

THIRD INTERNATIONAL MEDICAL CONGRESS

Healthcare Systems in Southeastern Europe

12- 15 September 2012
Belgrade, Serbia

Sofia, Bulgaria
2019





**SOUTHEAST EUROPEAN MEDICAL
FORUM
(SEEMF)**

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SOUTHEAST EUROPEAN MEDICAL FORUM

e-mail: seemf.congress@gmail.com

Website: www.seemfcongress.com

Tel./fax.: +359 2 854 87 82

**© Издателство: Сдружение "Югоизточно-европейски медицински форум",
2019г.**

© Publisher: Southeast European Medical Forum, 2019

ISBN 978-619-7544-05-3

THIRD INTERNATIONAL MEDICAL CONGRESS
organized by
SOUTHEAST EUROPEAN MEDICAL FORUM (SEEMF)
Dates: 12 - 15 September 2012
Venue: Belgrade, Serbia

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ABSTRACTS

DIABETES

ПРОБЛЕМЪТ ЗА АМПУТАЦИЯТА И НЕЙНОТО НИВО ПРИ СИНДРОМ НА ДИАБЕТНОТО ХОДИЛО

Ив. Ефремов , Вл. Костов, В. Василев ,проф. А. Атанасов
СБАЛ по ортопедия - София, ДМЦ " Св. Панталеймон", София, МБАЛ Бургас,
МБАЛ "Св. Ив .Рилски", Дупница

Синдромът на диабетното ходило обединява патологичните процеси и изменения в периферната нервна система, микроциркулацията, артериалната система, меките тъкани ,кости и стави.

Съществува становище ,че винаги при СДХ съществува непреодолима тенденция към ампутация и противно на него ,че с профилактика и лечение, могат да **се** отложат максимално дълго време ампутацията,или да се снижи нейното ниво.

Проследени са 247 болни, 186 мъже = 75.2 % и 61 жени = 25.9 % със средна продължителност на диабета от 9 г. и 3 мес.

Ампутация на различни нива- при 203 болни = 82.2 %. По видове ампутацията е била:

- на фаланги - 53.6 %
- на ходилото-33.9%
- на долна трета на подбедрица - 14.3 %

Диагнозата за определяне нивото на ампутация е осъществявана по единни алгоритми:

- анамнеза и общ статус,
- физикален локален статус,
- глюкозен и електролитен баланс,
- неврологичен статус,
- Доплер-сонография на долните крайници,вкл. и ходилата -ангиография на болното ходило с подбедрица,
- рентгенография на ходилото,

-пункционна мекотъканна биопсия на ниво ходило, долна и горна трета на подбедрицата, с хистологично изследване на материала. Наблюденията показват,че за определяне на нивото на ампутацията следва да се извърши доплерсонография,рентгенография, ангиография.

-многоетажна мекотъканна биопсия с последващо хистологично изследване на взетия при пункцията материал.Пункционна мекотъканна биопсия се извършва и на границата с очертаната некроза и подлежащите видимо непроменени тъкани.

RARE AND “SUPER-RARE” DISEASES, INSIGHTS FOR FREQUENT DISEASES FROM SEGMENTAL OVERGROWTH SYNDROME AND SOX3 DUPLICATION

Zoran S. Gucev,¹ Velibor B. Tasic¹

¹Medical Faculty Skopje, Macedonia

Aim: We present a novel disease of segmental overgrowth and the fourth patient with SOX 3 duplication. We discuss to impact of genetic data on other rare and frequent diseases.

Case 1 presentation. An 11 old patient with hypoplasia of the right kidney and hypospadias was found to be SRY negative, 46, XX. His parents and younger sister were healthy. His intelligence was normal (IQ 92) and he had no other anomalies. The behavior, growth and development were all normal. His testes were >4ml and the penis was 5 cm. Ultrasound and MRI did not show internal female genitals, while confirming right kidney hypoplasia (as did the DMSA scan). .

ACTH test showed normal basal and stimulated 17OH-progesterone excluding a form of 46XX DSD due to 21-hydroxylase deficiency. 11-DOC and 11S were normal at both baseline and after ACTH stimulation, excluding 11BHSD deficiency.

