunity, ferrodeficite anemia, increased infection tendency, slowed growth and development, etc.

Aim: Review of IND frequency in small children with LRTI and it's eventually interaction.

Material and methods: Retrospectively,we elaborated 665 histories of patients with IND and LRTI=Igroup,(2m-4yr.(mid.age:9,99month.), male:412(61,95%), female:253(38,04%), and compared them with 665 children(mid.age:10,26month, male:401(60,30%), female:264(39,70%).They were with similar-(almost the same)LRTI, but without IND=II-group; In both groups were followed: LRTI frequency(anamnestical), severity of actual pulmonal suffering(by clinical-score), Chest X-ray findings, and values of hematological, biochemical, biologic etc.(parameters-relevant for egzisting,and severity of bacterial infection), hospitalization duration,etc.

Results: Pneumonia, acute bronchitis, recidivate obstructive bronchitis, aspiration syndrome,were most frequent LRI associated with IND:(ferrodeficite anemia, rachitis, GER, hypotrophio, allergia nutritiva…).In I-group: 53,98% were with 4x times LRTI /yr, and during the actual LRTI=32,93% with>CRP, 38,95%with>SE(in elder>2yr), 72,18%=with>leucocytosis, 43,16%:with >neutrophylia, Chest X-ray=69,17%:with moderate to severe infiltrative shadows, 45,86%:with hospital stay longer than average. In II-group=35,79%:with 4xLRTI /yr; during actual-LRTI=25,86%:with>CRP, 27,06%=with>SE(in elder children), 60,90%=with >leucocytosis, 33,83%:with>neutrophylia, Chest X-ray=57,14%-with mild to moderate infiltrative shadows, 29,02%=with hospital treatment duration longer than average.

Conclusion: In I-group: children with LRTI associated with IND, frequency and severity of LRTI were increased and hospital treatment duration was longer, in relation with: control II-group. IND prevention and treatment contribute with LRTI prevention and treatment. Further studies: (wider, multicentric, independent, prospectively planed, double-blind, randomized, etc.) are necessary in relation with definite conclusion.

GASTROINTESTINAL INFECTIONS - NEW AND ALREADY KNOWN INTRUDERS IN INTESTINE

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Introduction: Globally, gastrointestinal infections are the most frequent infectious diseases after respiratory infections. Since diarrhea is dominant symptom, gastrointestinal infections are mostly classified as infectious diarrheas. It is considered that there are approximately 4 billion cases per year.

Etiology of infective diarrhea: Infectious diarrhea frequency in particular geographical regions is directly dependent on infectious diarrhea causes type. We may say that in undeveloped countries still dominates in high percentage bacterial and parasite diarrhea causes, while in developed countries the number of particular viral causess is increased, with constant number of bacterial causess and rapid growth of post-antibiotic diarrhea caused by different types of *Clostridium difficile.* Routine clinical microbiological procedures: fecal leucocytes or lactoferrin, coproculture, latex-agglutination tests, electronic microscopy, PCR, parasitological examinations and special staining and cytological examinations cannot still confirm diagnosis of acute

infectious diarrhea at no more than 35 – 50% of cases. Anyway, at large percentage of those unconfirmed infectious diarrhea cases, due to the clinical analysis and epidemiological investigations, there is a possibility to make a diagnosis of acute infectious diarrhea.

The most frequent division is to:

bacteria – food poisoners: *Staphylococcus aureus, Clostridium perfringens A,C; Bacillus cereus, Clostridium botulinum*

other bacterial causess: *Salmonella species, Vibrio cholerae NAG, Shigella, Escherichia coli - EPEC, ETEC, EHEC, EAggEC, DAEC; Yersinia enterocolitica, Campylobacter jejuni, Clostridium difficile, Aeromonas, Plesiomonas shigelloides, Edwardsiella, Vibrio parahaemolyticus*

viruses: *Rotavirus (A, B, C), Norwalk virus, Calicivirus, Adenovirus - 40,41; Astrovirus*

possible viral causess: *Coronavirus, Torovirus, Reovirus, Enterovirus, Parvovirus, Picobirnavirus*

parasites: *Giardia lamblia, Cryptosporidium, Isospora belli, Microsporidia (Enterocytozoon bieneusi, Septata intestinalis), Entamoeba histolytica*

Clinical expression

Non-inflammatory diarrhea is caused mainly by bacteria which produce enterotoxin: *V.cholerae*, *ETEC*, *Staphylococcus aureus*, *different type of viruses*, *Cryptosporidium, Giardia lamblia.* Sick person has liquid stool without pathological impurities and fecal leukocytes, with no temperature raised, and since fecal volume is large, dehydration is possible.

Inflammatory diarrhea is shown with causess that produce cytotoxs: *Salmonella species, Shigella, Campylobacter, EIEC, Clostridium difficile, Entamoeba histolytica, Yersinia enterocolitica.* They are clinically manifested with mucus and blood in stool, strong abdominal pain, fever, but relatively small fecal volume, although the peristalsis is strong, and in the stool there are leucocytes and blood, and different level of dehydration.

Conclusion: We should always be aware of the fact that acute infectious diarrheas are mostly with short duration, self-limited, nine of ten have no pathognomonic clinical features of particular causes, the major part of causess are not sensitive on antibiotics, the way it works in-vitro is often different from the way it works in-vivo, we often get analyses results after 48/72 hours and it is really difficult to prove that antibiotics really work in prevention of extraintestinal manifestations.

On the other hand, it is certain that antibiotics disturb intestinal flora, bring to resistant strains occurrence and often do not shorten but prolong carrier. For that reason, selective and controlled antibiotics usage is recommended and the importance of rehydration and the need of realimentation and probiotics in acute infectious diarrhea treatment is emphasized.

ILIZAROV METHOD FOR THE TREATMENT OF SEPTIC PSUDOARTHROSIS AFTER PREVIOUS SURGICAL TREATMENT OF OPEN TIBIAL SHAFT FRACTURES - CASE REPORT

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Background: Septic psudoarthrosis of lower leg are relatively frequent complication of open fractures associated with large soft tissue destruction, regardless of which method was primarily taken care of. Treatment is a very delicate misson, requires long-term hospitalization with doubtful outcome of the treatment. The goal of treatment is primarily to achieve healing of bone infection, then achieving healing at the pseudoarthrosis site, and finaly limb equalization. Extremely important is the fact that despite the severity of the general condition of the patient treated by the Ilizarov method, there is capability for immediately start of postoperative physical treatment and capacity for walking with the bearing on the operated leg.

Method and Results: It is about 52 years old man, who fell from a cliff approximately 30 m high, during the hunt and sustained an open fracture of the left leg. After stabilisation of general condition, at the other hospital was operated, made a external fixation with fixator by Mitkovic, and at the same surgical treatment plastic surgeon was repeared defected skin wound with Tiersch graft. Nine months after the injury patient was admitted in our institution, with a clear X-ray and clinical signs of septic pseudoarthrosis of the lower leg and infection around the pins and the fixator loosening. Immediately after receiving the external fixator is extracted. Two weeks after the operation was performed resection of septic pseudoarthrosis and the drainage flow was placed. 10 cm of bone was resected at both ends of septic pseudoarthrosis. When clinical and biochemical indicators indicate to calming of infection, surgery was performed by the Ilizarov method of osteosynthesis and corticotomy of tibia to compensate bone defect. Physical therapy and rehabilitation was started seven days after surgery and patent started walking with the baearing on the operated leg. At the same time the correction and distracton has been started, lasted in the next three months to obtain limb equalization. Distraction regenerate at the tibia was 11 cm and finaly result was equalization of the leg length. Eleven months after Ilizarov apparatus was extracted, with clinical and X-ray signs of pseudoarthrosis healing and complete recovery of infection. Eight months after removing the apparatus the patient was anatomically and functionally fully recovered.

Conclusion: The presented method of treatment is important and a very good option for the treatment of similar complications, for several reasons. Resection of the ends of the septic pseudoarthrosis gives capacity to bone healing. Corticotomy allows compensation of pseudoarthrosis defect to achieve limb equalization. The fixation is stable, and there is no additional soft tissue trauma. Only the Ilizarov method of

treatment improves the fight against infection. Physical therapy and walking with bearing on the operated leg may start immediately after surgery.

TUBERCULOSIS IN THE COMMUNITY OF TESLIC, FOR THE PERIOD BETWEEN 2000 AND 2009, AS ONE OF THE INDICATORS FOR TUBERCULOSIS MORBIDITY RATE IN THE REPUBLIC OF SRPSKA

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Tuberculosis is the leading cause of morbidity and mortality from infectious diseases in the whole world, as well as in the Republic of Srpska. The overall notification rate shows a slight decrease in the Republic of Srpska for the period from 2000 to 2009.

The aim of this study is to analyse the tuberculosis data in the community of Teslić and to compare those data with the ones in the Republic of Srpska.

We have analysed all tuberculosis cases in the community of Teslić for the above mentioned period and all data are presented according to sex, age, site of disease, sputum smear positive rate and socio-economical state.

During the period between 2000 and 2009 we have detected 380 tuberculosis cases (76 per 100 000 population), average age 57.89 years, most frequently registered age groups were from 55 to 64 and over 65 years of age, with a slight predomination of female cases. There were 93.42 % of newly detected cases, 76.32 % of culture confirmed cases, 91.58 % pulmonary tuberculosis cases and 39.74 % of these cases were sputum smear positive.

These results lead to the conclusion that the tuberculosis morbidity rate in the community of Teslić corresponds to the morbidity rate in the Republic of Srpska, and that the high morbidity rate among the elderly is present due to low socio-economic status and unemployment.

Key words: tuberculosis, morbidity

MATERNAL RISK FACTORS FOR INFECTION AND SMALL FOR GESTATIONAL AGE NEWBORNS

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Background: Newborn classification based on birth weight and gestation is valuable in predicting the outcome. At any gestation the poorest outcome is seen in infants with marked intrauterine growth retardation. Small for gestational age (SGA)

babies are those whose birth weight lies below the 10th percentile for that gestational age. There are plenty of risk factors for such a condition, and one of them is maternal infection.

The aim of this study was to investigate the maternal risk factors for infection and their possible contribution to intrauterine growth restriction, leading to small for gestational age infant, born at or near term. Methods: in the study group 300 successfully born term or near term (35 and 36 gestational weeks) newborns were included. Detailed data from maternal history were taken into consideration, and newborns were assessed for their gestational age after the birth, compared and plotted to the growth curves. As SGA were considered those whose birth weight was less than 10 percentile on the national curve. Included were only those SGA babies with maternal risk factors for infection, and no other factor for IUGR identified. Results: in the group, 25 SGA babies were diagnosed, and it makes 8,3%. In this group, in 5/25 SGA babies (20%), maternal risk factors for infection were identified. Some of them were: Gram positive Streptococcus of B-group in 1 case, maternal non-specific infection (long period positive biological markers of infection, no microbiological identification during the pregnancy) in one case, and positive early swabs on Chlamydia trachomatis and Ureaplasma urealyticum represented with one case respectively. All of these 5 newborns were term, over 37 gestational weeks, and 4/5 (80%) had positive biological markers of early onset infection. The early diagnosis and treatment was performed and all of them discharged in good condition.

Conclusions: in our study we had included small number of patients, having only a representative sample (non selected population). The incidence of SGA newborns is slightly higher than in literature data, but the possible reason is that our Clinic is working as tertiary level maternity, having intensive transport “in utero” from all over the country. The early onset of neonatal infection could be the direct consequence of the maternal risk factors, information that has to be proved designing study with higher number of patients and strongly specified inclusion and exclusion criteria.

MAPPING THE RISKS ASSOCIATED WITH COMMUNICABLE DISEASES

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Background: The maps are a tool for displaying data on hazards, vulnerability and risks in a particular area, thereby supporting the process of assessing the risk and overall strategy for risk management.On 23 February 2009, the European Commission adopted a Communication on a Community approach on the prevention of natural and man-made disasters1 setting out an overall disaster prevention framework and proposing measures to minimize the impacts of disasters. The Communication advocated the development of EU and national policies supporting the disaster management. From the list of the most important elements at risk from destructive events are people and animals, in which adverse impact can be direct, indirect and combined.

Material and methods: mapping the risks in terms of infectious diseases is (derived) based on previous experience and forecast (historical method) that are part of

the current situation and opportunities (analysis and synthesis as certain forms of logical method).

Results and discussion: In assessing the hazards that pose risk and procedures for documenting and mapping sluchenite (historical) hazards. Infectious diseases were one of the important problems in previous wars (Balkan wars, the First and Second World War) and elementary disasters-disasters that have occurred in the Republic of Macedonia. They came up suddenly and dramatically complicating the hygienic and epidemiological situation. Assessment of danger to life and health and living in a certain period of time in a particular region, essentially an assessment of the hygienic-epidemiological and epizootiological condition. For adequate assessment of these dangers, it is continuously monitoring the indicators of disease, mortality and other health disorders.

Since the epidemiological situation is related and dependent on hygienic condition in a given region, it is necessary to monitor and hygienic condition. Because at the same time and assessed the epidemiological, epizootiological and hygienic condition. Depending on the assessment of the hygienic-epidemiological and epizootiological situation are suggested and take appropriate preventive measures. The Republic of Macedonia such assessment is made in the national and regional level.Depending on what level are hygienic, epidemiological and epizootiological conditions in a region, hygienic-epidemiological situation can be assessed with five degrees of danger arising from the maps of danger: low risk, moderate risk, high risk and very high risk.

SPECIFICITY AND SENSITIVITY OF BIOLOGICAL MARKERS IN NEONATAL EARLY ONSET INFECTION

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Background: very frequently the fetus reacts to the maternal infections during the pregnancy. According to the current Guidelines, all newborns born of mothers with some detected risk factors have to be treated by antibiotics until exclusion of the infection, because the late treatment leads to adverse outcome. On the other hand, it is very difficult to confirm neonatal infections because of subtle and atypical clinical manifestations, and low sensitivity and specificity of biological markers. The objective of this study was to determine the sensitivity and specificity of the White blood cells count (WBC) and C-reactive protein (CRP), the correlation between granulocyte count/percentage and CRP. Methods): 3000 consecutively born term newborns were investigated. Inclusion criteria for the study were: maternal risk factors for infection listed in the evidence based Guidelines, clinical/ laboratory/ microbiological proof for infection. All of them were worked out completely, and antibiotics given immediately after taking blood for laboratory/microbiological testing. The blood for WBC and CRP was taken every second day until normalization.

Results: 37/3000 term newborns were proven with early onset infection (1,23%). WBC count was elevated in 31/37 (83,8%), granulocytes percent over 70% in

all 37 newborns, and CRP on the first day was elevated (>5 mg/l) in 5 cases (understandably, because of the late seroconversion). On the third day, WBC count was normalized in 25/31(80,6%) newborns, granulocyte percent in 21/37 (56,7%), and CRP was elevated in 15 more cases (total 20 cases, 54,1%), 3 of them with normal WBC and 2 with normal granulocyte number. On the day 5, all newborns had normal WBC, normal granulocytes in 16/21 (76,2%), and normal CRP value in 12 newborns. All newborns had normal clinical appearance. The results showed high sensitivity rate of the granulocytes and WBC in the early onset of infection (83%), and low sensitivity rate of CRP (63%). The specificity for the WBC was 78%, for the granulocyte percent was 82%, and for CRP value only 42%. The coefficient of correlation between granulocytes and CRP was 0,56 which belongs to the medium level.

Conclusion: although the sample size was not representative enough, it could be suggested that the WBC count and granulocyte number/percentage are more sensitive markers of neonatal early onset infection compared to CRP. Sometimes the CRP value can even mislead the physician to continue the treatment unnecessarily, which can also cause adverse effect to the treated patient. So, it is very hard to the physician to make decisions for the treatment ceasing in the cases with normal clinical manifestations, normal WBC and granulocytes, but slightly elevated CRP, which was the last normalized marker.

SEROPREVALENCE OF HEPATITIS B VIRUS INFECTION MARKERS AMONG THE DENTISTS IN THE CLINICAL HOSPITAL IN BITOLA, REPUBLIC OF MACEDONIA

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Background: To present the Hepatitis B virus (HBV) seroprevalence among the dentists in the Clinical hospital in Bitola, R. Macedonia.

Methods: Serum samples were taken from 195 dentists and the presence of HBV markers: HBsAg, antiHBc IgG, antiHBs, was tested. The analyses were made with the ELISA method (ABBOT).

Results: Out of 195 tested dentists, 136 were HBsAg negative, as well as anti HBs and anti HBcIgG negative (69.8%). The rest 59 (30.2%), were HBsAg (8.5%), anti HBs, and antiHBcIgG (91.5%) positive. 58 out of the negative ones, were males and the rest 78 were females. In the 59 sensitive to the HBV markers, 28 were males and 31 females. 124 (91.2%) out of the negative ones, were completely immunized, 8 (5.9%) were not completely immunized and 4 dentists (2.9%) refused the immunization. Seroconversion was achieved in 100% of the immunized dentists (anti HBs positive).

Conclusions: HBV is still a major infectious agent and a great health problem all over the world and of course in the R. Macedonia, especially among the health workers such as dentists. Therefore, all people must be examined and vaccinated for HBV, especially in the countries with high risk of HBV infection, such as our country and our region.

BRUCELLOSIS-DIAGNOSTIC PROBLEM

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Background: To present that the heterogenic and atypical clinical manifestations of brucellosis is one of the reasons for often delays in diagnosis and treatment.

Methods: During period of 10 years in our department were hospitalized 117 patients diagnosed with brucellosis. 25 (22%) of them were previously treated in the ambulance and other departments of the hospital. In setting the diagnosis, beside the anamnesis and epidemiological data, we used standard laboratory and biochemical analyses, serologic analyses (BAB, RVK, WRIGHT, COOMBS), X- rays, bone scan, CT.

Results: Out of 117 hospitalized patients, 25 were previously treated in other departments: 8 in orthopedic, 5 in physiatrist, 5 in internal, 4 in urology, 3 in ambulance, with different diagnosis: Lumboischyalgia, Coxitis, Spondilitis, Discopathia, Tu vertebre, Status febrilis prolongata, Orchiepididimitis, Laesio hepatic. Average time for setting the diagnosis in those patients was 96 days, while in other patients 18 days.

Conclusions: Despite the fact that R. Macedonia is an endemic regions for brucellosis, still it is not often considered in everyday medical practice. Setting the diagnosis and giving therapy on time reduce the possibility of chronic development, recidivisms and permanent sequels, which are not only individual but also socio-economic problems.

IRRATIONAL USE OF ANTIBIOTICS IN PEDIATRIC PULMOLOGY

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Background: Unstoppable trend of excessive and irrational malpractice abuse of antibiotics continue instead of great number of appeals for its reduction and indications for alarming increase of bacterial resistance, but: toxic, allergic, immuno-depressive, cancerous acting, and etc. also. There is insupportable overload capacity and overwhelming burden for health budget, even for the richest countries. Sanctions are introduced for irresponsible physicians in some countries.

Aim: Presentation of really malpractice abuse of antibiotics in ambulatory-policlinic practice in our country.

Material and Methods: This is retrospective review of our policlinic and ambulance data books. We have analyzed 1000 patients with acute respiratory infections, (who have previously received, and still now, are receiving antibiotics (not rare 2, even 3 antibiotics previously), prescribed by their's family doctor in the town of

Skopje. (Infant and small age ≤3 years were=670(67%), preschool and early school age(3 -10yr.)= were=284(28,4%), and elder children-(10 – 18 yr.) were=46(4,6), male=527, female=473.

Results: 873(87,3%)-from investigated patients have clinical-physical findings attached to upper respiratory infections, but only 116(11,6%)-were with low airway clinical-physical findings, 11(1,1%)were with otitis. One or more positive hematological finding: (>SE↑, >CRP↑, >Le↑, >Gran (Ne↑)-were only in=287(28,7%)= (according to bacterial infection); positive microbiological (sputum isolate, or pharyngeal swabs, or nasal swabs), were=328(32,8%) or/and positive ENT. X-Ray of lung was made on 103(10,3%) patients, of which 94(91,26%)-were with positive X-Ray findings (infiltrative shadows…)

Conclusion: Arbitrary, uncritical and indiscriminate use of antibiotics (just because of: febricity? fever? cough? rhinorea?, red throat? etc. and/(or) weakening on parents pressure is unjustified and unreasonable, as well as: arbitrary, unprofessional, and incompetent, ignorant, and uncritical, interpretation (with lack of knowledge) of-anamnestical, clinical, laboratory, epidemiology assessment or/and coherently and literally microbiological interpretation, is absurd, unreasonable and irresponsible.These authors appeal for responsible and critical use of antibiotics today - to preserve them for tomorrow.