The hCG test found testosterone in the low normal range for male sex and age at baseline. It rised up to 146 ng/mL indicating the presence of functional Leydig cells targeting by the hCG. The stimulated ratio T:DHT was 5.6, not supporting 5 alpha-reductase deficiency.

SNP array for copy number variations (CNV's) showed a unique 550 kb duplication involving SOX3, RP1-177G6, and CDR1 genes, and the microRNA MIR320D2. This CNV was absent in 13,839 controls.

Case 2 presentation. This is a five year old girl with large overgrowth of the right foot (triple siae), moderate overgrowth of the right vulva and suprapubic region.

The phosphatidylinositol 3-kinase (PI3K)-AKT signaling pathway was investigated because of its key role in cellular growth and metabolism. Interestingly, loss of function of PTEN (a negative regulator of PI3K), or activating mutations in AKT1, AKT2 or AKT3 have been observed in syndromes of overgrowth or hypoglycemia. The exome sequencing of DNA from unaffected and affected cells from the patient identified the cancer-associated mutation encoding p.His1047Leu in PIK3CA, the gene that encodes the p110 α catalytic subunit of PI3K. The alteration was detected only in affected cells. Those data were found in additional 10 patients indicating that they represent a distinct overgrowth syndrome.

Conclusions. 1. This SRY negative 46,XX male with renal hypodysplasia and an exceedingly rare duplication involving the SOX-3 gene, suggests a role in both sex determination and kidney development.

2. Sequencing of PIK3CA in ten additional individuals with overlapping syndromes identified either the p.His1047Leu alteration or a second cancer-associated alteration, p.His1047Arg, in nine cases. The identification of new genes causative for diseases identifies a rational therapeutic target. In addition, identifying genes with known role in cancer and/or other frequent diseases sheds novel insight in their genesis and therefore yields novel therapeutic aims.

PROTEOMICS IN CLINICAL PRACTICE – CAN WE PREVENT DIABETIC NEPHROPATHY

Goce Spasovski

University Department of Nephrology, Medical faculty, University of Skopje, R.
Macedonia

Diabetic nephropathy (DN) is a progressive kidney disease, a well-known complication of long-standing diabetes which represents the major pool of patients recognised to have chronic kidney disease (CKD). DN is the most frequent requirement for a renal replacement therapy in many Western countries and a largest burden of the Medicare expenditure, while only a minority of other CKD entities will progress to end-stage renal disease requiring dialysis or transplantation.

Here, the most important issue for eventual prevention of disease development would be a precise identification of those at higher risk of progression or death. Currently available diagnostic and staging tools frequently fail to differentiate these important steps. A second priority within the specific disease entities would be the prediction of a need for therapeutic intervention or the response to different forms of therapy. Thus, patients at risk for diabetic nephropathy will be easily identified in the presence of an already established microalbuminuria. On the other hand, it is much more difficult to identify among diabetics with normoalbuminuria those who are at risk to develop microalbuminuria or those in whom will kidney function decline without ever developing overt albuminuria.

Kidney and urine proteomic biomarkers are considered as promising diagnostic tools to predict CKD progression early in diabetic nephropathy which may enable development of specific drugs and early initiation of therapy. Thus, it seems that the need for renal replacement therapy could be postponed and related health-care expenditures reduced accordingly.

It is supposed that a combination of tissue and urine biomarkers should be more informative than individual markers use, but certainly, it would be more difficult for implementation into the current clinical practice. Other shortcomings of these recent innovative diagnostic approaches are lack of validation in between the independent groups and most importantly, the technique is still not available for routine clinical practice. In addition, while there are gaps in understanding of predictors of progression or need for therapy in non-diabetic CKD, there is an evident need for an early diagnosis and identification of progressors and their response under the certain therapy in diabetic nephropathy.

It was recently demonstrated with urinary proteome analysis as a tool for prediction of DN that the previously generated CKD273 classifier, when applied to normoalbuminuric patients, identifies patients who will develop diabetic nephropathy during follow-up, performing better than or equal to urinary albumin excretion rate (UAER). In the investigated cohort, the CKD273 classifier was showing consistently higher values in patients who did develop DN up to 5 years prior to development of macroalbuminuria.

In conclusion, before albumin excretion starts to increase, there is a decrease in collagen fragments. A non-invasive assessment of DN risk at an early stage is possible via determination of specific collagen fragments by the urinary proteomic analysis.

GLOBAL PROBLEMS OF DIABETES AND PARADOXES RELATED TO THEM

Prof. Ramaz Kurashvili MD

National Center for Diabetes Research, Georgian Union of Diabetes and Endocrine Associations (GUDEAS), Tbilisi, Georgia

Diabetes (DM) is a chronic, progressive endocrine disease characterized by cumulative costs. Diabetes like disease was first described in the ancient Egyptian papyrus dated 1550 BC, that was translated in the 19-th century.

DM became the world pandemic and the threat for the human development in the 21-st century. The rise in DM prevalence is awaited in all age groups, both males and females and independent of the level of the GNP of the countries. Chronic diseases are no longer the privilege of the rich, they hamper the poorest populations, "this represent a public health emergency in slow motion". Adoption of the Political Declaration (2011), EP Resolution (2012) and World Health Assembly Position Statement (2012) shows growing interest towards the prevention and control of the NCDs. IDF plays important role in all political processes that took place today.

There are modifiable and non-modifiable risk factor of DM; environment causes DM in 70-80 % of cases. Diagnostic tools for diabetes management have been significantly developed and changed; lately PPG has become important for early revealing of the condition, as 70% (vs 30% - FPG) of time a person is in the post-prandial state. In practice we measure PPG only in 30%, and FG – in 70% of cases.

It is known that beta-cell distraction starts several years prior to DM manifestation, that takes place when 50-60% of the cells are destroyed. In 55% of fresh DM micro- and macro-vascular complications are present. In 53% DM is manifested with classic symptoms, while in remaining 47% DM is diagnosed accidentally, during a visit to any doctor. Still many National and In-hospital Guidelines recommend to initiate diabetes management with only dietary therapy. If DM were only a glycemia disorder, it would remain a disease, that could be treated simply with diet and walking! It is proven that the delay in treatment initiation may lead to serious debilitating conditions. Thus, smart therapy, that includes diet, should be initiate at diagnosis. Thus, dietary intervention and increased physical activity are recommended only for high risk population.

While managing DM we should keep in mind both glycemic (glycotoxicity, metabolic memory, hypoglycemia) and non-glycemic (obesity, dyslipidemia, inflammatory markers, hypertension, depression, etc) factors. Initiating DM therapy we should remember new approaches to DM management – smart therapy, treatment individualization. New generation of glucose lowering drugs do not cause severe and frequent hypoglycemic episodes, weight gain, dyslipidemia, hypertension and inflammation progression. In the past century it was accepted that it was enough to maintain optimal glycemia control to stop DM complication. Today we know that together with optimal glycemia control it is important to influence pathologic chains of CV disorders. Paradoxically, that though a large number of recommendations were naïve from the point of view of today's knowledge, Prof. J. Campbell called DM "not a simple disease, but a silent killer".

DM is integrated with various medical disciplines, like cardiology, psychiatry, obstetrics-gynecology, osteo-arthritis, oncology and others. In 2005 there was no

information about the relationship between DM and cancer at the EASD Meeting in Athens, while today links between the conditions are revealed. Even the relation of some hypoglycemic agents to cancer development is being studied. It is in the center of attention of the world diabetes community and world healthcare system.

Unfortunately the system still invests in infectious vs NCDs in proportion typical for the end of the 19 century (5X1) – resources invested in NCD control are not adequate to the scope of the problem.

When we speak about the awaited rise in the prevalence of DM and other NCDs, reality always comes ahead of the prognosis. New approaches and new technologies, safe, accessible and affordable drugs, diagnostic technologies and education of people with diabetes, HCPs and the society will permit to demolish myths and paradoxes of DM and related conditions.