CONTRIBUTION OF CAREFUL PHYSICAL OBJECTIVE EXAM IN SOME EARLIER DIAGNOSIS OF MEASLES

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Measles is very contagious virus caused illness, vaccine-preventable with possible complications. Epidemic occurs when in population accumulate over 30-40% nonimmunized persons. Unfortunately measles diagnostic arises even in late eruptive stage when is too late to prevent infection spreading. Due to high contagious earlier detection and earlier patients isolate would reduce their further contacts with uninfected or nonimmunized persons and prevent spreading of infection. Careful oropharyngeal and physical objective examination is required.

Case report: In March,during the morbilli epidemic,and fly,in RM,a dental ordination was visited by subfebrile 4 years old unvaccinated,boy,from kindergarten where it contacted acute respiratory infections and home contacts with morbilli registered in neighborhood. Objectively:-mild lymphadenopathy, rhinitis, conjunctivitis, hyperemic mouth and oropharynx, palate enentem and Koplik's white spots on erythematous buccal mucosa opposite the molar and pre-molar teeth. Exanthema was not yet presented on the skin. Suspicious for measles home quarantine was advised, interrupting furder contacts. Tonsils swab–microscopically founded giant

cells confirmed the diagnosis in early-prodormal-(before rush) stadium without more sophisticated diagnostic; Blood count=unspecific with mild leucosis, microscopically peripheral blood smear: with plasma cells and mild eosinophiles. Bacteriological investigations of pharynx and nose swab=negative; Valid lung auscultatory findings. Child was directed to infectologist.

Conclusion: Measles should be assumed not only in times of epidemics.Non-immunized persons must be carefully examined for suspected signs including palate enanthem and Koplik's spots. Every physician:-(pediatrician infectologist general physician otorhinolaryngologist even dentist with carefully exam of oropharynx and mouth is able to make earlier diagnosis of morbilli.Earlier detection and earlier isolate of patients would possibly assist in shortening the time of their further contacts by some earlier interrupting contacts with an uninfected or non-immunized persons, which may slow spreading of infection.

ONCOLOGIC DISEASES

ОНКОЛОГИЧНИ БОЛЕСТИ

PAP SMEARS CHARACTERIZATION BY IR AND OPTO-MAGNETIC SPECTROSCOPY: TOWARDS A WATER BASED NANOMEDICINE

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Cervical cancer and endometrial carcinoma are the most common invasive cancers of the female genital tract and account for 12% of all invasive cancer in women, excluding skin cancer (1-3).

In this study, we used samples prepared for PAP test and examined them using IR (Infra Red) spectroscopy and digital imaging spectroscopy (DI-OMS) from the same excitation source of light (FTIR 660 Spectra-Microscopy, JASCO, Japan). In this device two different techniques are integrated: spectroscopy and microscopy (capable to make digital image). We analyzed the similarity and difference between these two methods, in order to detect normal, dysplastic and cancerous cells, with as high as possible accuracy. Samples were prepared, according to standard and staining procedures used for Pap smear tests during regular colposcopic examination.

DI-OMS method is based on image analysis using red and blue channels of water and tissue. Algorithm for analysis of light-matter interaction is based on spectral convolution (4). According to data from 40 cases, sensitivity of DI-OMS method compared to Pap test is 93.9% and specificity is 87.5%, while sensitivity and specificity of IR method is few percentages less. The goal of this study is to use the standard Pap test and improve its efficacy by providing means for more rapid and accurate prediction potential.

Presented research study is only a part of preliminary investigation. Acquired results indicate that both classical IR spectroscopy and opto-spectroscopy are valid to characterize PAP smears. However, digital opto-spectroscopy method is much chipper than PAP and classical IR spectroscopy methods, and it is much faster, about 30 times faster comparing to PAP method. More research has to be done for final conclusion.

Our future work is directed towards water based medicine and water behavior on nano scale (5). These two aspects could contribute with finding larger area that is sensitive to tissue changes and will enable us to conduct a more objective systematization of the results and fully appreciate the possibilities that are offered.

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BLADDER CANCER IN AREA OF BALKANS ENDEMIC NEPHOPATHY

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Background: Bladder cancer is the most frequent urinary system neoplasm. The incidence worldwide is 10.1-27.1 per 100,000 men and 2.5-5.4 per 100,000 women

per year, which makes it the nineth most frequent cancer. Between 75-85% of the first listed diagnozed bladder cancers are a non-invasive forms, while smaller part has invasive charasterisctics. Although urothelium represents histological and functional unit, incidence and nature of urothelial carcinoma varies geographically, which is especially visible in Balkans endemic nephropathy (BEN) area.

Objective: Identify characteristics of bladder cancer in focus of BEN.

Method: Retrospective analysis of bladder cancer: by incidence, by sex and age variations, stage, histological grade and grouping with proximal urothelial neoplasm. First group of patients were from endemic area, without clinical picture of BEN, operated in the Urology department of Doboj general hospital, and on the chronic dialysis treatment of dialysis center (DC) Samac (endemic area average was 82 patients/year). Second group of patients were from non-endemic area of Doboj region operated in the Urologiy department of Doboj general hospital and on the chronic dialysis treatment of DC Doboj (non-endemic area average was 99 patients/year). Duration of observation was 5 years (2006-2010).

Results: During the period of 2006-2010, 109 patients had primary diagnosed bladder cancer-35 bladder cancer patients were from endemic area (population of 34,400)-incidence of 101.6/100,000, 19/35 patients were men (54.3%) while 16/35 were women (45.7%). Ratio male/female was 1.2:1. Average age of patients was 74.5 and the most frequent occurance was in patients who were in their eighties. 33/35 (94.3%) patients in endemic area had non-invasive bladder cancer (Ta, CIS, T1), while 2/35 (5.7%) had an invasive forms. Histological grade was G1(54.3%), G2(40.0%) and G3(5.7%). Association of bladder cancers and proximal urothelial tumors in endemic areas had 6/35 (17.1%), and only 1/74 patients (1.4%) in non-endemic area.

On the other hand 74/109 patients were from the non-endemic area of Doboj region (population 235,600) what makes the incidence of 31.4/100,000. 58/74 (78.3%) were men, and 16 (21.7%) were women. Ratio male: female was 3.6:1. Average age was 70.2. Most frequent occurance was in patients in eightees. Non-invasive form was present in 68/74 (91.9%) while 6/74 (8.1%) had invasive bladder cancer. Histological grade distribution was G1 (74.3%), G2 (17.6%), G3(8.1%).

With p=0,05 error and P>95% accuracy with coefficient of contingency C=0,57 near C_{max}=0,707, influence of BEN area on distribution of tumors by sex is confirmed. Histological grade of tumor is not depended to endemic or non-endemic area ($\chi^2 = 5{,}69 < \chi_o^2 = 5{,}991$). Invasiveness of cancer in time of primary diagnosis was not determined by endemic or non-endemic area $\chi^2 = 0{,}57 < \chi_o^2 = 3{,}841$.

Conclusions: Bladder cancer has certain characteristics in area of Balkan endemic nephropathy.In area of BEN in Samac and Modrica municipalities, bladder cancer incidence was 3.2 times higher than the incidence in non-endemic areas of Doboj region.In the endemic area, occurance of bladder cancer is more likely in men than women.Average age of patients is 74,5 in endemic area, and 70,2 in non-endemic area. Highest frequency of bladder cancer is with patients in their 8th decade-62,8% in endemic, and 47,3% in non-endemic area. Histological grade as well as invasive nature of the bladder cancer was not in correlation with the analysed areas. Association of bladder cancers and proximal urothelial tumors in endemic areas had 17.1% patients.

CANCER PAIN

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Over 50% of cancer patient have sever pain. The cause of this pain are changes in the cells, tissue, organs, systems and the whole organism. In this painful process take part the cancer cells, the cells of the immune system (macrophages, neutrophils, T lymphocytes, mast cells) and the nervous system. The role of tumor-associated immune cells is extremely important, because the leukocytes infiltrating the tumor mass represent in some cases up to 80% of the tumor cell population. The pain information is accepted and conducted via Aδ and C nerve fibers. The nociceptors for cancer pain are mechanical (mechanically gated channels, purinergic receptors), TRPV1 (temperature nociceptors), chemical (receptors for protons, prostaglandins, endothelins) receptors.

It must be mentioned that in cell membrane of pain-conducting nerve fibers there are numerous receptors – metabotropic and ionotropic glutamate receptors, serotonin receptors, somatostatin receptors, opioid receptors, cannabinoid receptors, protease activated receptors, bradikinin receptors, TNFα and NGF receptors). Three main features are basically important for the cancer pain: the location of primary tumor, histological type of tumor and location of metastases in the body. Many chemical compounds (prostaglandins, some interleukins, growth factors, proteases, leukotriensare secreted in high levels in the cancer microenvironment, which play important role in generating cancer pain. These secretory products excite or sensitized sensory afferent nerve fibers. Tumor cells and tumor-associated inflammatory immune sells release protons and acid metabolites that stimulate TRPV1 and acid-sensing ion channels (ASIC), which are membrane receptors. The tumor growth injures sensory and sympathetic peripheral nerves and causes compression, ischemia and proteolysis, which leads to neuropathic pain. Cancer pain induces central sensitization, which amplified pain stimuli.

There are different causes for the cancer pain as tumor pressure, poor circulation as a result of blocked blood vessels, inflammation, bone fractures as result of metastasis, emotional problems (lost of job, financial costs, fear, grief) and cancer treatment. Cancer pain could be described in many different ways, but usually is calcified as acute and chronic.

OBSTRUCTIVE NEPHROPATHY CAUSED BY METASTATIC COLON CANCER AFTER RENAL TRANSPLANTATION - A CASE REPORT

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Background: Kidney transplant recipients (KTRs) are at greater risk for developing cancer compared to the general population. This is especially true for cancers associated with viral infections (e.g. EBV- associated lymphomas). On the other

hand, some common cancers in the general population occur at a higher incidence rate in KTRs (e.g. colon cancer).

Case report: We report an unusual case of a 54-year-old male with medical history of diabetic nephropathy and no family history of colon cancer, found to have advanced colon cancer causing urinary obstruction at four years after living-related kidney transplantation. Induction therapy consisted of methylprednisolone and Daclizumab and no complications were encountered during transplantation procedures. At the time of discharge there was a standard maintenance triple post-transplant immunosuppression with prednizolone, mofetil mycophenolate and cyclosporine A. He was visiting our outpatient clinic at each regular interval of a few months and serum creatinine levels were stabilized in between 180-220 μmol/l. At 6-month protocol biopsy the histology of tubular atrophy, intimal fibrosis, chronic allograft nephropathy and initial diabetic nephropathy characteristics were found. In December 2009, at four years after transplantation, the patient was admitted to our Department with urine retention into the bladder causing increase of the degradation products because of an obstructive nephropathy. In addition, he admitted having intermittent rectal bleeding, sporadic fever, feeling malaise and fatigue. The ultrasound examination revealed tumor mass adjacent to the urethral neck and urinary retention into the bladder. Urinary catheter was placed, and a diuresis of more than 3000 ml was obtained. The tumor mass was highly suspicious for metastatic colon cancer that was confirmed by rectoscopy and abdominal CT scan (showing solid colon tumor and enlarged paraaortal lymphatic nodes). The patient was immediately transferred for surgical intervention with the histology of colon adenocarcinoma from the surgery.

Conclusion: We highlight the possibility of development of fulminant cancer with metastases within relatively short period after renal transplantation and the importance of periodic colorectal cancer screening pre and post-transplant in this population. At best of our knowledge, the survival of KTRs with cancer is poor, and treatment options are limited by the transplant and comorbidities. It is thus important to consider options for preventative measures and malignancy screening in KTRs which could in turn deliver benefits of lower morbidity and mortality through reduced incidence and/or early interventions in such cases.

ATYPICAL FACIAL RESECTIONS

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Goal: To present the possibilities of major facial resections in cases of advanced facial tumors.

Introduction: Unfortunately in the clinical practice of the Maxillo- Facial Surgery we sometimes encounter with tumor processes that for different reasons are in an advanced stage and are defined as un-operable. In some of these cases, based on clinical and laboratory screening, analysis of the risk and lack of any other options we are forced to perform major and atypical resections.

Methods: 2 clinical cases are presented for atypical facial resections of advanced tumors.

A clinical case of giant-cell retinoblastoma in 3- year old child, the tumor weighing 950gr. and extremely exteriorized from the right orbit.
The operating approach is presented by 2 operating accesses: direct and coronary, as well as the post-operative result.

A clinical case of extremely advanced Ackerman' s cancer of the right facial half in 32-year old woman.

The operating approach is presented for hemi-facial resection (right orbit, upper and lower jaws) and radical neck lymph dissection at the same time. The post-operative result is presented 3 years post-surgery.

Conclusion: With some of the patients with advanced tumors, when we are depleted of any other alternatives for treatment, it is possible sometimes an atypical resection to be performed and patients saved and good quality of life ensured. Unfortunately these operating approaches can't be applied for all patients.

ЗЛОКАЧЕСТВЕНИ ТУМОРИ НА КОЖАТА-ЕПИДЕМИОЛОГИЧНИ ДАННИ И ТЕРАПЕВТИЧНО ПОВЕДЕНИЕ

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Най-честите кожни тумори са базалноклитъчният карцином, спиноцелуларният карцином и малигненият меланом. В последните десетилетия се наблюдава тенденция за повишена честота на тези заболявания в световен мащаб, както и епидемиологично изместване в по-млада възрастова група. Наследствената предразположеност и UV-радиация са основните етиологични фактори. Възможни са различни терапевтични подходи според вида и стадия на тумора. Златен стандарт в терапията на кожните тумори остава хирургичното лечение и последващото клинично проследяване.

ЛЪЧЕЛЕЧЕНИЕ ПРИ МОЗЪЧНИ МЕТАСТАЗИ

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Цел: Цел на настоящата презентация е да покаже мястото, приложението и ефективността при облъчване на целия главен мозък (ЦМО, целомозъчно облъчване /whole brain irradiation/WBI/) при лечението на пациенти с мозъчни метастази.

Материал и методи: През периода 2009 – 2011 г. в Токуда Болница София са лекувани общо 51 пациенти с мозъчни метастази. При всички пациенти е проведено ЦМО до обща доза 30 Gy, разпределена в 10 фракции по 3 Gy, давани 5 пъти седмично, с едновременно прилагане на стероидна и дехидратираща терапия. При 30 от тях е проведено проследяване повече от 6 месеца. Анализирана е общата преживяемост по метода на Kaplan-Mayer.

Резултати: При всички пациенти лечението е завършено без прекъсване, като е получена назначената доза от 30 Gy, без съществени странични ефекти. Неврологичната симптоматика е повлияна при 75% от пациентите, а при 25% е

постигнато стациониране. При нито един пациент не е настъпила прогресия в хода на лъчелечението. Средната продължителност на живот е 43 седмици (от 3 до 72 седмици). Преживяемостта е разглеждана по групи в зависимост от пол, възраст, хистология, предходна оперативна интервенция и брой на метастазите.

При пациентите с метастази от карцином на гърдата е постигната значимо по-добра обща преживяемост (median 69 седмици) в сравнение с пациентите с карцином на белия дроб (median 39 седмици) (log rank test, p=0.02). Предоперативното отстраняване на мозъчните метастази при пациенти с белодробен карцином подобрява общата преживяемост (median 58 седмици) в сравнение с неоперираните (median 10 седмици), но след първата година статистическата значимост на тази разлика се губи.

Изводи: Препоръчва се лъчелечение при пациентите с мозъчни метастази. Поносимостта на лъчелечението е добра и няма странични ефекти. Повлияването на неврологичните симптоми е от пълно до стациониране. При единични пациенти повишеното вътречерепно налягане и свързаната с това симптоматика, могат да се овладеят успешно с медикаментозно лечение. Наличието на големи вариации по отношение на преживяемостта и ефекта от лъчелечението се обясняват с хетерогенността на лекуваните болни по отношение на хистология, брой и големина на метастазите, предходно оперативно лечение и не на последно място, контрол на онкологичното заболяване извън мозъчните метастази.

OUR MODIFICATION OF RISK OF MALIGNANCY INDEX IN PATIENTS WITH OVARIAN TUMOR

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Background: estimation of the predictive values of our modification of the Risk of malignancy index (RMI) in 86 women with ovarian malignancy.

Methods: 86 women with ovarian tumor were estimated with our new RMI, as a simple sum of different points given regarding: familiar data, personal data, age, ultrasound characteristics of the tumor and serum CA-125. RMI≤6 predicted benign disease, RMI of 7-15 points predicted probably benign disease (endometriosis, inflammation); and RMI>15 predicted malignant disease.

Results: in 45 patients (group A) the histopathology of the tumor was benign and all these patients had RMI≤15; in other 41 patients (group B) the histopathology was malignant. In this group, 39 patients had RMI>15, but 2 had RMI=7-15 and borderline histopathology. The predictive values of our RMI were: very high NPV (1.0 i.e.100%); high NPV (0.85 i.e. 85%), and also very high sensitivity and specificity (0.91; 1.00, respectively).

Conclusions: It seems that our modification of RMI has high predictive values, but it has to be conformed in bigger study group of patients.

RISK FACTORS FOR CANCER OF THE BREAST IN REGION OF STIP

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Background: Like all other cancers that occur in humans, the main reasons for the breast cancer are also unknown. Regular medical checks are effective for early detection and diagnosis of the disease and it increases the possibility of full healing of breast cancer. The primary prevention is also very important. The aim of the study: To preventing the disease by detecting and removing the risk factors for the cancer of the breast.

Methods: The research included 100 women in their reproductive age in region of Stip, R.of Macedonia

Results: 54% of them doesn't have an inherited factor for a female line. 80% have been pregnant and 70% eestablished breastfeeding; 30% are uninformed for cancer of the breast. In the last few years, apart from the great achievements in medicine, yet the morbidity increased from 2-3 % and the mortality from 1-2%. The main raisons are: increased number of older population suffering of breast cancer, changes of lifestyle (western style) increased consumption of fats and oils. Most important problem in the treatment of disease mechanisms remain genesis and the factors that contribute to the development of the disease probably due to the inability days and fully explain the long remain in the realm of speculation in the area of the samples and the efforts of pharmaceutical industry to find right treatment.

Conclusion: Today, it is considered that there are many biological reasons for the appearance of the breast cancer. Therefore, particular attention has been paid to the so-called biological parameters of tumour: the status of hormone receptors (AIR, PR) and HER2.Identification of patients with HER2 positive is essential for adequate treatment of patients with early and metastatic breast cancer.

DUODENAL ADENOCARCINOMA – A CASE PEPORT

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General incidence of duodenal tumors is low, they constitute less than 0,05% of all tumors, i.e. 1-2% of all gastrointestinal tumors, which is very disproportionate to the length of duodenum, that represents over 75% of the total length of gastrointestinal tract. Duodenal tumors are very rare and constitute about 0,3-0,4% of all gastrointestinal tumors. Classification of duodenal tumors is difficult due to the structures that surround this organ and participate in the formation of its pathology. Benign tumors amount to about 16%, and malign to 38% of the duodenum tumors, in 80-90% of cases the most frequent malign tumor is adenocarcinoma which accounts for about 2,5% of carcinoma of digestive tract. Primary adenocarcinoma is most often localized in duodenum.

The aim of this study was to show that clinical indications for malign neoplasm of duodenum, adequate diagnostic procedures and reaching an early diagnosis contribute to quick and correct therapeutical choice, i.e. adequate surgical resection, as method of choice in treating this condition.

In this study we have shown in retrospective analysis of the history of illness and operative protocol a female patient, aged 63, with primary malign tumor of the 3rd portion of duodenum (PH adenocarcinoma duodeni), who was surgically treated. In the case of this patient the complete diagnostic procedures as well as analysis of clinical parameters were applied, and the presurgical diagnosis of duodenum tumor was established. Consequently, the surgical treatment was applied, as the only correct treatment procedure, and the basic factor for the survival of the patient.

Primary duodenal carcinoma (PDC) is a rare illness, with low degree of resectability and bad prognosis. Considering the possibility of malign affection of duodenum is important in order to reach diagnosis as soon as possible, because the clinical picture often reminds of many benign lesions. Surgical treatment is the main kind of therapy. Tumors localized in distal parts of duodenum have better prognosis.

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PSEUDOPAPILLAR PANCREATIC CANCER-FRANZ TUMOR-CASE REPORT

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Background: Pseudopapilar tumor of the pancreas is a rare exocrine pancreatic tumor. Most common in women in the second decade of life. Tumor has low potential for malignancy, and therefore favourable prognosis. Usually is a large, encapsulated with a mixture of cystic and hemorrhagic components.

Can often be asymptomatic but can cause a number of serious complications such as pancreatitis due to ischemia, can cause distension and obstruction of pancreatic and bile ducts, and can occur hematoperitoneum due to rupture of tumor. Malignant form occurs in 13-15% of cases and is manifested angioinvasion, perineural invasion and invasion of adjacent organs. Metastases are rare, and if they occur primarily in the liver and a lymph gland.

Methods: A case report.

Results: Patient M.K., a girl 19 years old, medical student appeared in the general medicine clinic because touched globular creation in the abdomen by occasionally has touched, and occasionally the move.

Clinical examination in the supine position, careful palpation of the abdomen cannot establish the existence of the same but in a standing position can touch a creation around 10 cm size, round and medium hardness. Do the emergency ultrasound examination of the upper abdomen and both kidneys, which are established with the oval hyper-echoic shadow near left kidney and tail of the pancreas size 11x10 cm. The same day in a private clinic to do the MRI of the abdomen to determine the existence of expansive sharply limited change 10x11 cm, below the stomach, mostly well-vascularised, solid tissue structures with zones that correspond to the signal intensity cystic changes. There are not sure signs of a change of origin. No detailed laboratory processing the patient is sent to the Clinic of Digestive Surgery in Belgrade where she carried out further investigation and treatment. In operation for a tumor found to belong to the same pancreas, in fact it was a spherical creation pedicellate related to the narrow tail of the pancreas. A detailed histopathology analysis and immunological treatment showed that it was a solid, pseudopapilar neoplasm of the pancreas (Franz tumor).

Therapy included only radical surgery: the tumor was completely removed and the tail part of the healthy tissue of the pancreas where the tumor was fixed. Metastases are not established. One year days after surgery the patient is feeling well. Regularly performs prescribed ultrasound abdominal control and laboratory blood tests that are currently normal. Also and control abdominal MRI after 6 months after surgery was normal. The patient feels good, does not take any treatment and returned to their normal duties.

Conclusion: The presence of tumor in the abdomen and requires prompt diagnosis and adequate treatment. The correct treatment of the tumor improves patient quality of life and length of survival. Since in this case a young person and the tumor with low malignancy hope that the treatment is completed, i.e. there will be no recurrence and metastasis. Patient are recommended healthy lifestyles and regular check-ups.

KIDNEY CANCER - A CASE REPORT

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Background :The most common kidney cancer is adenocarcinoma, which arises from the tubular epithelium and is 80-90% of all the kidney cancers and 2% of all malignant tumors in adults. The disease is usually occurs between 50 -70 years of age and affects men twice as often than women. When we discover this cancer it can be great from 3-15 cm. Arise anywhere in the kidney, usually round but may use canes or lumps which indicates the aggressiveness of the lesion. If the tumor does not grow on the kidney channel system can long remain asymptomatic. The most common metastases in bones and lungs.

Purpose: To show how kidney cancer can be asymptomatic and thus accidentally discovered.

Method: HEALTH reviewed medical records documentation-women JD 56 years old from Sabac, treated the last ten years from diabetes and hypertension with insulin and ACE inhibitors. Because of disease patient is listed once a month in the relevant clinics check with values of glycaemia and complete laboratory findings annually.

Results: At the regular control of complete laboratory analysis, patient was observed at low hemoglobin values 80g/li elevated sedimentation 78, and the identified need for further examination of the causes of anemia are evident.

The patient complains of occasional pain in his right shoulder, and often taking NSAIDs (diclofenac). The following is done. Rtg tests are normal: left shoulder, cervical spine X-ray: narrowing intervertebral space and cervical lordosis of the spine. Rtg lung: regular, Rtg gastroduodenuma: gastric mucosal folds of coarse, symmetrical peristalsis without visible signs of erosion, duodenal bulb tests are normal.
Ultrasound of the abdomen and both kidneys: normal-sized liver homogeneous light, gallbladder, pancreas, spleen, aorta area, right kidney tests are normal. Left kidney with a hypoechoic shadow 4.5 cm x6 promines outside contour of the kidney. For verification of tumor formations do the CT of the abdomen to confirm the presence of expansive processes 7x5, 3x7 cm. Patient referral to a urologist for surgery, which prior to receiving a request to do bone scintigraphy. Findings were normal. The patient is referred back to the urological department, where do the extirpation of the tumor and diseased kidney as a whole. Histopathologic analysis of tumor tissue was diagnosed comfirmed: Carcinoma renocellulare. T3N0M0.After operating course duly passed. The patient is feeling well, pain in left shoulder unnoticeable.

The control abdominal ultrasound shows left nephrectomy. CT scan of the abdomen 6 months after surgery: The torax scans through the base-level segment of X to the left shows bullous changes 19 mm and several lymph nodes - 10 mm paraaortal. From the laboratory findings: SE 63 HGB 118 g / l, urea 14.6 mmol / l creatinine 134 mmol / l, blood glucose 6.5 mmol / l, HbA1c 8.2%. The patient is under regular control of urologists and urological consulting team. In addition to therapies for diabetes and hypertension does not take other medicines.

Conclusion: Each new symptom and occurrence must be carefully observed as they usually mean the occurrence of a serious illness. Often the diagnosis is pending due to unavailability of some search for a few months (waiting lists). In this particular

case, waited four months from early diagnosis until the end of surgery, which is a long time and a dangerous waste of time for oncological diseases.

ANALYSIS OF RISK FACTORS FOR CERVICAL CANCER

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Introduction: Premalignant and malignant changes on the cervix may be associated with different risk factors. Cervical cancer is a malignant diseas that has the characteristics of sexsual transmited diseas. According of date WHO cervical is ranked second as a causa of death for women in the word.

Methodology: The stady included 101 patients aged 25-70 years treated in the 2009/10 year in gynecology policlinics of public health institutions Health Center Banja Luka. It was used independently created the questionare. In 101 patients made a gynecological examination done in 99 Papa test, done in 76 test for the hpv infection. In patients with abnormal Pap we compare the risk factors.

Results: Of total 101 patients with a clinical examination in 2(0,19%) diagnosed with invasive cancer. From 98 patients who made Papa 48(48%) were abnormal Papa it was negative 51(52%), 36(36%) were positive for hpv infections, 9(0,9%) was negative. Of the 48 patients with abnormal Papa 18(18%) belonged to age group 31-40 years, 14(14%) 41-50 years, over 50 were 15(15%) and 3(0,30%) between 20 and 30 years. 33(33%) had secondary education, 5(0,51%) with higher, 4(0,40%) with high, 6(0,61%) primary school; 38(70%) were married, 2(0,41%) unmarried, 6(0,12%) divorced, 3(0,62%) widows; 17(35%) had one partner, 33(68%) had multiple partners; 17(35%) had consumed tobacco, 23(47%) are not consumed 8(16%) were former smokers. 45 women tested for hpv infection from abnormal Papa test, findings of 36(80%) had positiv test, 9(20%) negativ test.

Conclusion: We conclude that there are factors high, moderate and law risk. In high risk factors can be factored in factors from the sphere of sexsual behavior, infection (viral) of hpv. The intermediate risk factors include socio-cultural factors in intermediate risk factors include age, childbirth, abortion etc.

Key words: factor risics, cervical cancer, hpv infection.

HUMAN CHORIONIC GONADOTROPIN LEVELS IN PATIENTS WITH ECTOPIC PREGNANCY

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Background: An ectopic pregnancy is a complication of pregnancy in which the fertilized ovum is implanted in any tissue other than the uterine wall. This is medical emergency and if notreated properly can lead to the death of mother. Early diagnosis of ectopic pregnancy is now possible, thanks to the development of radioimmunoassays and antiserum that together allow sensitive and specific assays of the β-subunit of

human chorionic gonadotropin (HCG) and high resolution ultrasonography with vaginal probes. The aim of this study is to evaluate the influence of human chorionic gonadotropin levels in treatment of patients with ectopic pregnancy.

Methods: In retrospective study we evaluated the results of treatment of 184 patients with ectopic pregnancy on Clinic for gynecology and obstetrics in Skopje in the last three years. Diagnosis of ectopic pregnancy is confirmed after clinical investigations, quantitative measurement of serum concentration of β-human chorionic gonadotropin (HCG) levels and transvaginal ultrasonography. For measurement of serum concentrations of HCG we use method of hemiluminiscency.

Results: The mean age of the patients was 30±5 years. From 184 patients with diagnosis of ectopic pregnancy in 94 cases (51%) treatment was with laparoscopy, in 30 cases (16.3%) with laparotomy, and in 60 patients (32.6%) conservative treatment with methotrexate. In group with laparoscopic treatment values of β-HCG were between 151 IU/l and 5900 IU/l, with mediana of 5320 IU/l. In patients treated with methotrexate levels of β-HCG were under 10 000 IU/l. We followed-up this patients with serial measurements of serum concentration of β-HCG until complete resolution (levels of β-HCG<5 IU/l)\.

Conclusions: Methotrexate is used for medical treatment of patients with ectopic pregnancywho are hemodynamically stable, with lover concentration of β-HCG. Surgical treatment is used for patients with higher levels of β-HCG (usually β-HCG levels>1000 IU/l). If persistent trophoblast is a risk, follow-up with serial measurements of serum concentrations of β-HCG is necessary.

HEALTH IMPACT OF TRADITIONAL AYURVEDIC PREPARATIONS WITH ANTIOXIDANT ACTIVITY

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In the past twenty years the scientific data concerning the role of oxidative stress in the pathogenesis of various diseases and cancerogenesis tremendously increasing. In combating the negative effects caused by oxidative stress the traditional Indian medicine Ayurveda represents very promising source of potent antioxidants. This study is focused on some of the most exploited plants with antioxidant properties in Ayurveda, their active ingredient composition and use in the light of current scientific data – 86 publications 1990-2010. In addition some specificities of Ayurvedic preparations *Triphala* and *Chyawanprash* were also within the scope of this study.

Based on the current scientific evidence the health impact of antioxidant selected combinations of antioxidant medicinal plants *Curcuma longa L. / Piper longum* L.*, Phyllanthus emblica L., Terminalia bellirica (Gaertn.) Roxb., Terminalia chebula Retz.* and Ayurvedic formulas *Triphala* and *Chyawanprash* were analyzed. The antioxidant properties and health benefits are known results from supplementation with

traditional Ayurvedic preparations and have been proven by current scientific data. The impact of antioxidant products could not be ascribed only to single class of phytochemicals and there is evidence that different active compounds produce in vivo additive and/or synergistic effects.

A better comprehension of traditional methods for preparation of Ayurvedic preparations gives valuable guidance how to improve the bioavailability of antioxidant compounds in order to correctly evaluate their bioactivity and to gain maximum benefit from supplementation.

СЛЕДОПЕРАТИВНО КОМБИНИРАНО ХИМИО-ЛЪЧЕЛЕЧЕНИЕ ПРИ ВИСОКО РИСКОВИ БОЛНИ С КАРЦИНОМ НА МАТОЧНАТА ШИЙКА – ПРОГНОСТИЧНИ ФАКТОРИ

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Цел: Анализ на прогностичните фактори при болни с рак на маточната шийка в в група с висок риск (позитивни илиачни лимфни възли и позитивна резекционна линия) по отношение на общата преживяемост, локалните рецидиви и далечно метастазиране.

Материал и метод: Анализирани са данни за 165 пациенти с рак на маточната шийка, диагностицирани и лекувани за периода 2002–2010 година. Болните са провели следоперативно лъчелечение в Клиниката по Лъчелечение на СБАЛ по Онкология. Всички пациенти са след лапарохистеректомия по Wertheim и преценени, като високорискови за локален рецидив и метастази. Проведено е перкутанно лъчелечение, като при ДОД 2Gy до ООД 50Gy и едновременно химиолечение с цисплатина 40 мг/м^2 еднократно - седмично до обща доза 150-200 мг. Изследваните фактори са: възраст при поставяне на диагнозата, размер на тумора (T), брой метастатични илиачни лимфни възли (N), степен на диференциация на тумора (G), лимфноваскуларна инвазия (LVI), позитивни резекционни линии (R+), наличие на хидронефроза. За анализа на преживяемост са използвани метода на Kaplan Meier и Log-rank тест.

Резултати: Пациентите са на средна възраст 46.4 години. От тях 87 (52.7%) са с позитивни тазови лимфни възли N+ и 58 (35.1%) са с позитивна резекционна линия (R+) по отношение на параметриумите. При 71 болни (43%) се установяват локални рецидиви за областта на малкия таз, при 50 (30.3%) са налице далечни метастази в областта на парааортални лимфни възли, както и белодробни метастази - (4%). Средното време на проследяване е 33.1 месеца (1.23-156.3). Наблюдаваната средна преживяемост е 101.6 месеца (95%CI: 83.8 – 119.3). Пациентите на възраст < 50 г., с тумор (T2), илиачни метастатични лимфни (N+) възли, позитивна резекционна линия и наличие на хидронефроза имат по-ниска средна преживяемост. Разликата в преживяемостта е статистически значима при наличие на хидронефроза ($p < 0.0001$) и при T2 тумори ($p = 0.012$). Степента на диференциация и инвазията в лимфни и кръвоносни съдове (LVI) не очертават статистически значимо повлияване на лечебните резултати.

Изводи: Наличието на позитивна резекционна линия, както и на хидронефроза при провеждане на комбинирано следоперативно химио-лъчелечение на болни с рак на маточната шийка в група с висок риск редуцират общата преживяемост. Обсъжда се въвеждане на сбор от прогностични фактори за оценка на риска и интензификация на следоперативното лъчелечение.

CARDIOVASCULAR DISEASES

СЪРДЕЧНО СЪДОВИ БОЛЕСТИ

STRESS ECHOCARDIOGRAPHY IN PATIENTS WITH HEART FAILURE

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Echocardiography has the ability to noninvasively explore hemodynamic variables during pharmacologic or exercise stress test in patients with heart failure.The identification of viable hibernating myocardium in patients with coronary artery disease and chronic left ventricular (LV) dysfunction is the most common use of stress echocardiography (SE) in patients with heart failure.

However, some other important potential applications of SE in patients with systolic heart failure include: assessment of exercise capacity, the presence and the behaviour of concomitant mitral regurgitation, assessment of ventricular asynchrony and the prediction of response to resynchronization therapy.

Systolic heart failure: The most common cause of heart failure is coronary artery disease. In patients with coronary artery disease and chronic LV dysfunction, it is important to distinguish between viable and fibrotic tissue in order to make adequate clinical decision. Viable myocardium may correspond to different states that are important but difficult to distinguish: ischemia, stunning, nontransmural infarction or hibernation, and in individual patients these pictures may coexist.

Echocardiography can detect viable myocardium during infusion of dobutamine or enoximone. Routinely, the dobutamine is the most common stressor used, whereas the enoximone is particularly useful in patients on beta-blocker therapy. It has been also showed that dipyridamole echocardiography can identify regions with myocardial viability. Combined low-dose dipyridamole followed by low-dose dobutamine, has been proposed for assessment a contractile reserve in some asynergic segments that were nonresponders after dobutamine or dipyridamole alone.

During stress echocardiography it is possible to observe four response patterns based on regional wall function: normal, ischemic, viable and necrotic. In the normal response, a segment is normokinetic at rest and normal or hyperkinetic during stress. In the ischemic response, a segment worsens its function during stress from normokinesis to dyssynergy. In the necrotic response, a segment akinesia remains akinetic during stress. In the viability response, a segment with resting dysfunction improves during stress. During pharmacologic stress, a viable response at low dose can be followed by ischemic response at high dose (biphasic response). This response is suggestive of viability and ischemia, with jeopardized myocardium fed by a critically stenosed coronary artery. A resting akinesia which becomes dyskinesia during stress reflects a purely passive mechanical phenomenon and should not be considered a true active ischemia.

The main clinical issue to search the myocardial viability is that patients with evidence of viable myocardium who undergo revascularization have longer survival and improvement of left ventricular function and symptoms. However, the presence of myocardial viability is only relevant in patients with severely depressed left ventricular function and has a prognostic impact only when a significant amount of viable myocardium is present.

The final end point of searching the myocardial viability is to predict the recovery of global myocardial function after revascularization.

A level of ≥ 4 viable segments, which corresponds an improvement in wall motiuon score index (WMSI)>0.25 (about 20% of LV), is advised as a cutoff value to predict improvement of LV ejection fraction. However, despite the presence of viability, in some patients LV ejection fraction does not improve after revascularization and those are the patients with a high end systolic volume (≥140ml) due to LV remodeling.

Myocardial deformation imaging (strain and strain rate) is recently introduced echocardiographic technique, which provides more information about regional myocardial function. The increase of peak systolic myocardial strain rate during low-dose dobutamine stimulation allows accurate assessment of myocardial viability in patients with depressed LV function after myocardial infarction. Evaluation of myocardial strain and strain rate during stress echocardiography, increase sensitivity, spesificity ang diagnostic accuracy in the detection of viable myocardium.Stress echocardiography may be also an practical method in the assessment of functional capacity and prognosis in patients with heart failure.Exercise (using either treadmill or bicycle exercise protocols) rather than dobutamine is the stressor of choice to evaluate functional capacity due to the possibility to combine echocardiographic variables with common parameters available during exercise.

In the ischemic cardiomyopathy stress echocardiography is focused to find the presence of myocardial viability and its possible effect on global systolic LV recovery after revascularization. In dilated cardiomyopathy the primary end point is to evaluate the presence of residual global contractile reserve. Both dobutamine and exercise testing have been used in the study patients with dilated cardiomyopathy , but there is clear predominance for the use of dobutamine test. The critical level to define the presence of contractile reserve is defined as an increase of at least 5% in the global LV ejection fraction at stress echocardiography compared to baseline values. In the interpretation of stress echocardiography results of WMSI and the LV volume to derive left ventrivular ejection fraction must be calculated. It has been showen that patients with significant improvement in their WMSI and LV ejection fraction during dobutamine infusion have a better survival rate and increase in the LV ejection fraction during follow-up period.

The same stress echocardiography study offers assessment of systolic pulmonary artery pressure (sPAP) and right ventricular (RV) function.The change in the sPAP at rest and during exercise is frequently utilized echocardiographic variable. Pulmonary hypertension determined by echocardiography has been defined as a peak of sPAP>30mmHg at rest and >45mmHg during exercise.Right ventricular dysfunction predicts impaired exercise capacity and decreased survival in pts with heart failure. The evaluation of tricuspid systolic annular tissue Doppler velocity has been introduced as index of RV function and a value less than 10.8cm/s indicates patients with abnormal RV function.

Additional great value of stress echocardiography is its prognostic role in pts with intermediate values of VO2max (10-14ml/Kg/min). VO2max <10ml/Kg/min defines high risk, a value >18 ml/Kg/min defines high risk, while values in between represent a grey zone.

Stress echocardiography in the form of standard exercise or pharmacologic protocols can be useful in the assessment of mitral regurgitation (MR), which is common finding in patients with heart failure. Left ventricular contractility, in the presence of MR, can impair or improve during exercise with modification of MR. Patients with presence of contractile reserve show a decrease in MR, while a fall in

stroke volume is associated with an increase in MR volume during exercise. In patients with ischemic MR and left ventricular dysfunction significant exercise-induced increases in MR unmask patients at high risk of poor prognosis.