DIABETES IN PREGNANCY AND NEONATAL MACROSOMIA

Zisovska Elizabeta, Professor, PhD

University Clinic for Gynecology and Obstetrics, Skopje, Macedonia

In general, macrosomia, or large for gestational age newborns (LGA) is defined as a birth weight greater than the 90th percentile for age. However, it has been suggested to restrict the definition to infants with birth weights greater than the 97th percentile (2 standard deviations above the mean) as this more accurately describes infants who are at greatest risk for perinatal morbidity and mortality. Diabetes is one of the most frequent medical condition resulting in LGA newborns, and may be induced by pregnancy or, if pre-existent, affects the pregnancy. Unfortunately, pregnancy makes diabetes much harder to control. High blood sugar levels (BSL) in pregnant women could be complicated by vasculopathy, and if it not, fetal hyperinsulinism and macrosomia are mostly present. They may have large organs, particularly the liver, adrenal glands, and heart. These infants may have episodes of low blood sugar (hypoglycemia) shortly after birth because of increased insulin. However, an enlarged heart may take several months to get better. In this study, our objective was to present some indicators in LGA babies, comparing them in relation to diabetes in pregnancy. Methods: prospective study, monitoring few biochemical, clinical and other indicators. The identification of the LGA newborns was performed using WHO growth standards for both sexes (male/female) issued 2009. Results: during the first six months of 2012, 2396 full term newborns were examined, divided in three groups: A-56 LGA babies (20,8%) whose mothers had no history of Diabetes; B-116 LGA babies (43,1%) of mothers with pre-gestational Diabetes; C-97 LGA babies (36,1%) of mothers with Gestational diabetes. Parameters compared between the three groups were: Body mass index (BMI), initial glycaemia, perinatal outcome. BMI was in normal range in group A, border-line in group B and statistically not significant higher in group C (BMI=16,9). Glycaemia was taken according to the National Guidelines (30 minutes after the second feed) and the results showed significantly lower BSL in group C, mean $1,7 \pm 0,2$ mmol/L (OR 2.19, 95% CI, 1.25–3.82, P=0.01). Both groups of newborns (A and B) had no significant difference in the mean value of BSL. The ratio male/female was significantly higher in the group A (1,4) compared to other two groups, suggesting that associated factors other than diabetes are responsible for the macrosomia. Regarding the overall

perinatal outcome, significantly higher adverse outcomes were found in the group C of newborns (infants of mothers with gestational diabetes), (OR 1.9; 95% CI 1.2-2.9). Such outcomes were: death, hypertrophic cardiomyopathy, congenital heart defects, death, birth trauma and polycythemia. The results showed that LGA babies have much higher risk if their mothers have gestational diabetes compared to pre-existing diabetes, and particularly with those whose mothers had no history or parameters of diabetes. These findings suggest that pre-existing diabetes is known risk factor before the conception, the glucoregulation is established well, and if controlled, the adverse outcomes are rare. On the other hand, the gestational diabetes occurs during the pregnancy, and the impact on the fetus depends strongly on the early identification and good management.

КЪМ СИНДРОМА НА ДИАБЕТНОТО ХОДИЛО

В.Костов , В .Василев,А.Кехайов ,Е.Лефтеров ,М. Савов ,В .Прнчев,Б.Полянов,
проф.А Атанасов,д.м.н.

ДМЦ, "Св.Пантелеймон*"София ,МБАЛ Бургас ,МБАЛ "Д-р Бр.Щукаров"
Смлянон ,МБАЛ " Св.Ив .Рилски 2003 "Дупница

СЗО / Световна здравна организация /определи като отделна нозологична единица синдромът на диабетното ходило.

Чрез стандартизирани наши анкетни карти , анализирахме получените данни от 14467 болни от диабет,60.5 % мъже и 39.5 % жени,със средна възраст 59 г. и 6 месеца .По давност на диабета болните са разпределени:

-с давност до 3 години - 0 болни,

-3-5 години- 574 болни = 3.96%

-5-10 години - 2576 болни = 17.8%

-над 10 години - 11317 болни = 78.2 %

Ние се придържаме към класификацията на СЗО на синдрома на диабетното ходило и според нея анкетираниите болни са разпределени:

а.с невропатична форма - 1015 болни =10.84%

б.с невроисхемична форма - 5062 болни =54.1%

в.с исхемична форма - 3277 болни = 35.03 %

Данните посочват ,че невропатичната форма е открита при по-млади болни с краткосрочност на диабета.Като усложнения са открити гнойно-некротични

DIABETES MELLITUS AND END STAGE RENAL DISEASE RELATED TO HEMOSTASIS IMBALANCE

Petar Dejanov, MD, PhD

Clinic of Nephrology, Medical Faculty, University Ss. Cyril and Methodius, Skopje,
Macedonia

Background: Chronic diseases are often related to hemostasis imbalance due to vascular affection which may cause further disease complication. The aim of our study was to examine hemostasis in patients with diabetes mellitus (DM), end stage renal disease (ESRD) and arterial and venous thrombosis.