Diastolic heart failure accounts for more than 50% of all heart failure patients. In patients with suspected diastolic heart failure and normal systolic function, symptoms of effort intolerance and dyspnoea commonly occur during exercise. Stress echocardiography is useful method in the assessment of pathophysiologic components of diastolic heart failure: elevated LV diastolic pressure, elevated pulmonary venous pressure and latent systolic dysfunction. All these aspects can be evaluated during exercise echocardiography. Combining transmitral flow velocity with annular velocity obtained at level of the mitral annulus with tissue Doppler (E/E`) has been proposed as a tool for assessing LV filling pressures that combines the influence of transmitral driving pressure and myocardial relaxation.

A rest E/E`<8 suggests normal filling pressure, E/E` >15 suggests elevated filling pressure, while a range of 8 to 15 represents a gray zone. Normaly, during exercise E and E` velocity proportionaly increases, so the E/E` ratio do not change significantly, which means normal diastolic response during exercise.

If E/E` ratio increases up to 15 we can suppose a pathological increase of LV filling pressure during exercise. This finding may unmask the presence of subclinical diastolic dysfunction, and it can be helpfull for further diagnostic and treatment algorithm. Evaluation of exercise E/E` ratio must be associated with the assessment of cardiac output and sPAP during exercise. Finally, in patients with predominant diastolic abnormality, evaluation of systolic LV function during exercise may discover the patients with concomitant latent myocardial dysfunction.

Conclusion: In patients with systolic and diastolic heart failure stress echocardiography is useful test to: detect viable hibernating myocardium, assess different patophysiologic component of heart failure syndrome, assess prognosis and make appropriate clinical decision.

КАРДИОХИРУРГИЯ – НАСТОЯЩЕ И БЪДЕЩЕ

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В настоящата лекция ще бъдат разгледано състоянието на кардиохирургията в България в момента. Ще бъде обърнато внимание на препоръките за миокардна реваскуларизация при лечение на пациентите с исхемична болест на сърцето с цел да се оптговори на въпросът „стентиране или операция“. Ще бъдат разгледани транскатетърните методи на лечение – ендопротезиране при аортна патология и транскатетърното аортно клапно протезиране. Ще бъдат засегнати средствата за механична циркулаторна поддръжка и минимално ивазивната хирургия. Ще бъде обсъдено и „бъдещето“ на кардиохирургията в България.

CARDIAC SURGERY – PRESENT AND FUTURE

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One of the scopes of this lecture will be present status of Cardiac surgery in Bulgaria. Contemporary Guidelines for myocardial revascularization in patients with coronary artery disease will be discussed in order to answer the question "Stenting or By-pass surgery". Transcatheter methods for treatment both endovascular stent grafting and transcatheter aortic valve replacement will be discussed. Ventricular assist devices and minimal invasive cardiac surgery will also be mentioned. The "future" of Cardiac surgery will also be discussed.

ПЪРВОНАЧАЛЕН ОПИТ С TAVI ПРИ ПАЦИЕНТИ СЪС СИМПТОМАТИЧНА АО СТЕНОЗА И ВИСОК ОПЕРАТИВЕН РИСК

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Увод: Дегенеративната аортна стеноза е най-често срещаното клапно заболяване в Европа. По правило тя се среща при възрастни пациенти с множество придружаващи заболявания.

Основен метод за лечение е оперативният /Ао кл. протезиране/ с нисък процент оперативна смъртност при стандартна операция /2,5%-4,0%/.

При възрастни пациенти обаче и наличие на коморбидност този риск може да надхвърли 25%.След появата на първите симптоми средната продължителност на живота е 2,5 – 3 години. Само 20% до 50% от пациентите с високостепенна, симптоматична Ао стеноза се оперират, поради напреднала възраст, висок оперативен риск, придружаващи заболявания и други.

По настоящем съществуват две по-малко инвазивни методики за терапия:

- Балонната валвулопластика – прилага се рядко, поради лошите дългосрочни резултати.
- Транскатетърно аортно клапно протезиране (TAVI) – терапевтичен метод, който търпи бурно развитие в последните години след първата имплантация на пациент публикувана през 2002.

Цел: Целта на настоящото проучване е да оцени ранните и едногодишни резултати след TAVI (трансфеморален /TF/ и трансапикален /TA/ достъп) при пациенти със симптоматична аортна стеноза и висок оперативен риск, след имплантация на протеза Edwards Sapien® (Edwards Lifesciences Inc., CA, USA).

Материал и методи: За периода януари – 2009 - май 2010 г в СБАЛССЗ "Св. Екатерина" бяха проследени 19 пациента след перкутанно аортно клапно протезиране (чрез трансфеморален и трансапикален достъп), със симптоматична аортна стеноза и висок оперативен риск. При всички пациенти предпроцедурно бе проведено CT и TEE, с оглед определяне на достъпа (TF или TA) и размера на био-протезата .

След аортна балонна валвулопластика бе имплантирана аортна протеза Edwarts-Sapien, по време на високочестотно пейсиране, под TEE и флуорографски контрол при 10 пациента с TF достъп и при 9 пациента с TA достъп.

Резултати: Процедурният успех бе 100%. Среден клапен градиент след имплантацията 15 ± 5 мм жив. Без значима аортна регургитация и мозъчно-съдови усложнения и при двете групи пациенти.

Ранна болнична смъртност бе установена при 1 пациент от групата с TA достъп(ОЛСН) и при 1 пациент от групата с TF достъп (периферно съдово усложнение/. Преживяемостта на пациентите при период на проследяване (12 +- 4 месеца), бе 79%. Смърт от екстракардиална причина се установи при 1 пациент след 3-ти месец от процедурата. Клиничното и ЕхоК проследяване показа значително подобрен ФК и нормална протезна ф-ция и при двете групи пациенти. Аортната регургитация:без динамика – 12 пациента; с намаляване (от II на I) – 2пациента; с нарастване (от I/II на II) – 5 пациента.

Заключение:TAVI е революционна методика в кардиологията. Добрите ни резултати се потвърждават и от излезлите наскоро резултати от PARTNER I и II както и Европейския Регистър SOURCE. Не трябва обаче да се забравя, че методиката все още се развива и засега метод на избор остава оперативното аортnоклапно протезиране. По тази причина методът следва да се прилага само при високорискови пациенти, които са контраиндицирани за конвенционално клапно протезиране.

МЕНИДЖМЪНТ НА ПАЦИЕНТИ С КОМПЛЕКСНА АОРТНА ПАТОЛОГИЯ – ОПИТ НА ЕДИН ЦЕНТЪР

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Цел: Целта на настоящата работа е да представи опитът на СБАЛССЗ „Св. Екатерина“, София при хибридното лечение на високорискови пациенти с комплексна аортна патология.

Пациенти и методи: От 2003 до 2011 общо 12 пациента, 11 мъже и 1 жена със средна възраст 49 години (от 26 до 69 години), бяха лекувани хибридно, поради наличие на комплексна аортна патология. Патологията беше както следва: аортна дисекация (9 пациента), аортна аневризма след оперативна корекция на коарктация (2 пациента) и ИБС в комбинация с високостепенна аортна стеноза, ХАНК и порцеланова аорта (1 пациент).

Бяха извършени следните процедури:

- Аорто-каротиден байпас с последваща имплантация на ендопротеза – 5 пациента;
- Имплантация на ендопротеза след конвенционална хирургия – 4 пациента;
- Едноетапно извършване на операция на Bentall/De Bono и имплантация на ендопротеза – 1 пациент;
- Конвенционална хирургия след имплантация на ендопротеза – 1 пациент;
- Транскатетърно аортно клапно протезиране след ОРСАВ хирургия – 1 пациент.

Резултати: Един пациент от групата пациенти с аорто-каротиден байпас с последваща имплантация на ендопротеза почина, поради руптура на аортата. Двама пациента от групата хирургия + имплантация на ендопротеза починаха поради усложнения на основното заболяване (аортна дисекация), като непосредствената причина за смъртта беше интестинална исхемия при единия пациент и бронхомалация при другия. Един пациент от групата с аорто-каротиден байпас с последваща имплантация на ендопротеза получи инсулт.Всички останали пациенти се възстановиха напълно и бяха изписани без усложнения.

Заключение: Нашият опит сочи, че при пациенти с комплексна аортна патология транскатетърните процедури са адекватен метод за лечение с приемлива смъртност и болестност. Бихме могли да твърдим, че хибридният мениджмът, включващ конвенционална хирургия и транскатетърни интервенции, може да се приеме за оптимален при лечението на тези високорискови пациенти.

MANAGEMENT OF PATIENTS WITH COMPLEX AORTIC PATHOLOGY – SINGLE CENTER EXPERIENCE

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Objective: The aim of present work is to overview the experience of "St. Ekaterina" University Hospital, Sofia with hybrid management of high risk patients with complex aortic pathology.

Methods: From 2003 to 2010 a total number of 12 patients, 11 male and 1 female with average age 49 years (from 26 to 69 years), underwent hybrid management of complex aortic pathology. The pathology was aortic dissection in 9 patients, aneurysm after aortic coarctation surgery in 2 patient and coronary artery disease, combined with severe aortic stenosis, peripheral artery disease and lead pipe aorta in 1 patient.

The procedures were as follows:

- Aorto-carotid bypass with consecutive endovascular stentgraft (EVSG) implantation – 5 patients;
- EVSG implantation after conventional surgery – 4 patients;
- Single-stage Bentall/De Bono procedure + EVSG implantation – 1 patient;
- Conventional surgery after EVSG implantation – 1 patient;
- Transapical aortic valve replacement after OPCAB surgery – 1 patient.

Results: One patient died in aorto-carotid bypass + EVSG group, because of aortic rupture.

Two patients died in surgery + EVSG group, because of aortic dissection complications – one from intestinal ischemia and one from bronchomalacia. One patient in aorto-carotid bypass + EVSG group developed stroke.All other patients had uneventful recovery and were discharged home.

Conclusions: Our experience shows that transcatheter management in patients with complex aortic pathology is a reasonable approach for management with acceptable morbidity and mortality. We can say that hybrid management, including transcatheter and conventional surgery, could be claimed an optimal therapy for these high risk patients.

СЪРДЕЧНА ТРАНСПЛАНТАЦИЯ: ОСОБЕНОСТИ НА РАННИЯ И ОТДАЛЕЧЕНИЯ СЛЕДОПЕРАТИВЕН ПЕРИОД

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Сърдечната трансплантация е средство на избор при крайната степен на сърдечна недостатъчност, когато е изчерпан ефакта от медикаментозната и интервенционалната терапия. За добрия резултат на трансплантацията са от значение характеристиките на донора и реципиента, както и самото донорско сърце; антропометрични данни, инфакциозен статус (особено вирусологичен), исхемично време, както и съвместимостта донор/реципиент и нивото на преформираните в реципиента антитела. Като правило резултата от крос-мач теста е налице след трансплантацията, обаче изпреварваща информация може да се получи с разширено имунологично изследване на реципиентите и потенциалния донор. Непосредствените следоперативни проблеми обикновено са свързани с ранна дисфункция на трансплантираното сърце. Последното е резултат на имунологичен конфликт между донорското сърце и реципиента, (различен от реакцията на отхвърляне) и/или на повишеното натоварване на дясната камера от хронично повишеното белодробно съдово съпротивление. В единия и другия случай нерядко са налице циркулаторни нарушения, водещи до хипоперфузия на тъканите и развитие на множествена оганна недостатъчност. Имуносупресията, включваща калциневринови инхибитори, антиметаболити и гликокортикоиди е утвърдена практика. Отхвърлянето на трансплантираното сърце, клетъчно или хуморално е с най-висок интензитет през първата година след трансплантацията, като антирежекционното лечение включва пулс терапия с кортизон, поликлонални/моноклонални антитела, плазмафереза. Стадирането на реакцията на отхвърляне се основава на приета хистологична скала. В по-отдалечен период от време се наблюдава ускорена атеросклероза със засягане на коронарните съдове, лимфо-пролиферативни заболявания и инфекциозни усложнения. Независимо от това до края на първата година са живи над 85%, на 5-та година 70% и на 10-та година над 50% от трансплантираните.

ANTIHYPERTENSIVE TREATMENT AND CIRCULATION OF THE TARGET ORGANS. THE J –CURVE: REALITY OR MYTH?

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The relationship between blood pressure (BP) and risk of cardiovascular events is continuous, consistent and independent of other risk factors. The mean reduction of the events from the treatment is 35-40% for stroke, 20- 25% for coronary heart disease , and 50% for heart failure. The decades ago , Stewart cautioned against too aggressive antihypertensive therapy, because cardiovascular complications might be increased with a fall especially in diastolic blood pressure (DBP). L .Farnett et al analyzed a series of large hypertension studies demonstrated a constant J- shaped relationship for cardiac events and DBP but not between BP and stroke . The explanation of this phenomenon is in the existing pathophysiologic consideration of coronary flow and BP. The coronary

circulation is unique in that most of the coronary blood flow to the left ventricle(LV) occurs in diastole. During systole, the contracting LV myocardium compress intramyocardial vessels and obstruct its own blood flow. Auto-regulation ensures relatively constant myocyte perfusion over a wide perfusion pressure range of 45 to 125 mmHg. However, in patients with coronary artery disease (CAD), auto -regulation can be compromised. A fall in DBP might lower perfusion pressure distal to a stenosis below the critical level at which auto -regulation is effective, thereby compromising myocardial perfusion, increasing myocardial ischemia and LV filling pressure. In patients with left ventricular hypertrophy (LVH), subendocardial ischemia might occur even in the absence of stenosis.

Three pathophysiologic mechanisms have been proposed to explain the existence of J- curve: 1) low DBP could be an epiphenomenon to coexisting or underlying poor health or chronic illness, leading to increasing morbidity and mortality; 2) low DBP could be caused from an increased pulse pressure reflecting advanced vascular disease and stiffened large arteties;3) overaggressive antihypertensive treatment could lead to too-low DBP and thus hypoperfusion of the coronaries resulting in coronary events .

Increase of pulse pressure has been shown to increase the risk of a coronary events: in fact, an increased pulse wave velocity is a powerful independent predictor of cardiovascular events, especially of coronary heart disease. With aging, the reflected waves travel faster and return to the central aorta in early to mid systole where they augment the already elevated systolic BP.

In general, blood flow to vital organs of the body such as the heart, kidney and the brain, is normally auto- regulated and within wide limits, blood flow remain constant within the organ in the face of changes in perfusion pressure. Auto-regulation is mediated by changes in the caliber of small arteries and arterioles. Below a certain pressure the mechanism begins to fail. Unlike the coronary regulatory mechanism, the brain's compensatory system can increase oxygen extraction, when perfusion pressure falls below the limits of auto-regulation and can, therefore, better tolerate reduction in DBP.

The INVEST study was an ideal model to analyze the significance of the J-curve because all patients had CAD and hypertension. The primary outcome in the INVEST study doubled when DBP was below 70 mm Hg. In contrast to the risk of acute myocardial infarct, the risk of stroke did not increase with low DBP.

Although there is substantial evidence to support an association, between antihypertensive therapy and J –curve phenomenon, a causal relationship has not been established . Although we agree that SBP reduction should be the goal, caution has to be exercised in lowering the diastolic component beyond a critical "J-point". This might be even more important in elderly patients here DBP might already be reduced due to age at onset of therapy.

The interaction of antihypertensive drugs and coronary hemodynamic status is complex, and head-to- head comparisons among drugs or drug classes are lacking. Although all antihypertensive drugs lower BP, they do not have quantitatively similar effects on pulse pressure. Most drug classes, such as blockers of the rennin angiotensin system and calcium channel blockers, as well as the diuretics, improve arterial compliance and thus lower SBP more than DBP, and therefore diminish pulse pressure. Antihypertensive drug class that reduce LVH and hypertensive vascular disease are

more effective over the long term in improving coronary flow reserve than drug classes that have little or no effect.

An analysis of BP and cardiovascular events in the Treating to New Targets(TNT) trial, revised the J- curve hypothesis. In patients with CAD, a J-curve relationship or a non-linear relationship was found to persist between BP and cardiovascular events such that a low BP, (< 110-120/<60-70mmHg) increase risk of future cardiovascular events.Numerous study have documented an inverse relationship between DBP and CHD (i.e. J-shaped curve). In most study, the J-shaped curve was found to be below 70-80 mm Hg. At the same reduced DBP levels, there are little if any evidence of a J-shaped curve with regard to other target organs, such as the brain and kidney. Few, if any J-shaped curve phenomena have been documented between systolic BP and coronary, renal or cerebrovascular events. Careful scrutiny of the available data seems to show a J-shaped relationship between DBP and coronary heart disease in high –risk patients. These are often characterized by being elderly, having LVH and/ or coronary heart disease, and by exhibiting a wide pulse pressure.

VASCULAR CALCIFICATIONS AND CARDIOVASCULAR DISEASE MORBIDITY AND MORTALITY

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Introduction of the CKD-MBD concept: The term mineral and bone disorders (MBD) in patients with chronic kidney disease (CKD) have been recently introduced as a systemic condition comprised of mineral, hormonal and bone disorders, coupled with vascular calcification (VC) and increased cardiovascular morbidity and mortality [1]. There is a continuous effort of the nephrological community to produce-update guidelines in this complex issue trying to help practitioners to prevent possible detrimental outcome [2], although there is still insufficient evidence and a need for a concerted action trying to bridge those huge gaps [3].

The link between kidney dysfunction and cardiovascular risk in the presence of even subtle kidney dysfunction is considered as one of the conditions necessitating intensive prevention of this cardiovascular risk [4]. Moreover, the risk of cardiovascular disease (CVD) in patients with CKD appears to be 10 to 20 times higher than in the general population [5]. Thus, in addition to the traditional risk factors as hypertension, diabetes, smoking, dyslipidemia etc., uremia specific factors (anemia, uremic toxins, hyperhomocystinemia and vascular calcification) are crucial to explain the increased CVD mortality in CKD patients. Nowadays, it is known that hyperlipidemic intimal plaque when coupled with calcium/phosphate deposits occlude the lumen and lead to an insufficient blood flow of the perfused organ. Conversely, in cases of medial VC the elasticity of the vessel wall is lost leading either to indirect overload of the hearth function or ischemic hearth disease especially in cases of a low diastolic blood pressure.
Vascular calcification and related bone changes
The finding that VC of the large and medium calibre arteries in CKD patients is associated with an increased risk of vertebral fractures and increased mortality in women especially [6], reflects on the issue of bone health and VC relationships in CKD [7]. It is assumed that a prerequisite for successful control of calcium/phosphate

metabolism is the preserved bone health, i.e. the absence of alterations in bone morphology (high or low bone turnover) associated with CKD. Such bone has the capacity to buffer the efflux/influx related to the level of bone minerals (calcium/phosphate), reducing the possibility for deposits and calcification in soft tissues and especially VC. Expectedly, there is evidence of a negative relationship between low bone turnover and the degree of coronary artery calcification [8]. Moreover, there is data demonstrating an inverse relationship between mineralized bone volume and both coronary calcification and vascular stiffness [9]. However, in despite of all evidence the relationship between low and/or high bone turnover and VC remains under debate. Nevertheless, it is considered that not bone turnover itself but rather the excessive bone resorption which can occur at any rate of turnover may be related to VC. In accordance with this concept, the correction of this balance in bone turnover, (high or low), could protect against the progression of VC [10]. *Vascular Calcification and CVD Morbidity and Mortality*

CVD mortality, which occurs at a rate up to 500 times higher than in the general population, increases exponentially with age [11]. The number of arteries calcified is reported to be an independent risk factor for CVD and mortality in addition to the established conventional risk factors [12]. However, the background for VC is viewed through the relationship between individual disordered abnormalities in mineral metabolism (Ca, phosphorus, PTH, vitamin D) and various CVD outcomes already described in CKD populations [13-16]. Finally, the growing worldwide public health problem caused by CKD and its related vascular problems has consequences beyond the clinical bedside, and now represents a substantial socioeconomic burden for health care systems and the medical community.

From the experiments *in vitro*, it's known that VC represents an active process of transdifferentiation of vascular smooth muscle cells to osteoblike cells, based on the excessive balance either of VC promoters (hyperphosphatemia, hypercalcemia, chronic inflammation, elevated PTH levels, and exogenous vitamin D therapy), or VC inhibitors (matrix GLA protein, osteoprotegerin, fetuin A etc.) [17]. In order to implement this evidence into the clinical practice, it's important that nephrological community adopts same definitions of referent or abnormal parameters according to the standardised assays employed over the years, especially for PTH analysis. Moreover, the reported mainly observational studies that indicate an association between mineral metabolism categories and mortality imply the need for an international harmonization of existing clinical practice guidelines for mineral metabolism and standardisation of available therapeutical strategies. However, we should be aware that neither currently available Kidney Disease Outcomes Quality Initiative (K/DOQI) [18] nor recent Kidney Disease: Improving Global Outcomes (KDIGO) practice guidelines [19], could superimpose a defined standard of care or an exclusive course of management. The last version has been already challenged by the European Best Practice Group [20], trying to help further clinical guidance in the field of CKD-MBD for the practising nephrologists. Thus, it is obvious that the possibilities for treatment or prevention of VC development should be reviewed.

Can we prevent development of Vascular Calcification and CVD Morbidity and Mortality In order to prevent CVD all aforementioned risks should be considered as one of the conditions necessitating intensive prevention of such risk. Apart from the conventional factors such as hypertension, dyslipidemia, and hyperhomocysteinemia

and the specific condition of CKD population such as oxidative stress of uremia and hemodialysis [21], hyperphosphatemia, hypercalcemia, and elevated calcium-phosphorus product remain as major contributors to the development of VC and CVD in this population [22,23].

Over the years, various drugs (basically non-calcium based phosphate binders (non-CBPB)) have been introduced with limited evidence from RCTs in CKD that the reduction of arterial calcification progression impacts mortality [24-26]. In the period of current economical crisis, the uncertainty in the nephrological community about the most cost-effective way to treat hyperphosphatemia in patients with end-stage renal disease is becoming even more prominent [27]. Although there is a consensus among the nephrological community that known vascular/valvular calcification and its magnitude identify patients at high cardiovascular risk and there is suggested treatment according to all available guidelines on CKD-MBD [18,19], the widespread utilization of non-CBPB is yet challenged as exceeding what would usually be considered good value for the money [28,29].

At present, the actual treatment should be a preventive one with as great as possible reduction in calcium load from calcium based phosphate binders. Moreover, the presence of vascular/valvular calcification should be regarded as a complementary component to incorporate into the decision-making of how to individualize treatment of CKD-MBD in each patient along with the evaluated trends rather than based on single serum mineral values.

Finally, while awaiting positive evidence for various treatment strategies from new randomized clinical trials, the current clinical perspective for treatment should be to “do no harm” [30].

ACUPUNCTURE METHOD FOR CURING OF HYPERTONIE

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It is done a research of the world situation on the deaths by cardiovascular reasons. Bulgaria is a world leader in this bad statistic.

It was checked the alternative medicine possibilities of curing hypertonie. By acupuncture method was treated 78 years old female with brain insult and 10 years of hypertension background. She has been treated first by Clophadon, Nitrolong Isodinit, after that by Vasopren, Atenolol and Presstarium (twice daily by 1 tabl). In the first visit the blood pressure before treatment was 193/105, after treatment 160/90. On the second day the start pressure was 165/95, after treatment 155/90. During first three days the patient have been receiving her medicines, so on the third day after treatment the medicine have been cut on a half, after two days doses were cut again on a half, and after two more days the medicine was stopped at all. Since this day\7 procedure\ the patient stopped receiving any medicine for regulating of the blood pressure.

For two years the patient came every month. After a year and a half the blood pressure was around 145/90, after that coming to 135/85.

For the period twice the patient had accidently high blood pressure – 180/90, which was corrected by acupuncture.

Conclusion. Acupuncture has high potential for helping the patients with essential hypertonie.

СЕРДЕЧНО-СОСУДИСТАЯ ПАТОЛОГИЯ ПРИ НАРУШЕНИИ СКОРОСТИ УТИЛИЗАЦИИ УГЛЕВОДОВ У БОЛЬНЫХ ДЕТСКИМ ЦЕРЕБРАЛЬНЫМ ПАРАЛИЧОМ

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Клиницисты и исследователи, занимающиеся проблемами больных детским церебральным параличом (ДЦП), неоднократно отмечали наличие в клинической картине этого заболевания нарушения со стороны сердечно - сосудистой системы. Эти нарушения, проявляющиеся чувством резкой слабости, профузной потливостью, тахикардией, артериальной гипотонией, похолоданием и синюшностью кистей и стоп, трактовались обычно как вегетативно-сосудистый синдром и по своей клинической картине были чрезвычайно близки к гипогликемическим состояниям.

В связи с этим представлялось целесообразным изучить состояние углеводного обмена при различных формах и различных степенях тяжести поражения у больных ДЦП

Работа носит клинико-лабораторный характер. У больных церебральным параличом детей исследовался неврологический статус, данные электрокардиографического исследования, динамика артериального давления, пульсометрия и кардиоинтервалография. содержание глюкозы крови натощак и четырехкратно после нагрузки глюкозой.

Всего обследовано 276 детей, страдающих детским церебральным параличом в возрасте от 5 до 7 лет. У 101 ребенка были выявлены дистрофические изменения сердечной мышцы на ЭКГ, профузная потливость, гипотония и тахикардия, нарастающие через 2-2,5 часа после приема пищи. Глюкозотолерантный тест выявил в этой группе больных отчетливую тенденцию к ускорению утилизации глюкозы (3.01±0.3). Все больные относились к тяжелой степени заболевания с наличием выраженной мышечной гипертензии и распространенными глобальными синкинезиями.

Анализ данных показал, что сердечно-сосудистые расстройства у больных ДЦП совпадали с ускоренной утилизацией углеводов и связанной с этим гипогликемией и выявлялись у наиболее тяжелой категории больных (индеек корреляции 0.85). Это позволяет высказать предположение о связи вегетативно–сосудистой патологии у больных ДЦП с вызванным спастически напряженными мышцами повышенным потреблением глюкозы и вызванной этим перманентной гипогликемией, что позволяет наметить принципиально новые пути коррекции этой патологии.

MODERN SOLUTIONS FOR DIFFICULT CARDIAC PATIENTS CASES IN TOKUDA HOSPITAL-SOFIA

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In the recent years the advancement and improvement of the diagnostic and medical technologies and methods, largely increased the number of complicated patients, treated by various methods of invasive cardiology and cardiac surgery. This faced us with complicated and unusual cases and made us make difficult and non-standard medical decisions. Here we present some of them.

The end-stage heart failure due to ischaemic cardiomyopathy is a great challange after ICS implantation and maximal surgical revascularization. In such patient we used a one-stage stem cells intracoronary injection and CRT-P implantation with good effect.

The ventricular tachycardia and fibrillation are a life-treat condition, especially in patients complicated with heart valve disease, We treated such a patient after mitral valve replacement, dilative cardiomyopathy and life-treat ventricular arrhythmia, dependent on a standard pacemaker with low ejection fraction, by one-stage pacing system extraction and ICD implantation.

Hydatid cysts are with a rare localization in the human heart. A rare case of such localization in the ventricular septum, causing a complete A-V block with bradycardia and syncope was treated with a pacemaker and conservative treatment. 5-years follow-up showed we had chosen the right strategy.

RELATIONSHIP AMONG SERUM LIPIDS, FIBRINOLYTIC ENZYMES AND FACTOR VII IN WOMEN DURING MENOPAUSE

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Background: Hyperlipidemia is seen as an important risk factor for coronary artery disease (CAD) in women during menopause. However, hypercoagulability and reduced fibrinolytic capacity, often seen in menopausal women, are associated with hypertriglyceridemia (possibly concomitant with low levels of high-density lipoprotein cholesterol).

Aim of the study. The mutual correlation among serum lipids, fibrinolytic enzymes: tissue type plasminogen activator (t-PA), plasminogen activator inhibitor type 1(PAI-1), and factor VII in women during menopause was studied.

Material and methods: Study comprised a total number of 76 women divided into two groups: group of women in perimenopause and group of women in postmenopause. The first group consisted of 36 women in perimenopause, with irregular menstrual cycle and FSH level under 25 mU/ ml. The second group encompassed 40 women in postmenopause, with anamnestic data indicating last menstruation at least 12 months ago and FSH level above 25 mU/ml. Lipid level (HDL-CH, LDL-CH, TG, total cholesterol) was determined with colorimetric-spectrophotometric method, fibrinolytic

enzymes were determined using immunoenzyme sandwich method (Elissa) and factor VII of coagulation with the method of deficiency plasma. Data were entered into a data – base and were statistically analyzed. Correlation analysis (Pearson·s coefficient) was used for assessing the relationship between examined parameters.
Results: Fybrinolytic activator (t-PA) was in poor negative correlation with fibrinolytic inhibitor (r = - 0.18) factor VII of coagulation (r = - 0.28), total cholesterol (r= - 0.17) and triglycerides (r = - 0.35), but in weak positive correlation with HDL-CH (r = 0.73) as well. There was a positive correlation between PAI-1 on one hand and factor VII (r = 0.18), triglycerides (r = 0.245) and total cholesterol
(r = 0.14) on the other hand, but there was also a weak negative correlation between PAI-1 and HDL-CH (r = - 0.048).

Conclusions. These data suggest that serum lipids, particularly triglycerides have a close relationship with thrombogenesis as evidenced by activated f. VII in the extrinsic coagulation system and also by elevated PAI-1 activities in fibrinolysis. Therefore, we ought pay attentions not only to serum cholesterol or LDL-cholesterol for their atherogenic actions, but also to triglycerides because of their close correlation with extrinsic coagulation system and anti-fibrinolytic activities.

РОЛЯ НА ФАРМАЦЕВТИТЕ В МЕНИДЖМЪНТА НА СОЦИАЛНО ЗНАЧИМИ ЗАБОЛЯВАНИЯ

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Увод: Заболеваемостта и смъртността от хронични заболявания, както и разходите за тяхното лечение постоянно нарастват. В световен мащаб, хроничните заболявания с изключение на района на Субсахарска Африка са водеща причина за смъртност, като се очаква, че до 2030 година, дори в този район смъртността от хронични заболявания ще изпревари тази от инфекциозните болести. В условията на финансова криза и недостиг на средства, правителствата са склонни да съкращават разходи за здравеопазване и да осигуряват само основни здравни услуги, за сметка на средствата за превенция и адекватна терапия на хроничните заболявания. Хронифицирането на заболеваемостта променя задачите и приоритетите на здравното обслужване. Фармацевтите, като здравни специалисти в непосредствен контакт с пациентите са доказали, че могат да подобрят мениджмънта на редица социално значими заболявания, като диабет, астма, сърдечно-съдови и др.

Целта на това изследване е да анализира някои успешни програми за мениджмънт на социално значими заболявания с участието на фармацевти, в различни региони от света и да коментира възможностите им за приложение в български условия.

Метод: Обобщени са резултатите от 17 публикации за период от 1999-2010 г.

Резултати: Резултатите показват, че ангажирането на фармацевтите в мениджмънта на редица социално значими заболявания подобрява грижата за пациентите по отношение на оптимизиране на терапията, осигурява подкрепа за придържане към терапията и е оценена високо от пациентите и техните лекари. Включването на фармацевтите е в посока на предоставянето на по-добър достъп до информация на хората. Така те могат да поддържат здравословните аспекти на своя начин на живот и да намаляват влиянието на рисковите фактори.

Изводи:В България за лечението на много хронични заболявания са включени лекарства в позитивния списък, но те се предписват на един напреднал етап, когато пациентите са изразходвали значителни ресурси, те са на политерапия и няма ефективни програми за профилактика. Терапията на хронични заболявания често е ненавременна и следователно по-съпа.

Фармацевтите представляват един неизползван ресурс по отношение на превенцията и мениджмънта на социално значими заболявания. Необходимо е тези дейности да се подкрепят освен на съсловно, и на държавно ниво в посока включване на фармацевтите в национални програми за борба със социално-значими заболявания.

QUALITY OF LIFE IN PATIENTS WITH HIPERTENSION

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Introduction: Definition of the quality of life to the WHO QoLiy group in 1995. is individual's perception of their environmental positions in the existing culture and system of values and establishes indicators that show how patients are functioning and how the disease limits their activities.

The aim is to measure quality of life for patients with hypertension and discover the quality of certain areas that are not satisfactory.

Method: The method is completing 15D questionnaire (Harri Sintonen). The questionnaire contains 15 questions with 5 gradations and covers physical, mental and social aspect of life. Questionnaire completed by patients with hypertension and control group of patients without hypertension, in February 2010. Medical Center in Kruševac. Results: The study included 121 patients with hypertension, mean age 68.86, and 29 subjects without hypertension, mean age 66.7 year. Average quality in hypertensives was 0.7633 ± 0.153 and in those without hypertension was 0.7852 ± 0.138. In the area of individual subjects without hypertension are more alert, breathing is better, easier to feed, are preserved, mentally and perform activities with less discomfort. Patients with hypertension have less discomforts and symptoms. Gender differences are statistically significant and breathing and sleeping (men with other diagnoses). Women sleep worse than men. Most symptoms and discomfort of women have other diagnoses. Quality of life declines with age. Differences of mean values hypertensive groups and those without hypertension is not significant.

Declining of quality in those without hypertension is gradually (0.8557, 0.8483, 0.7269,) and significantly after 70 years is 0.5720, ($t = 2.14$ $p = 0.05$) and in hypertensives is blinder especially in age groups 60-69 and 70 -79 years which was statistically significant (0.8922,0.8413,0.7027**,0.6076*) **p=0.001 *p=0.05.

Quality of life in hypertensives decreases in all characteristics with the years of life. At least declining eyesight, the ability of food and speaking. Statistically significant decreasing we have in breathing and mental activity. The high statistical significance found in usual activities. There are differences in motion but not statistically significant. The difference is evident by the disease by breathing in hypertensives. Mental functions and perform common activities are worse for those without hypertension who also have more discomfort and symptoms compared to hypertensives.

Conclusion: Quality of life declines with age and disease-especially patients with hypertension.

Key words: 15D, hypertension, quality of life

IS THE PERIDONTITIS A SOURCE OF SYSTEMIC INFLAMMATION IN PATIENTS UNDERGOING PERITONEAL DIALYSIS OR HEMODIALYSIS?

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Background: Periodontitis contributes to generalized inflammation and development of systemic diseases, including atherosclerosis and cardiovascular disease. Studies have reported that moderate to severe periodontitis can precipitate an acute-phase response and based on this we studied the relationship between periodontitis and two measures of systemic inflammation, serum albumin and C-reactive protein (CRP) among patients who were receiving chronic outpatient hemodialysis and peritoneal dialysis treatment.

Methods: 93 patients (63 on HD, mean age, 49.34±10.98years, average duration of dialysis 49.79±39.46 months; 30 pts on CAPD, mean age 51.22 ±16.18years, average duration of dialysis 26.10±18.93 months were enrolled in the study. Periodontal examination was carried out by a single professional stomatologist and the measurements were recorded according to WHO recommendations. A periodontitis case was defined as > 60% of sites with attachment level ≥4 mm. Binary logistic regression was used to determine the association between periodontitis and two measures of systemic inflammation, low serum albumin (defined as <3.5 mg/dl) and high C-reactive protein (defined as >5.0 mg/dl).

Results: Fifty of all subjects (54.2%) were diagnosed as periodontitis cases. There were no significant difference between the prevalence of periodontal disease in pts on HD or PD therapy (53.9% vs 47%).The average number of teeth was 20.08 (SD 6.12). Plaque index score, gingival index score, papillary bleeding index, loss of Clinical attachment level,and Community Periodontal Index were 2.11 ± 2.26; 1.31 ± 1.0; 2.05 ± 1,35 mm; 5.12 ± 1,23mm and 1.61± 1.11 respectively. Periodontitis cases reported being uncomfortable when eating or swallowing. 91.2% of them were sensitive to hot or cold; 93,8% had a worse sense of taste and 87,5% had painful aching in the mouth. Periodontitis was associated with low serum albumin (OD=4,93, CI95%: 1,298-14,866, p =0,017) compared with individuals without periodontitis disease after adjustment for age, gender, diabetes, hypertension, body mass index, smoking, total

cholesterol, serum calcium, serum phosphorus. The serum CRP levels between the groups with or without periodontitis were no significantly different (OD=0,910, CI95%: **0,826-1,002, p=0,055).**

Conclusions: The results of the study showed that periodontal disease is prevalent, severe and under recognized in dialysis patients. Periodontitis was associated with low serum albumin level but we didn't found a positive correlation with CRP. This finding is probably due to uncomfortable eating. Althought highly prevalent it doesn't seems to be a great source of inflammation in end-stage renal disease patient on dialysis therapy.

THE CORRELATION BETWEEN THE CARDIO-VASCULAR RISK FACTORS AND DEEP VEIN THROMBOSIS IN PATIENTS TREATED AT THE CLINICAL HOSPITAL IN STIP

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Background: To determine the influence of cardio-vascular risk factors for deep vein thrombosis.

Methods: The following risk factors were examined In patients with deep vein thrombosis hospitalized and treated in the departments at the Clinical Hospital in Stip: arteriosclerotic risk factors, cigarette smoking, hypertension, dyslipidemia, physical inactivity, obesity and alcohol consumption.

Results: In total, 88 patients with deep vein thrombosis hospitalized and treated in the departments of the Clinical Hospital in Stip were followed during the period of five years (2006-2010). It was confirmed that 22 patients (25%) had higher glycaemia level, 18 (20.45%) had higher cholesterol or triglycerides, and 15 (17.04%) had higher body weight.

Conclusion: Cigarette smoking, hypertension, physical inactivity and alcohol consumption are not related with the risk of deep vein thrombosis. Diabetes, hyperlipidemia and higher body weight with physical inactivity are risk factors for deep vein thrombosis. There is a need for bigger vigilance and prophylaxis in patients with Diabetes mellitus, hyperlipidemia, higher body weight and physical inactivity in order to decrease the incidence of deep vein thrombosis.

CARDIOVASCULAR RISKS ASSOCIATED WITH FOOD SUPPLEMENTS CONSUMPTION IN ATHLETES

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A large number different in structure, origin and physiological action compounds determine diversity in the composition and the widespread use of food supplements in athletes. This study focuses on assessment of composition, possible interactions and cardiovascular risks, associated with consumption of proclaimed food supplements in athletes, on the basis of actual regulatory requirements and current scientific data – 27 publications in Scopus, PubMed, Dietary Supplements database US National Institutes of Health Office of Dietary Supplements, World Anti-Doping Agency (WADA) and FDA rapports during 2000 – 2010 period. The label's information of 43 food supplements, containing *Citrus aurantium* extract, Synephrine, Octopamine, Methylsynephrine, Hordenine, Phnethylamine , Beta- methylphenethylamine and methylxanthines available on Bulgarian market were evaluated according safety criteria.

The covered compounds and food supplements are popular among consumers due to their potential to optimize body composition, to improve physical performance, recovery process and psychostimulating activity. Besides their benefits, there is a serious risk for the health of consumers including cardiovascular adverse reactions when the production, distribution and administration of food supplements is not controlled or correct especially for those containing phenethylamines and methylxanthines in combinations or contaminated products. On the labels information of covered food supplements often are not clearly indicated contraindications, precautions, significant adverse reactions and interactions. In order to optimize control and provide updated information to the physicians and pharmacists it is very important to establish and maintain a database of food supplements with standards for data transfer.

ТАБЛЕТКИ ДИСПЕРГИРАЩИ СЕ В УСТАТА В ПЕДИАТРИЧНАТА ПРАКТИКА - ПРЕДИЗВИКАТЕЛСТВА И ПЕРСПЕКТИВИ

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Увод: Повишаването на регулаторните изисквания удължава времето за създаване и внедряване на иновации във фармацията и повишава стойността им. Този факт наред с намалената производителност, повишените изисквания на платците в здравеопазването и все по-сложната комуникация със специалистите, предписващи лекарствени продукти подлагат под съмнение ефективността на бизнес модела донесъл успехи на най-големите фармацевтични компании в края на миналия и началото на настоящия век. Всичко това действа като катализатор за развитие на нови системи за доставка на лекарства и внедряването им в нови пазарни продукти, както от страна на притежателите на изтичащи патенти, които виждат в тях възможности за повишаване на ефикасността на съществуващите продукти, увеличаване на одобрението на пациента към предписаната терапия и разширяване на патентната защита, така и от компаниите разработващи подобрения на базата на генеричното производство.