Material and methods: Patients with chronic diseases were divided as following diseases: DM (n=129); ESRD (n=412); arterial and venous thrombosis (n=165). The number of 125 healthy subjects served as a control group. The performed global hemostasis tests were: prothrombine time (sec); caolin-cephaline time (sec); trombine time (sec); fibrin degradation products (FDP) (mg/ml); platelet count and aggregation in adenosine diphosphate (ADP). These parameters were compared between chronic patients and control group. The biological activity of von Willebrand factor (vWf) (%) was examined in each of patient groups and was compared to the control group. For statistical analysis, student t test was used with statistical significance for p less than 0.05.

Results: Examined parameters showed impaired values in chronic disease v.s. control group as following: for prothrombine time - 12.6 ± 0.6 sec. v.s. 12.0 ± 0.2 sec. ($p < 0.01$); for caolin-cephaline time - 54.1 ± 6.6 sec. v.s. 51.2 ± 1.9 sec. ($p < 0.05$); for thrombine time - 19.8 ± 3.4 sec. v.s. 15.4 ± 0.6 sec. ($p < 0.001$); for FDP - 16.5 ± 3.6 mg/ml v.s. 2.4 ± 0.8 mg/ml ($p < 0.001$); platelet count - $356 \pm 112 \times 10^9$ v.s. $285 \pm 61 \times 10^9$ ($p < 0.01$); aggregation in ADP - 140 ± 112 v.s. 48 ± 21 ($p < 0.001$). For vWf in all chronic patient groups were found increased values: diabetes mellitus - $271 \pm 174\%$ ($p < 0.01$); ESRD - $128 \pm 62\%$ ($p < 0.05$); arterial and venous thrombosis - $128 \pm 72\%$ ($p < 0.02$). Referent value for vWf was obtained as $101 \pm 35\%$ (control group).

Conclusion: Obtained results obviously confirmed the role of chronic diseases in hemostasis imbalance which accelerate endothelial dysfunction related to unstable patient condition with worse disease prognosis and its outcome.

THE CORRELATION BETWEEN DIABETES MELLITUS AND DEPRESSIONAL DISORDERS

Vesna Galić, doktor medicine, Dom zdravlja Prijedor, Bosna i Hercegovina

Depression disorder occurs in 6-35% of patients in the primary health care. Problem becomes more complicated if it is taken into account that depression is often followed by other co-morbid mental disorders, and that depression itself often follow somatic diseases, which represents a major problem of diagnostics and treatment in the primary health care institutions. Diabetes as a metabolism disorder is often combined with depression, and it is considered that such patients have two to three times higher chance of depression than general population.

The aim of this work was to determine the number of diagnosed depressive disorders at patients suffering from diabetes.

The research was done as a retrospective study of 80 patients, both sexes, from rural and urban communities, 18 years and older, living on the area covered by the clinic of family medicine of the Healthcare facility of Prijedor. By checking the medical database, it was found that 80 patients are suffering from both diabetes and depressive disorders. 59% of those patients were female, while 41% were male.

According to many studies, more than a half of depressed persons connect their “psychological condition” with a certain stressful event or a long-term stressful situation which occurred in the last 6 months. According to the results of this study, 80 patients are getting a treatment for depression, and there are probably many more patients, because, in their opinion, they do not need professional help because they are already

on a lot of medication and they do not need any more. Patients suffering from type II diabetes have a two to three times higher chance of suffering from a depressive disorder as opposed to general population. Such results correlate with this research which shows that depression appears more often at type II diabetes (69%). Using meta-analysis of the study it was discovered that a prevalence of depression is from 30 to 40% in comorbidity with diabetes, and only a third of patients is being treated. Two thirds of patients suffering from diabetes and depression are ill for two or more years and a large number of examinees already had several depressive episodes, while the recidivism of depressive disorders in the timeframe of 5 years was discovered in 80% of examinees, which complies to this research in fullest.