Наред с това нараства значението на продуктите предназначени за лечение на детската популация, като вниманието на експертите се насочва отвъд традиционните и добре развити сегменти, като детските противовъзпалителни средства, в посока на перспективни области като сърдечно-съдовите заболявания.

Резултати: Понастоящем в глобален мащаб се наблюдава липса на лекарствени форми, които са специално предназначени за приложение при пациенти в детска възраст, като този дефицит въздейства негативно върху тяхното здраве.

Разрастването на пазара на системи за доставка на лекарства се дължи до голяма степен на иновативни перорални форми като таблетките диспергиращи се в устата, които предлагат стабилността, точността при дозиране и удобството на твърдите перорални лекарствени форми и лекотата на приемане на течните лекарствени форми. Тази комбинация, е оценена високо, особено що се касае за пациенти в детска възраст.

Посредством използването на различни технологични подходи се постига усъвършенстване на лекарствената форма в следните направления: механична якост и разпадаемост; прикриване на неприятния вкус; приятно усещане в устната кухина; чувствителност към факторите на околната среда; цена.

Изводи: В съвременните условия постигането на положителни резултати са невъзможни без колаборация между бизнеса, фармацевтите в аптечната мрежа и академичната общност.

По отношение на таблетките диспергиращи се в устата, постигането на необходимия баланс между подходящите характеристики и цената на лекарствената форма налага търсенето на иновативни технологични решения и нови помощни вещества. Прилагането на последните при производството на детските лекарствени форми е свързано с редица ограничения. Един от подходите за тяхното преодоляване е използването на помощни вещества с натурален произход.

Наред с технологичното усъвършенстване, съществено значение за навлизането и утвърждаването на таблетките диспергиращи се в устата придобива и обучението на пациентите и здравните специалисти.

OXIDATIVE STRESS IN HEALTH AND DISEASE

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Background: Oxidative stress (OS) is a condition of free radicals (FR) overproduction accompanied with no sufficient antioxidative defense within many consequences such as accelerated aging and apoptosis, atherosclerosis, hypertension, chronic diseases like diabetes mellitus, autoimmunity, malignancy, etc.

The aim of this study was to examine OS in health conditions and in some chronic diseases.

Material and methods: A number of 185 healthy subjects and patients was included into the study. The healthy subjects (n=70) were divided regarding: age, young - 20-39 years old (n=35); middle aged - 40-59 years old (n=20); old - 60-79 years old (n=15); gender, male (n=38) and female (n=32); type of living conditions, from city (n=42) and from village (n=18); lifestyle habits: non smokers (n=20); smokers (n=18); and former smokers (n=14); and lipid profile, without dislipidemia (n=20) and with dislipidemia (n=10). All healthy subjects did not have any chronic or acute disease and did not take any medication. The examined patients were with end stage renal disease (ESRD) (n=85) and with diabetes mellitus (DM) (n=30) regarding their disease duration: <5 and ≥5 years. The examined patients on different substitution therapies were on: iron (n=10), erythropoietin (n=27) and L-carnitine (n=17). Lipid peroxidation (LP) method was used to clarify the OS level, using malonyldialdehyde (MDA) as its end product.

Results: Concerning the age in healthy subjects, LP increased from 3.3±0.9 μmol/l in young group, 3.91±0.8 μmol/l in middle aged and 3.94±0.9 μmol/l in the old group ($p<0.05$). No significant differences were noticed between gender groups of healthy subjects. Smokers showed higher level of LP, 4.3±1.3 μmol/l compared to non smokers, 3.42±0.9 μmol/l ($p<0.01$) but no significant difference with former smokers LP level was found. In subjects without dislipidemia LP level was lower, 3.57±0.7 μmol/l than in those with dislipidemia, 4.24±1.1 μmol/l ($p<0.05$). Average LP level in ESRD was 4.5±1.5 μmol/l which showed significant increase within disease duration ($p<0.05$). Average LP level in DM showed high value of 4.8±1.65 μmol/l but even higher value in the group of ≥5 years was considered ($p<0.05$). Patients showed changed LP level depending on supplementation therapy: 5.2±1.95 μmol/l with iron; 4.2±1.4 μmol/l with erythropoietin; and 4.1±1.5 μmol/l with L-carnitine ($p<0.05$).

Conclusion: These findings suggest that OS is present in older healthy subjects, preferably with smoking habit and impaired lipid profile, thus increases the risk of accelerated aging and disease appearance. Chronic diseases like ESRD and DM showed evident OS that might be changed under supplementation therapies, which may be useful biomarker of the disease evaluation and its prognosis, respectively.

HEALTH REFORMS AND FUNDING

ЗДРАВНИ РЕФОРМИ И ФИНАНСИРАНЕ

THE WORLD MEDICAL ASSOCIATION
Presented by Wonchat SUBHACHATURAS M.D.
President of the World Medical Association 2010-2011

Background and preliminary organization

During World War II, the BMA House had been the focal spot at which doctors of all the allied nations congregated from time to time to discuss problems of medical practice and peacetime and to compare the conditions of medical service and medical education in their respective countries. In July, 1945 an informal conference of doctors from several countries convened in London to initiate plans for an international medical organization to replace l'Association Professionnelle Internationale des Médecins", which having been organized in 1926 and having reached a maximum membership of 23 countries, had suspended operations with the advent of World War II. Accordingly, a second conference was held in London in September 1946. Medical associations of 31 countries were invited and 29 of them sent representatives. An Organizing Committee was appointed and directed to draft a Constitution, and plan for the First General Assembly. This Conference decided that the name of the new organization should be "The World Medical Association" and that it should have broader activities and wider membership than the former l'Association Professionnelle Internationale des Médecins. APIM officers attending the Conference agreed to dissolve the APIM in favor of the WMA, and generously turned over its remaining funds to the WMA.

Those named to the Organizing Committee were:

- Dr F. de Court, France
- Dr Pierre Glorieux, Belgium
- Dr Dag Knutson, Sweden
- Mr Otto Leuch, Switzerland
- Dr John A. Pridham, Great Britain
- Dr T. Clarence Routley, Canada
- Prof. I. Shawki Bey, Egypt
- Dr Lorenzo Garcia Tornel, Spain
- Dr A. Zahor, Czechoslovakia

The Conference further agreed that a provisional joint Secretariat should be established in London and Paris. Dr Charles Hill, Secretary of the BMA, was designated as the English Secretary, and Dr Paul Cibrie, Secretary of La Confédération des Syndicats Médicaux Français, as the French Secretary. Dr Otto Leuch was appointed as temporary Treasurer.

The second meeting of the Organizing Committee was held in Paris in November 1946. Further progress was made on the Constitution and Bylaws and it was decided to invite the American Medical Association to name one of its members to serve on the Organizing Committee. Dr Louis H. Bauer - the first Secretary General of the WMA - was named by the AMA to serve on the Committee, and Dr Elmer L. Anderson to serve a alternate.

The final draft of the Constitution and Bylaws was approved at the third meeting of the Organizing Committee held in London, April 1947, and plans were made to hold the First General Assembly in Paris, September 1947. The draft set dues at 20 Swiss centimes per member of the national medical association with a minimum subscription of 1,000 SFrs, and a maximum of 10,000.

The fourth and final meeting of the Organizing Committee was held in Paris 1946 the day before the convening of the General Assembly (September 18, 1947). The proposed Constitution and Bylaws was adopted on the first Assembly day with minor amendments. The meeting became the First General Assembly of the WMA, and 27 national medical associations represented became the founder member associations. These associations were:

- Federal Council of the BMA in Australia
- Osterreichische Arztekammer (Austria)
- Fédération Médicale Belge
- Canadian Medical Association
- Chinese Medical Association (dropped in 1952)
- Ustredni Jednota Ceskych Lekaru (ceased to exist in 1948)
- Den Almindelige Danske Laegeforening (Denmark)
- Medical Association of Eire (changed to Irish Medical Association)
- La Confédération des Syndicats Médicaux Français
- British Medical Association
- Association Médicale Panhellenique (Greece)
- Laeknafelga Islands (Iceland)
- Indian Medical Association
- Palestine Jewish Medical Association (later changed to Israel Medical Association in 1949)
- Federazione Nazionale degli Ordini dei Medici d'Italia
- Syndicats des Médecins du Grand Duché de Luxembourg
- Koninklijke Nederlandsche Maatschappij tot Bevordering der Geneeskunst (Netherlands)
- Den Norske Laegeforening (Norway)
- Palestine Arab Medical Association (ceased to exist in 1949)
- Naczelna Izby Lekarska (dropped in 1949)
- Medical Association of South Africa
- Colegio Oficial de Médicos de Espana

- Sveriges Lakarforbund (Sweden - Fédération des Médecins Suisses
- Turkish Medical Chamber (later replaced by the Union of Turkish Physicians)
- American Medical Association

Prof. Dr Eugène Marquis, France, was elected as the first President of WMA, Dr Jar. Stucklik, Czechoslovakia, was elected President-Elect, Dr Otto Leuch, Switzerland, was elected Treasurer, and Dr Charles Hill, UK, was elected as temporary Honorary Secretary. The first Council, composed of 10 members, was elected, and the World Medical Association was fully launched.

The Constitution, as adopted, provided, among other things, for membership of national medical associations fully representative of the medical profession in their countries or territories, but only one member association from each country. The General Assembly was vested with the general control of the policies and the affairs of the association, and was to meet annually in a different country. The executive body, the Council, was directed to administer the affairs of the association and report annually to the Assembly. The Council to consist of three elected officers, and ten members elected by the Assembly.English, French and Spanish were declared the official languages of the association, and a bulletin or journal was to be published and known as the official organ of the WMA.

In order to facilitate financial support from its member associations during a period when monetary exchange was restricted by many national governments, Switzerland and the USA were considered the most advantageous locations for the Headquarters Secretariat of the new association. In 1948, the executive board, known as the Council, established the Secretariat of the WMA in New York City in order to provide close liaison with the United Nations and its various agencies. Dr Louis H. Bauer was appointed as Secretary General. The WMA Secretariat remained in New York City until 1974 when for reasons of economy, and in order to operate within the vicinity of Geneva-based international organizations (WHO, ILO, ICN, ISSA, etc.) it was transferred to its present location in Ferney-Voltaire, France.

In July 1964 the WMA was incorporated as a non-profit educational and scientific organization under the laws of the State of New York, USA. This Incorporation established the legal and financial status of the WMA in the USA, with elected members of Council to serve as the Association's Board of Directors. It also made possible to obtain a tax-free status recognition on funds donated to the WMA and for donors of financial contributions. WMA's Incorporation was adopted at the XIXth World Medical Assembly held in London, UK, 1965.

The annual meeting of delegates was changed in 1962 to "World Medical Assembly" following revision of the Constitution and Bylaws at the XVIth General Assembly.

WMA Headquarters since foundation to 1974: NEW YORK CITY, USA

From 1975 to present: FERNEY-VOLTAIRE, FRANCE

What Does the WMA Do?

As an organization promoting the highest possible standards of medical ethics, the WMA provides ethical guidance to physicians through its Declarations, Resolutions and Statements. These also help to guide National Medical Associations, governments and international organizations throughout the world. The Declarations, Resolutions and Statements cover a wide range of subjects, including an International Code of Medical Ethics, the rights of patients, research on human subjects, care of the sick and wounded

in times of armed conflict, torture of prisoners, the use and abuse of drugs, family planning and pollution.

Other areas of service:

- Health-related human rights - promoting and defending the basic rights of patients and physicians
- Medical education - helping physicians to continuously improve their knowledge and skills
- Human resources planning for health care services
- Patient safety
- Public health policy and projects such as tobacco control, immunization
- Democracy building for new medical associations, especially in new or developing democracies
- Leadership and career development
- Advocacy for physicians' and patients' rights
- Occupational health and safety

What is the structure of the WMA?

The main decision-making body of the WMA is the General Assembly, which meets annually. The Assembly comprises delegations from the National Member Associations, the officers and members of the Council of the WMA, and representatives of the Associate Members (Associate Members are individual physicians who wish to join the WMA).

The Assembly elects the WMA Council every two years with representatives drawn from each of the six WMA regions, namely Africa, Asia, Europe, Latin America, North America and the Pacific.

The Chairperson of Council, elected by the WMA Council every two years, is the political head of the organization. The Ceremonial Head of the WMA is the President, elected annually by the Assembly. As Chief Executive of the operational units of the WMA, the Secretary-General is in full-time employment at the Secretariat, appointed by the WMA Council.

The WMA Secretariat is situated in Ferney-Voltaire, France, adjacent to the City of Geneva.

CASE STUDY: POSSIBLE DIRECTIONS OF FURTHER DEVELOPMENT OF THE HEALTHCARE LEGAL FRAMEWORK IN SERBIA

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Background: The health care system in Serbia in the 21st century is exposed to many challenges, which are reflected in the insecurity of the patient and the public, but also of the healthcare workers as well, especially physicians.On the other hand, the confidence in the management is fading away, especially with regard to jobs cutback. The physicians have lost their status of an elite group in the fifties, but also the decision-making status in the relationship with the government.

In the last years the physicians have been constantly exposed to public scrutiny and pressure, media hunt and pressure due to "mistakes", incompetency. On the other hand technology developments and knowledge explosion represent new challenges for the medical profession.

Legal security in the society means that the law is clearly defined in advance and applied precisely. Legal norms are obligatory codes of conduct defined by the constitution and laws adopted by the respective authority. In case of non-compliance with these norms, the government will apply sanctions.Legal aspects of health care are complex and refer to the statutory right, employment, rights and responsibilities, institutionalization, intellectual property, business law and also to the source of the rights.

The constitution of the Republic of Serbia refers to the rights as follows: the right to life, right to inviolability of physical and mental integrity, personal data protection, right to be informed, right to work, children's rights, right to health care, right to a healthy environment, freedom to give birth to a child.Health care is regulated by the Constitution, Article 68. "Everyone has the right to protect their own physical and mental health. Children, pregnant women, mothers during maternity leave, single parents with children up to seven years of age and elderly have the right to state-funded health insurance if not provided otherwise pursuant to the law.Health insurance, health care and health funds are stipulated by law.The Republic of Serbia is promoting the development of health and physical culture."

The Health law has its own set of regulations to regulate the following areas:
-health law basics
- functioning of the health care system and organizational structure of healthcare services in Serbia
- Health care providers
- Patients as health insurance holders
- Relationship between the healthcare workers and health services beneficiaries
- Responsibility of health workers
- Chambers of healthcare workers
- Provision of healthcare services - monitoring

The term medical law differs from the term health law

Conclusion: It is necessary to adopt a medical law that defines physicians as officials and it is necessary to define better the rights of the medical profession.
The process of adopting a law in the healthcare system plays an important role in the formation of a sustainable healthcare system in Serbia.

THE PORTUGUESE HEALTHCARE FINANCING SYSTEM

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Executive summary: The present abstract aims to present a summarized profile of the Portuguese Health Care Financing System while provides a description of the health system framework and policy initiatives, namely financial, in progress or under development.

The abstract is organized in three blocks with the following goals: 1) To describe the organization, financing and delivery of health services and the role of the main players in the Portuguese health system; 2) To highlight the evolution of major financial figures, challenges and constraints in financing the health system, and; 3) To present current trends financing in the Portuguese health care sector as whole, namely the public-private partnerships.

Introduction: The Portuguese population enjoys good health and increasing life expectancy, though at lower levels than other most-developed western European countries. All residents in Portugal have access to health care provided by the National Health Service (NHS), financed mainly through taxation, co-payments mechanism (which have been increasing over time), and also through co-insurance (remarkably higher for pharmaceutical products). Approximately a quarter of the population enjoys a second (or more) layer of health insurance coverage through health subsystems and voluntary health insurance (VHI). Health care delivery is based on public, social and private providers. Public provision is particularly present in primary care and hospital care, with a gatekeeping system in place for the former, Social provision (hospitals of religious charities called *Misericórdias)* focuses more on continuing care, while Private provision is present on both primary care and hospital care. Furthermore, pharmaceutical products, diagnostic technologies and private practice by physicians constitute the bulk of private health care provision.

The Portuguese health system has not undergone any major changes on the financing side since the early 1990s, despite the steady growth of public health expenditure. On the other hand, many political and public financial measures have been adopted to improve the performance of the health system. For instance, measures since 2002 have included: public–private partnerships (PPPs) for new hospitals; a change in NHS hospital management rules towards a more entrepreneurial approach and a more effective purchaser–provider split; promoting generic substitution of pharmaceuticals; liberalization of prices and entry onto the over-the-counter (OTC) market; administrative price reductions for pharmaceutical products; introduction of a reference pricing mechanism for pharmaceuticals facing competition from generics; regular updates of the co-payments for public health care services; reorganization of the public network of services (closure of delivery rooms in some hospitals, reshuffling of emergency departments, mergers of hospital management teams); definition of a national health plan; reform of primary care (creation of Family Health Units); and, creation of long-term care networks. Some of these measures have faced opposition from the (local) population, namely those related to the closure of health care facilities.

There is an overall awareness, and concern, about the rise in health care expenditure in Portugal. Most of the reforms undergone in the recent past are being evaluated at the time of writing this paper.

Organization and delivery of health services : The Portuguese health care system is not a "pure" (theoretically speaking) national health system once it is characterized by three coexisting systems: (i) the NHS; (ii) Health Subsystems (special public and private insurance schemes for certain professions); and (iii) Private Voluntary Health Insurance (VHI).

In practice, the Portuguese NHS guarantees the universal coverage of the population, but the State's role is decreasing as a provider and as financial source to guarantee a free of charge access to the NHS, which instead is being substituted by health care providers and VHI funding. So, generally speaking, the health system in Portugal is a network of, mostly, public and private health care providers, regulated and connected to the Ministry of Health. Moreover, there is a third entity in the system, the charity organizations, which act at a lower but increasing scale-level. So, on the supply side, the providers can be public, social or private, with different agreements with respect to their financing flows, ranging from historically based budgets to purely prospective payments.

Regarding the administrative structure of the NHS, we can organize it among several key players (not all):

a) Ministry of Health, whose responsibility is to develop the health policy, overseeing and evaluating its implementation. Furthermore, it is responsible of the regulation, planning and management of the NHS as a whole while also audits and inspects the private and social health care providers, regardless of their integration in the NHS.

   Under the Ministry of Health there are several other institutions under direct or indirect management whose activities are defined to support the entire role of the Ministry, as for instance, the General Directorate of Health that plans, regulates, directs, coordinates and supervises all health promotion, disease prevention and health care activities, institutions and services, whether or not they are integrated into the NHS.

b) Health subsystems, which are in practice, health insurance schemes for which membership is based on professional or occupational category. The health subsystems can be either public subsystems or private, depending on the entity that is financing the subsystem is public or private and can the health care can be provided either directly or by contract with private or public providers (and in some cases by a combination of both). Finally, the access is generally limited to beneficiaries of a specific profession and their families.

   Approximately 25% of the population is covered by the health subsystems or VHI. Where, approximately 16% of the population are covered by a health subsystem, approximately 10% are covered by VHI and less than 2% have cumulative coverage from both VHI and health subsystems.

c) Charity Organizations (Misericórdias) are independent non-profit-making institutions with a charitable background. These institutions currently operate very few hospitals, despite their historical role as one of the main providers of health care.

d) Private health care providers provide diagnostic, therapeutic and dental services as well as some ambulatory consultations, rehabilitation and psychiatric care services. And, they have a supplementary role to the NHS rather than being a full alternative to the NHS.
These private providers range from private health care groups, which have under their control private hospitals and ambulatory clinics, to private practitioners.
The private expenditure increased from 31% in 2000 to 33% in 2007, approximately 1/3 of the total expenditure is being provided by the private sector and is being increasing each year. This is mainly due to the incapacity of the NHS to respond to almost all medical appointments by the NHS' specialists and/or General Practitioners. And, of course, patients with less severe conditions and/or with the necessary financial means may opt for private practice specialists in ambulatory and/or hospital care, which explains their role and market share.

e) Private health insurance companies, which are one of the main private actors in the NHS and where people can benefit from an additional coverage, that is, from the NHS, a health subsystem from their job (either public or private) and finally through a Private Voluntary Health Insurance (VHI).
The VHI expenditure has been steadily increasing from 3,5% in 2000 to 4,7% in 2007 when compared to the total health expenditure.

f) Professional associations and unions whose three main representative ones are: 1) Medical Association; 2) the National Medical Federation; 3) the Independent Medical Union. On the first case, memberships in the Medical Association is mandatory for all practicing physicians, where its functions are: i) accreditation and granting of licenses to practice; ii) accreditation and certification of specialist training; iii) application of the disciplinary code, with powers to warn and punish doctors. Whereas, the unions (unions as in case 2) and in 3) role is to defend physicians' rights/interests as employees, mostly concerning wages and employment issues.

The following chart provides an overview of the Portuguese system, not only of the financial relationships between all players but also an overview of how are the interrelationships between these providers.

Major financial figures evolution, challenges and constraints in financing the health system: The Portuguese healthcare system is a combination of both private and public financing. The Portuguese NHS is generally financed through taxation while the Health subsystems are mainly financed by employees' monthly contributions (discounted on their salaries) whether the company is public or private. Moreover, there are private financing into the system materialized through co-payments and direct payments made by the patient when accedes to the NHS and, finally, the private insurance schemes which are volunteered payments to provide an extra health coverage. The next Table (Funding mix for the health system) shows the percentage of total health expenditure financed through public and private sources. Public expenditure, which represents 67% and comes mainly from taxation (over 90%), includes funding of direct care provision within the NHS and subsidies to the health subsystems for public sector employees. Private expenditure, which represents 33% and mainly includes OOP payments and VHI (28,7% and 5,1% of the total funding on health in 2008 respectively).

As a conclusion, one may state that the THE is increasing as a % of the GDP and the problem in Portugal as for many other European countries lays on how flexible and innovative funding schemes can be found in order to still provide a national and almost free public health coverage whilst the financial constraints, population ageing and new health technologies put pressure on the NHS's finances. Furthermore, the % of OOP and VHI of the THE will increase and we will assist of a divesture of the NHS while will assure health coverage through private-public partnerships whether by clinical services contracts, concessions or even management.

Current trends in financing the Portuguese health projects: Portugal has initiated a recent utilization of the Public-Private Partnerships in the health care sector due to the lack of public budget restrictions as well as due to the incapacity to manage the incoming hospital's projects.

There was a 2nd wave of PPP projects, although due to financial constraints and recurrent high public deficits, but was annulled.Generally speaking the PPP model used for the 1st wave is the DBFO (design, built, finance and operate) almost equal to the model used in Great-Britain but with two major differences: 1) the Portuguese PPP model doesn´t use a consortia in the form of *special purpose vehicles* (SPV) but instead the partnership contract is celebrated between two entities (one public and the other private or social), with defined contract terms, duration and financial budget payments and investment; 2) the Portuguese model includes the provision of health care services, namely clinical services.

Furthermore, in the Portuguese PPP model there is a separation between the management of the hospital infra-structure (HFM - hard facilities management) and between the management of the hospital itself as a health care provider (SFM - soft facilities management). The aim is to separate the risks and adequate the type of management to both societies involved in the PPP contract and to facilitate the process of negotiating and regulating the contract.

Concerning the PPP contract itself, the Portuguese Government aims to closely link the duration of the contract to the type of management. For instance, the HFM contract can be a maximum of 30 years (equal to the life expectancy of the hospital infra-structures) where the hard facilities are transferred to the State ownership at the end and, on the other hand, the SFM contract can last with a maximum of 10 years, to a maximum of three successive equal time extensions (a maximum of 30 years).

To sum up, the PPP model has fragilities and some virtues. Among the fragilities there is some ambiguity in the PPP contract definitions and lack of specific definitions (such as quality) to which clinical services are to be contracted – thus it is really difficult to evaluate the quality standards as well as to assure the necessary equity on health. On the other hand, there are some virtues, which can be summarized as: it aims to pay incentives to innovation and increases the contractual flexibility, where the contracts duration is adjusted accordingly to the services contracted and the demographic changes over the contractual time.

Conclusion: The Portuguese health system is organized around an NHS, which is managed by the Ministry of Health. Overlapping with the NHS are certain special public and private insurance schemes for certain professions (termed "health subsystems"), which are compulsory for groups of employees, and private VHI.

Total health expenditure (THE) in 2008, as a percentage of gross domestic product (GDP) was approximately 10 - public health expenditure has grown since the early

1990s. The Portuguese health system is primarily funded through taxation. Public sector funding as a percentage of total expenditure on health care fluctuates around 70%.
The Portuguese health system has not undergone any major changes in terms of financing, despite the steady growth of public health expenditure during the last two decades. Although, some measures were adopted in order to improve the performance of the health system. One of these measures have included: PPPs for new hospitals; a change in NHS hospital management rules towards a more entrepreneurial approach and a more effective purchaser–provider split; and so on.
Regarding the PPPs it is yet to be proved whether the Portuguese innovative PPP model will provide the necessary efficiency and quality of the "public" health care services. On the other hand, one may state, that considering time-consumption and cost-efficiency of the new hospitals facilities (Loures and Cascais) have been improved and saved up-front money and time to the Portuguese State.

APPROACHES TO REFORM THE SYSTEM OF PUBLIC HEALTH IN UKRAINE: CONCEPTUAL, SYSTEMATIC AND PROFESSIONALISM

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Over the past 20 years, each new government in Ukraine declared its intention to reform the system of public health. However, unfortunately, none of these intentions have not been implemented.

The system of public health in Ukraine continues to be in a deep systemic crisis. In Ukraine are among the lowest in Europe indices of health, a deep demographic crisis, high mortality, especially among men of working age, a crisis of medical personnel and specialists, is extremely outdated infrastructure of health facilities, a deep depreciation of medical equipment, high public dissatisfaction with medical care. All signs of the crisis deepened with each year increase.

One of the main factors of the annual deterioration in the system of public health of Ukraine is the monopolization of the management in this system. Management is entirely in state hands since the Soviet Union times. The main factors of inefficient public management in the system of public health is the management imbalance that is the absence of professional medical self-government. This complements such systemic flaws in Ukraine's system of public health as the absence of different sources of funding and compulsory state social medical insurance, inconsistency in the actions and lack of real political will and vision in state rulers the ways changes in the system of public health, is not predictable medical personnel policy, lack of motivation of health personnel to provide quality services, lack of modern information provision of the system of public health, ignoring the views of non-government sector about reforms etc. Reliance by the state rulers on the existing Ministry of Health as the chief reformer of the system of public health leads not only to the absence of real change for the better, but also to deepen the existing crisis.

For the success of future reforms in the system of public health in Ukraine, we offer the following successive the systems steps:

- establish a temporary (up to 3-4 years) the separate central state executive body for the development and implementation of public health reform which has the status and powers of a separate ministry ("the Ministry of reforms");
- "the Ministry of reforms" necessarily well be provide participation of all partners (medical, scientific and patient associations, lawyers of medical law, experts and consultants from leading European countries, journalists, financiers, etc.) in the developing a new system of public health;
- during the election the new Parliament of Ukraine forming a powerful medical lobby for legislative support of the proposed reforms and adoption of necessary new laws;
- develop a new version of the basic medical laws and pass new laws, to adopt new programs of the system of public health on the level of the laws;
- learning of a new personnel of health management.

In the proposed new laws, regulations and resolutions of the Cabinet of Ministers of Ukraine and Ministry of Health of Ukraine, provide in particular:
- implementation status of the physician as the subject of law;
- transition to contractual relationships between health care providers, their managers and specialists;
- ensure the existence of a unique medical space through provide management functions in new system of public health for professional organizations of doctors and pharmacists.

It is necessary to conduct a broad public discussion, explanation and popularization of all steps in the formation of a new system of public health. Obligatory to obtain a positive result is a public and professional support this reforms.

As a result, after agreeing with each other and with all existing laws to organize accepted the new legislation in the Parliament of Ukraine - in the form of special session of health.

After this "the Ministry of reform" as a body which has fulfilled his task, disband. And existing the Ministry of Health convert a ministry with new functions and powers.Other ways to reforms of the Ukrainian medicine well be unproductive.

BULGARIAN PHARMACEUTICAL UNION VISION ON NATIONAL DRUG POLICY

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Introduction: The pharmaceutical industry is one of the driving engines of gross domestic product and value added tax worldwide. In Bulgaria the impact of commercial interests in the past years can be strongly felt both on public-media level and in the implemented governmental regulatory policy. Consequently, certain unfavorable tendencies are formed like liberalization, lack of control, sale of drugs from unauthorized premises, online sale of forbidden in Bulgaria drugs, creation of vertical and horizontal integration in particular segments of production/wholesale/retail, reduction of retailers' income and creation of favorable conditions for retailers' monopoly among others. In such an environment, after more than 20 years as of the start of democratic changes, in 2011 the first steps towards development of National Drug Policy (NDP) in Bulgaria have been implemented.

Method: A variety of Bulgarian legislative acts (statutes and regulations) as well as of World Health Organization (WHO) guideline for development and implementation of NDP and of other countries' methods of implementation of National Drug Policies has been analyzed. The attempted implementation of NDP in Bulgaria has also been presented in the perspective of the lack of such policy till the present moment.

Results: WHO develops drug programs since its establishment in 1948. The resolution of the World Health Assembly (WHA 47.13/1994) in 1994 outlines four key elements whose development should grant better access to quality medications to the population. One of those elements is development of NDP. Every nation should implement its own drug policy bearing in mind its specific political and economic conditions, problems and abilities. The choice of drug policy reflects the nation's social value and culture.

The analysis of the implemented National Drug Policies of developed countries indicates that such a policy is developed in a wide range as a consensus document by all interested parties and its elements are provided and analyzed. The development of NDP is a process that requires a lot of responsibility and lack of such a policy also indicates certain degree of responsibility as in Bulgaria this led to the consolidation of retailers, the existence of vertical structures of manufacturers (importers)/wholesalers/retailers, the sale of drugs in beauty shops, the aggressive promotion of certain drugs, the lack of qualified pharmaceutical help, restricted access to drugs in the scarcely populated regions and so on.

An objective approach to the elaboration of NDP has been used in the formation of work groups in the spring of this year. This approach follows the positive legislation in the Law on Human Medicines and the Health Law. The above-said, however, does not correspond to worldwide recognized standards for development of NDP. On the contrary, after the development of the basic elements of NDP, which represents a fundamental act for the regulation of the sector for a period of 10 to 30 years, the next step is to start preparation of relevant legislation which is only one element of NDP that follows the rest logically. The work groups are not backed by data from the healthcare system that can help them make relevant analysis in order to improve processes effectively. Days before the formation of the work groups, without public discussion and outside of the thus publicly developed concept of drug policy, the Ministry of Health introduced Bill on Human Medicines which directly affects the National Drug Policy but which was not discussed by the work groups for development of NDP.

Conclusion: The development of NDP in Bulgaria has been initiated spontaneously and lacks basic and mandatory elements like methodology of development of concept, time limit, and allocation in temporal terms of the different structures, anticipated results and documents which should be prepared. The body of the formed working groups is composed of nongovernmental organizations without clearly defined representative functions and which directly protect interests of corporative stakeholders, wholesalers and retailers. Thus, regulators effort to meet public expectations is not adequate step toward the enactment of NDP with regards requirements of WHO and practice of the developed counties.

PATIENT SAFETY AND MEDICAL ERRORS

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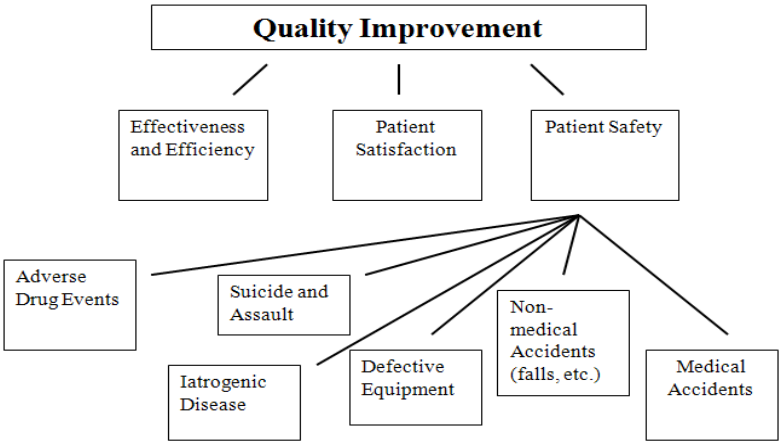
President of Macedonian Medical Association and
Vice President of SEEMF

In each country there are shocking cases of wrongly made operations (amputated the wrong leg, operated healthy hip, removed healthy kidney, eye, in patient with infertility performed hysterectomy etc). In industrialized countries nearly half all adverse in hospitalized patients are related to surgical care. At least half of the cases in which surgery led to harm are considered to be preventable. Almost half of surgery led to harm are considered to be preventable.

Those shocking cases are not merely isolated incidents. According to the U.S. Institute Medicine (IOM), at least 44,000 people die every year in U.S. hospitals from medical errors that were preventable. Therefore, in the USA, more people die from medical errors than from car accidents, breast cancer, or AIDS.

Having in mind that Patient Safety is a real big global problem, WHO in October 2004, launched the World Alliance for Patient Safety in response to a World Health Assembly Resolution (2002) urging WHO and Member States to pay the the closest possible attention to the problem of patient safety. The patient safety is in close relation with quality improvement.



Patient Safety is more than merely preventing medical errors in diagnosis or treatment. In fact, the most common problems of patient safety are not medical errors in diagnosis or medical errors in surgery. Rather, the most common problems of patient safety are adverse drug events and wound infections. Who is demanding improvements in patient safety? Government agencies, accreditation organizations (JCAHO), health insurance companies and employers, patients, doctors and other healthcare professionals. A case study in improving patient safety: anesthesia,. In the 1970's and

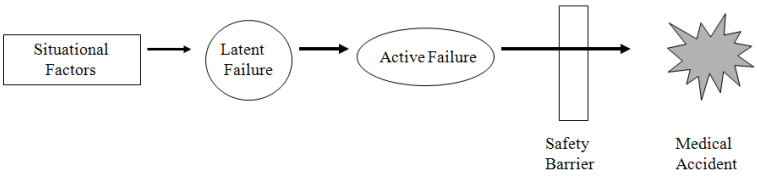
1980's, about 1 in 10,000 patients died from surgical anesthesia in the USA. Anesthesiologist had high premiums for malpractice insurance and bad publicity on television about preventable deaths. After about 10 years, the mortality rate from anesthesia was reduced to only 1 in 200,000 patients.

How to improved patient safety and reduce medical errors. We need to accept the fact that human beings will make mistakes. We cannot prevent errors by trying to prevent people from making mistakes. Therefore, the way to improve patient safety is to change systems and procedures, so that those human mistakes do not cause harm to the patients.

How was anesthesia made safer for surgical patients? In 1983, the American Society of Anesthesiologists (ASA) began a safety campaign. Medical records and malpractice claims indicated that many anesthesia injuries were caused by human error. The system for delivering anesthesia was improved so that human errors and mechanical failures do not cause harm. How was the system for anesthesia improved to prevent harm? The ASA adopted mandatory standards for patient monitoring and safety. Practice guidelines were issued. Equipment was redesigned, including standardization and safety devices. The hours of work for medical residents were reduced. These system improvements were successful in preventing harm. In a period of about 10 years, the mortality rate for anesthesia was reduced from 1 in 10,000 to only 1 in 200,000. Today, anesthesia is considered very reliable and very safe. This example proves that patient safety can be improved by changing the systems for delivering care.

Methods of analyzing and improving healthcare systems. Investigate ,,sentinel events,, that give a warning about a problem. Conduct a ,,root cause analysis,, to determine the basic reason for the failure: begin with the adverse event , look back in time, identify each event in the chain of causation, ask ,,why,, each event occurred, ask ,,how,, each of the errors led injured.

Analyze the *"accident trajectory"* to find the root cause (the system failure)



Source: Spath PL, "Error Reduction in Health Care" (2000), at 113.

What is an ,,active failure,,? An active failure is an error by an individual operator, such as a doctor or nurse, who perform healthcare processes. For example: picking up the wrong medication or the wrong blood, failing to confirm that the medication or blood was intended for that particular patient. What is a ,,latent failure,,? A latent failure is a fault in system of care that creates a potential for an active failure. For example: poorly designed procedures for preparing medications or distributing blood. Lack of rules about the minimum qualifications to perform particular tasks. What is a *"situational factor"*? A situational factor is an unfortunate or unlucky circumstance

which can activate a latent failure. For example: distraction of a doctor or nurse by another person or by a phone call, two patients in the hospital at the same time who have the same name or similar names. What is a *"safety barrier"*? A safety barrier is a defense that prevents an operator from making an active failure or prevents an active failure from causing harm. For example: A hospital's requirement that nurses re-confirm a patient's identity before administering a drug or a blood transfusion (an administrative barrier)ECG equipment is designed so that its electrodes cannot be plugged into the primary electrical power supply (a technical barrier). WHO Surgical Safety Checklist. How do these factors interact with each other to cause harm? Latent failures can exist for a long time without causing an accident. Then, a situational factor "activates" a latent failure. That latent failure contributes to an active failure and might even combine with other latent failures. Safety barriers fail at "just the wrong time."

Preventing future accidents by using "*anticipatory failure analysis*" In addition to looking *backward* to find the "root cause" of an accident, healthcare organizations can look *forward* to fix latent problems before they cause harm. Analyze the processes of delivering care to determine how an accident might occur. For example, in Failure Mode and Effect Analysis (FMEA), make a diagram of the processes, and ask "what if" any part fails.

Specific ways to improve patient safety and prevent medical errors several agencies and organizations have developed lists of specific ways to improve patient safety and prevent medical errors. A "patient safety solution" is defined as "any system design or intervention that has demonstrated the ability to prevent or mitigate patient harm stemming from the processes of health care. "

The "Ten Lifesaving Patient Safety Solutions" deal with these issues: Look-Alike, Sound-Alike Medication Names, Patient Identification, Communication During Patient Hand-Overs, Performance of Correct Procedure at Correct Body Site, Control of Concentrated Electrolyte Solutions, Assuring Medication Accuracy at Transitions in Care, Avoiding Catheter and Tubing Mis-Connections, Single Use of Injection Devices, Improved Hand Hygiene to Prevent Health Care-Associated Infection (HAI). Organize a team of health –care professionals working to gather within a supportive health system.

How to handle medical errors when they occur. Hospitals should have a *written* policy on adverse event response, including these steps: First, prevent further harm to the injured patient, Then, collect and save the drugs, equipment, and records that were involved in the incident, investigate and get all of the relevant information, perform a "*root cause analysis*", make the appropriate internal and external reports. Inform the patient and the family. First, prevent any further harm to that patient or to any other patient. The first duty of the doctor and hospital is to prevent additional harm to the injured patient by: stabilizing the patient, providing the necessary care, mitigating (limiting) the effects of the injury. Also, remove any remaining threat to any other patients, such as threats from: defective equipment, a healthcare worker who is impaired, an unsafe procedure in the system of care. Make the appropriate internal and external reports. Internally, the adverse event should be reported to the appropriate persons and departments within the healthcare facility, including: supervisors, facility administration, risk management department

Externally, laws might require the facility to make reports to specific government agencies. Also, the healthcare facility should notify its malpractice

insurance company. Notifying the patient and the family. According to many experts in medical ethics, doctors have an ethical duty to: disclose their errors to the patient; and apologize to the patient.

Research indicates that patients want to be informed about errors that affected their care. There is no persuasive evidence that apologizing will make the patient more likely to sue the doctor or hospital, Failure to communicate and apologize might make the patient angry and more likely to sue.

Work for continuous quality. improvement (CQI). Develop an organizational culture for quality of care. Use incentives for quality. A case study of successful quality improvement: cardiac care randomized trials were performed to determine the "best practices" for patients with acute coronary syndromes (ACS). Based on that data, medical professional organizations developed practice guidelines for treatment of ACS patients. However, many hospitals and doctors in practice did not follow the guidelines. How could hospitals and doctors be encouraged to follow guidelines? The Joint Commission (JCAHO) required hospitals to report their performance on quality measures, including cardiac care. Those reports on quality measures made it possible to compare different hospitals, and some data was available to the public. Performance measurement encouraged hospitals and doctors to improve. The result: cardiac care for ACS patients has significantly improved.

A recent study (May 2, 2007) shows significant improvements in clinical practice for ACS from 1999 to 2006.Now, more doctors use evidence-based treatments (both pharmacological and interventional treatments). These changes in clinical practice have improved clinical outcomes (such as fewer patients with ACS dying in the hospital). "*what receives attention gets improved*"! A recent report on quality was issued in July of 2008 by The Commonwealth Fund Commission on a High Performance Health System. According to that report, "all of the quality indicators showing significant improvement have been targets of national and collaborative efforts to improve, informed by data with measurable benchmarks and indicators reached by consensus.

Viewing quality improvement from the *facility* perspective. Also, we will consider the perspective of the hospital or other healthcare facility From this perspective, we are concerned about: Improving quality within the organization. Reducing variation among different parts of the organization. Comparing the performance of doctors within the organization. Measuring patient outcomes within the organization.

The quality problem in healthcare. Defining the terms , understanding the relationships, analyzing the causes of the problem How do we mean by "quality"? The Joint Commission (JCAHO) defines quality of care as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge."According to the U.S. Institute of Medicine, health care should be: Safe, Effective, Patient-centered, Timely, Efficient, Equitable.

According to Donabedian, there are 3 ways to evaluate quality of care. Structure (Does the organization have the necessary resources to provide adequate care?). Process (Do the healthcare professionals in that organization perform in accordance with accepted standards of practice?) Outcome (How the patients' conditions have changed after the treatment?) Quality improvement is *more than* patient

safety and preventing errors. Patient safety is only one aspect of quality improvement. Preventing medical errors is only one part of patient safety.

How to improve quality in healthcare organizations. The systems approach; Continuous Quality Improvement (CQI); developing an Organizational Culture for quality of care; financial incentives for quality. The systems approach to improving healthcare quality. This approach is based on improving a facility's *system* for delivering care.

Continuous quality improvement (CQI). CQI is a systems approach to improving quality, which is used in many hospitals, It is based on concepts developed for improving industrial processes, In general, CQI includes: focus on the facility's mission and values, use of internal Process Improvement Teams, use of data and evidence to make decisions.

In the USA, hospitals are required to have quality improvement programs. Hospitals accredited by the Joint Commission (JCAHO) are required to: meet standards on improving performance; implement a program to reduce adverse events and safety risks Non-accredited hospitals that want to participate in the federal Medicare program are also required to implement a program of quality assessment and performance improvement. China has similar requirements for quality improvement and safety China's Regulation on the Handling of Medical Accidents (2002) requires hospitals to: establish departments for quality control or arrange for persons to be responsible for that function, educate their staff members about legal requirements, standards of medical care, and professional ethics , develop plans to prevent medical accidents and limit the effects of injuries.

Developing an organizational culture for quality of care. Healthcare organizations need to develop a culture of quality. A culture of quality requires commitment by the management and cooperation by the workers.. It requires a system for workers to report problems, without fear of retaliation. It also requires efforts to control disruptive behavior (such as disruptive doctors).

How to evaluate an organization's culture for quality of care. Does the top management really care about providing high quality care? Is quality improvement considered in every employee's annual review and salary review? Are employees encouraged to report problems and potential problems in the facility? Can employees report problems without giving their names? Are individual employees blamed and punished when something goes wrong? Relationship between cost and quality Spending more money does <u>not</u> necessarily lead to better quality of care, But, good quality of care does <u>not</u> necessarily cost more money than bad quality of care.

International perspective on quality improvement, Additional issues of healthcare quality in developing and transitional countries. Actions by WHO for quality improvement and patient safety, Other international efforts to improve the quality of care. Other quality issues in developing and transitional countries. Many countries have wide variations in the training of their doctors and other healthcare professionals. Some are highly trained and highly skilled. Others have much less training and skill. Many countries do not have an effective system of government regulation and licensing of healthcare professionals.

WHO recognizes serious quality problems in developing countries. Poor quality of buildings and equipment. Supply of drugs is unreliable, with problems of

quality and counterfeiting. Low level of infection control and management of wastes, personnel problems, under-funding of healthcare costs.

Therefore, WHO created a "World Alliance for Patient Safety" The World Alliance for Patient Safety develops "Global Patient Safety Challenges" for action in each 2-year cycle, the first "challenge" for 2005-2006 was healthcare-associated infection ("Clean Care is Safer Care."), The second "challenge" is safer surgery ("Safe Surgery Saves Lives"), including the WHO Safe Surgery Checklist.

In Conclusion we can say: Conclusion 1 Patient safety can be improved and errors can be reduced. We need to accept the fact that human beings will make mistakes. We cannot prevent errors by trying to prevent people from making mistakes. Therefore, the way to improve patient safety is to change systems and procedures, so that those human mistakes do not cause harm to the patients. Conclusion 2: Quality in Healthcare Organizations Can be Improved by using the systems approach. Problems in quality are *not* caused by bad people or careless people, Rather, problems are caused by defects in the system for providing care, Therefore, do not blame individual doctors or healthcare workers for poor quality, Instead, fix the system for delivering care. Err is human est. Only God does not make errors, but humans can elaborate systems to prevent the errors as much as possible and to alleviate and mitigate the consequences.

VIENNA RESOLUTION OF THE EUROPEAN MEDICAL STUDENTS' ASSOCIATION

Elif Keles
European Medical Organizations Liasion Officer 2010-2011
European Medical Students' Association

European Medical Students' Council Resolution is called Vienna Resolution and is a policy statement about the "Future of European Healthcare", written in 2010. In this paper, we deal with the development of high common healthcare standards in Europe, the shortage of healthcare professionals, especially in rural areas ("Access to healthcare") and the intra-European mobility of healthcare professionals ("Mobility"). The EMS Council aims to give voice to the medical students in geographical Europe and does so by organizing an annual conference whose members express the results of their discussions in a policy paper on European healthcare matters. The theme of the 2010 conference was "The Future of European Healthcare", where we as future doctors intended to contribute to a better European healthcare. We would like to participate as a stakeholder in the discussion about the future of European health and healthcare with the help of our resolution.

Preamble

The European Medical Students' Council 2010 in Vienna,

- Intending to contribute to a better European Healthcare,
- Wishing to participate as a stakeholder in the discussion about the future of European health and healthcare,
- Strongly supporting the common values as defined by the European Ministers of Healthy (universality, access to good quality care, equity and solidarity) and adding integrity, transparency and confidentiality,

- Emphasising the importance of healthcare workers within the European society,
- Acknowledging current public priority to increase international collaboration and sharing of knowledge on improvement of healthcare,
- Observing the increasing complexity of healthcare and the changing roles of healthcare professionals,
- Taking into account the changing European demographics, the increasingly mobile workforce, the changing demands of society, technological development and the increasing costs of healthcare,
- Taking into account workforce migration which affects the accessibility of healthcare in rural areas,
- Building upon current European statements with regards to healthcare as well as related policy papers and scientific literature,
- Appreciating the efforts of all stakeholders in this field, from policy makers, through healthcare workers to patients,
- Expressing our belief that leadership skills are essential when dealing with patients as well as other stakeholders,
- Affirming the importance of the continuous development of Lifelong Learning strategies,
- Convinced that organizations providing healthcare must evolve into learning organizations1 in order to increase the quality of care,
- Keeping in mind that all our endeavours should be patient-centered, while taking into account their impact on society
- Contributing to a vision of the future of European healthcare, the European Medical Students' Council,
- Calls for attention to the topics of access to healthcare and mobility of students and healthcare workers,

ЗДРАВНОТО ЗАКОНОТВОРЧЕСТВО – МЕЖДУ ПРИОРИТЕТИТЕ И ПСЕВДОПРИОРИТЕТИТЕ

Проф. Веселин Борисов,
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Нарастващата и решаваща роля на приоритетите в провеждането на здравни реформи се признава от здравните политици в целия свят.
Ходът на съвременните здравни реформи показа категорично, че колкото по-ограничени са ресурсите на една национална здравна система, толкова по-належащо е да се спазва водещия стратегически принцип за УПРАВЛЕНИЕ ЧРЕЗ ПРИОРИТЕТИ.

В условията на ограничени ресурси за здравеопазването здравният мениджмънт е изправен пред решаването на следните неотменими проблеми:

- Всяка здравна организация да обосновава пределно ясни цели. Не цели въобще, а преориентация към високо приоритетни цели. Постигането на такива цели гарантира резултати с висока значимост.

- Здравната организация ще получава ресурси, строго адекватни на определените приоритети и ще разпределя и изразходва тези ресурси чрез бекомпромисен приоритетен принцип.
- Водещ критерий за оценка ефективността на всяка здравна организация ще бъде постигането на приоритетните цели.

За съжаление, както показват анализите, ресурсите в здравеопазването се разпределят и изразходват не по приоритети, а под натиска на моментните потребности.

Преобладаваща част от досегашните здравно-политически решения, намерили отражение и в законовата база, са фрагментирани, с вътрешни логически противоречия и без ясен фокус към конкретни приоритети. Многобройните здравни закони са изолирани един от друг, всеки е приеман сам за себе си, без единна концепция и национални здравни приоритети.

Нагледна илюстрация за липсата на приоритети или подмяната на приоритети с псевдоприоритети е практиката на клиничните пътеки. Със своята неприоритетна хаотична структура клиничните пътеки стимулират формализма и непрофесионализма в ежедневната медицинска дейност, изразяващи се в такива феномени като свръххоспитализация, документални фалшификации, доминиране на инвазивните и оперативни дейности, при силно подценяване на рехабилитацията и продължителното лечение.

Догматичният пазарен механизъм и необузданата *комерсиализация* на медицинската дейност са трудно преодолима бариера за приоритетния подход. Липсват целеви ресурси и конкретна система дейност за здравето на учениците и подрастващите, а в същото време лавинообразно нараства броят на всевъзможни нови и нови лечебни заведения, клинични лаборатории и други със съмнителна акредитация, но получили гарантиран достъп до публичните ресурси чрез договори с НЗОК.

Доминирането на затвореното технологично и икономическо мислене над здравно-политическото и медико-етичното мислене поставя тежки проблеми при избора на приоритети. В една концепция за приоритети винаги стои въпросът за скалата на ценностите, чрез тях и за етичните правила и отговорности, за етичния избор (проф. С. Попова).

За обективно и обосновано определяне на приоритетите е нужна разнообразна информация - епидемиологична, социално-медицинска, демографска, социологическа, икономическа и др. За съжаление, подобна комплексна информация почти липсва в официалните данни за здравеопазването. Практическата реализация на здравните приоритети изисква постоянен баланс на националната и регионалната здравна политика.

Адекватното определяне на здравните приоритети изисква интегрирането на четири критерия, отразяващи степента на нужното (потребности), възможното (ресурси), желаното (търсене, очаквания) и реално полезното (доказана ефективност).

Здравните приоритети не са неизменни, а са динамична подвижна величина във времето и пространството. Тяхната динамика трябва постоянно да се анализира, преценява и съобразява от стратегическия мениджмънт на националната здравна система.

PATIENT'S SATISISFACTION FROM THEIR PERSONAL DOCTOR IN HEALTH CARE ORGANIZATIONS

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Patient satisfaction is an important measure of quality of care. Patient satisfaction with personal physicians was studied within the "Analysis of transition of the health system in Macedonia."

Objectives. The purpose of this study was to investigate patient satisfaction with personal physicians exhaustive evaluation of some behavioral characteristics of the physician. The specific objectives of this study is to determine whether there are differences in assessment of patient satisfaction with physician behavior in terms of some characteristics of the respondents sociodemografski.

Methods: The study group consisted of 1000 respondents: 470 (47%) men and 530 (53%) women. Medical students interviewed the respondents' face-to-face "after consultation with the doctor. The anonymous questionnaire is provided responses to 10 questions on patient satisfaction. Sociodemografics results features were also provided answers and reasons for meeting participants.

Results. The average positive rating over 10 questions on patient satisfaction was 85.3%. There was a statistically significant difference in age distribution between geographic areas ($p < 0.001$). Differences in responses were found in terms of gender, age, education level ($p < 0.001$), and the reason for encounter ($P < 0.01$). Two factors were obtained by analyzing factors: the first could be called a doctor's competence / expertise estimated by respondents, and empathy by the physician respondents. Respondents were divided into two groups based on the reason for the meeting as a criterion for diskriminanten analysis: acute (symptoms and complaints, injuries; $n = 456$) and other reasons ($n = 544$). The discriminant function was obtained statistically significant ($P < 0.01$). Younger respondents, regardless of sex, whose reason for encounter was an acute condition, are less satisfied with the expertise of the doctor, consent during consultations, the interests of the physician or physician style.

Conclusion: Given the present difficulties in the health systems of countries in transition, the results of our study were surprisingly encouraging, showing that respondents are satisfied with the conduct of the doctor and that doctors meet the basic elements of professional behavior.

Key words: family practice, patient satisfaction, physician behavior.

MISCELLANEOUS

РАЗНИ

DYSLEXIA –STUDY OF CASE

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Dyslexia is not a disease, that is a lingual founded disorder with constitutional genesis that is manifested with difficulties in coding respective words, and which is usually expressed in a lack of the ability of the phonological processing. The difficulties in the decoding of a respective words are result of the common developing and sensor difficulties. According Orton Dyslexia Society, the dyslexia is defines as one of the difficulties in studying. What describes the dyslexia in a closer sense are the speed and the accuracy while reading. Usually the dyslexia is followed by dysgraphy – disturbances in writing. For the children with dyslexia reading is difficult, hard to be understood and it is a big problem for them because of which they feel tired and fail. Gradually that passes into frustration from the school and personal dissatisfaction. Basic symptoms of the dyslexia are: not recognizing or mixing of the graphemes / letters, difficulties when associating two letters (passing from consonant to vowel and vice versa), skipping letters in words, consonant groups, small- functional words, difficulties when reading words with more syllables, changing of vowels with vowels, changing of consonants by form, by sound, irregular orientation in space – inversion of the syllables, of the numbers, of the words, irregular rate – speed, depending of the age and understanding, disorder at keeping the line when reading, destruction of the understanding (he/she doesn't understand the content), disorder of logical reading with an appropriate intonation and accent.

The aim of the work is through the study of a case at a student with diagnosed dyslexia, the dyslexia to be presented from a medical aspect, the importance of the natural biological mature resources and the plasticity of the brain in the childhood. A sample of dyslexia is given from an educative and logopedical aspect through accenting the importance of the team work of the teacher, the parent and the logopedist for outdoing the state.

In the study of a case are given the results from the following assesses made: an Assess of knowing the parts of his/her own body, an Assess of imitation of complicated movements, an Assess of the dominant lateralization, an Assess of knowing the lateralization of himself/herself and another person, an Assess of the control of the motority while being still (Subiran), an Assess of the reproduction of the rhythmical structures, an Assess of the reproduction of the rhythmical structures, an Assess of perception of the relations in the space and the presented space, an Assess of the conscious functions, an Assess of the reading ability with a " test based of the difficulty of the text "(Kostic, Vladisavljevic), an Assess for the reading ability with a " Three-dimensional reading test". In the presentation are presented the results of the medical examinations and an assess made, defectological – logopedical assess, participative observations and assesses by the teacher. The structure and the principle of the logopedical treatment and the achieved results regarding the improving of the skills of reading is presented, decoding or encoding the graphemes / letters and their connection in words and sentences, overcoming the meaning of the punctuation marks

that make limit inside or between the sentences and with that they make it possible the meaning and making a text of a chain of words to be discovered, improving of the lingual meaning , knowledge of the words, the forms and the relations inside the sentence. Also giving an opportunity to the student with dyslexia a passage from the treatment of decoding of the graphemes / the letters to the treatment of understanding and thinking while reading, that will mark the beginning of the real reading, as well as decreasing and extirpation of the resistance to the reading with which the success in studying is increased, the conscience for his/her own abilities and the self-confidence is increased , as a base for health psychological development of the child.

Key words: dyslexia, logopedist, teacher, treatment

ЛЕКАРСТВЕНИ ФОРМИ С ИЗМЕНЕНО ОСВОБОЖДАВАНЕ В СЪВРЕМЕННАТА ПРАКТИКА

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При лечението на много състояния, идеалния дозов режим е този, при който приетото лекарство достига бързо терапевтичната концентрация и тя се запазва постаянна по време на целия период на приемане на лекарството(лечението). При приемане на една конвенционална форма, за да се поддържа необходимата терапевтична доза, се налага да се повтаря приемането на нова доза след недълъг период от време. Това създава неудобства за пациента и има редица недостатъци. Те могат да се отстранят с лекарствените форми с изменено освобождаване. Лекарствени вещества с продължително действие и лекарствени форми с удължено действие – принципна разлика .

Класификация на системите със забавено освобождаване на базата на кинетиката на освобождаване:
забавено освобождаване, повтарящо се освобождаване, удължено освобождаване, продължително освобождаване, контролирано освобождаване, поддържащо действие, изменено освобождаване и др.

Дизайн на перорални форми с модифицирано освобождаване. Физиология на гастроинтестиналния тракт и резорбция на лекарствата. Биологични фактори, влияещи върху резорбцията. Избор на лекарствена форма. Технологични подходи за удължаване действието на лекарствата при създзаване на : физични и химични системи. Фактори, влияещи върху дизайна на лекарствени форми.Механизъм на освобождаване на лекарственото вещество. Дифузионно контролирани системи - резервоарни и матрични системи. Хидрогелни монолити. Биоразграждащи (биоерозиращи системи).Осмотично контролирани и хидростатично контролирани системи.Микросфери и микрокапсули.Таргетинг – системи. Липозоми, продръгс, наноносители на лекарствени вещества.

LOCALIZATION OF THE CB1 TYPE CANNABINOID RECEPTOR IN IN RAT'S AMYGDALA AFTER IMMOBILIZATION STRESS. IMMUNOCYTOCHEMICAL STUDY

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The distribution of CBl cannabinoid receptors in the amygdala of immobilized and icontrol rats has been studied by means of irnmunocytochemical technique. The immobilization was found to modify the pain sensitivity. The nociception was measured by means of the paw pressure test. The endocannabinoid system plays a role in the regulation of synaptic transmission in stress-responsive neural circuits.

Endocannabinoids are signaling molecules in the nervous system that are recruited about the activation of G-protein-coupled receptors such as CB1. To elucidate the possible regulatory role of CB1 receptors in responsive neural circuits animals were exposed to acute immobilization stress.

Morphometric analysis revealed that immobilization stress exposure increased the density of CB1 receptors in the amygdale comparing with control rats. These data provide insights into the roles of the amygdala in the descending pain modulation system involved in the behavioral responses and synaptic effects typical of stress.

CB1 CANNABINOID RECEPTORS IN RAT'S STRIATUM AFTER IMMOBILIZATION STRESS

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The expression of CB1 cannabinoid receptors in striatum during exposure to stressful acute immobilization has been examined by means of the immunocytochemical technique. Striatum is an important neuronal network area of a descending analgesic pathway. The nociception was measured by the paw pressure test. The immobilization of the rats increased the pain threshold. The stress exposure alters endocannabinoid level and CB1 cannabinoid receptor-mediated control of synaptic transmission in the striatum.

Morphometric analysis revealed that the density of CB1 receptors in neuronal elements of striatum increases in the immobilized rats comparing with control rats. Further studies are needed to clarify the enhancing endocannabinoid-mediated distribution via activation of CB1 receptors in striatum.

IDENTICAL MONOCHORIONIC TWINS WITH DOWN SYNDROME AND PATERNAL ORIGIN OF THE EXTRA CHROMOSOME 21

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Trisomy 21, the cause of Down syndrome (DS), is the most frequent trisomy in humans. The risk for DS increases with maternal age: mothers under 25 years of age are known to have an average risk of a DS pregnancy of 1:1600, rising to 1:350 at age 35 and to 1:40 at 43, respectively.

Twins with DS are rare. We report on monozygotic (MZ), monochorionic twin sisters with DS, whose parents are young (24 and 26 years old, respectively) and healthy. Family history is non contributory; pregnancy and delivery were uneventful. Both girls presented at birth with clinical manifestations of Down syndrome, that was confirmed cytogenetically (47 XX,+21). Microsatellites analysis indicated that the twins are identical and that the extra chromosome 21 was of paternal origin.

Conclusions: For practical purposes, the causative non disjunction should be considered a single sporadic event, with an empirical recurrence risk estimated at about 1%.

Key Words: Down syndrome, identical twins, paternal origin.

SEEMF

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