Many studies show that the development of depression as a consequence of several years of uncontrolled or inadequate treatment of diabetes, and which as a consequence had an increased number of complications of the primary disease. In relation with these studies, the research in the Healthcare facility of Prijedor shows that much more women had this complication as opposed to the number of men. Depression is connected to a larger functioning inability, lesser care for nutrition and exercise suggestions, erratic therapies and irregular control visits to the doctors' of those suffering from diabetes.

The continued education of patients concerning these methods should be continued. Regular control visits at the doctors' are not something that we can be proud of. Usually patients only come to take their regular treatments, and out of those visits, the patients suffering from type II diabetes come most often (52%).

This research showed that diabetes and depressive disorders have been diagnosed at 80 patients, more often in women than in men, at the patients aged 50 or more, and that ailment lasted for more than two years. Even though the patients are educated, they do not care about doctors' orders received at every visit. Connected to that fact, we should do education more often, make plans along with patients themselves concerning their nutrition, inclusion of physical activity, try to reduce the stress factors as much as possible and include members of family. Only a good coordination between doctors, patients, their families and consultants will surely help deal with these health problems, which leads to lower medical bills, richer society and a better life quality of everyone.

The conclusion is that the monitoring and treatment of depression at those suffering from diabetes is becoming a necessity, and it should be done with a multidisciplinary approach in a team and should be individually adjusted taking into account all the needs and complications of every patient.

Key words: diabetes mellitus, depression disorders, patient education

TREATMENT OF DIABETIC FOOT IN THE PERIOD FROM 2009 TO 2011 KOCANI

G.Panova, B.Panova, N.Panov, N.Velichkova
FMN-UGD-Stip, Macedonia

Introduction: Diabetic foot is a chronic complications of diabetes and it is an open sore or wound that occurs mostly in the lower leg in 15% of patients with diabetes. Of them 6% were hospitalized because of infection or other complications

associated with diabetic foot. Diabetes is the leading cause of netraumatski amputations of lower limbs 14% -24% in developed countries.

Objective: The main objective is to promote the health of patients with diabetes and prevention to avoid Diabetic stapalo. Tuka include all measures and methods to be taken for proper education of these patients. . Risk factors for developing diabetic foot are: duration of diabetes over 10 years, male gender, chronic bad glikoregulacija, the presence of cardiovascular, eye and kidney complications typical of diabetes, smoking, poor education about foot care, inappropriate footwear.

Methods and techniques: Initial survey includes palpation of the pulse of the legs (a.dorsalis pedis and a.tibialis posterior). Absence of pulsacija indicates possible peripheral vascular disease and require further isleduvanja. Vazhna is the color of the legs and foot temperature kozhata. Naogjanje / brahijalen index of less than 1 indicates disturbance of the circulation in the legs, the findings of oscilometrija oscilografija and the extremities. Doppler-ultrasonography examination and measurement of toe pressure together with an estimate of the circulation are methods for examining the foot, angiographic examination.

Discussion: In Macedonia, about 70% of amputations of limbs due to untreated ulcers in diabetic stapalo. Progresivniot debridement (removal of dead / infected tissue), or operations to reconnect blood circulation, result: Between 2009god.ima registered 5298 patients with Diabetes melitus of which 34 have the appearance of diabetic stiipalo of them 24 are treated conservatively and 10 operatively lekuvani. vo 2010 registered 5428 patients with Diabetes melitus of which 46 have the appearance of diabetic stiipalo of them 34 are treated conservatively and 12 operatively treated and 2011god.5634 patients with Diabetes melitus in 30 of which have the appearance of diabetic stiipalo, of which 20 are treated conservatively and 10 operatively lekuvani.

Conclusion: diabetes mellitus is among the leading diseases causing death in 21 century of foot ulcer is the main precursor for amputation of a leg because they prevent Diabetic foot with; good checks of diabetes, regular samopregled and hygiene stalalata, skill recognition of complications, proper selection of appropriate footwear, implementation of moderate physical activity, avoiding injury and treatment is reduced to limit the skin area of amputation in order for it to expand.

Key words: diabetic foot, amputation, limb, diabetes.

INSULIN FOR TREATMENT OF GESTATIONAL DIABETES MELLITUS

G.Panova, B.Panova, N.Panov, N.Velickova, L.Nikolovska

FMN-UGD-Stip, Macedonia

Objective: To compare the use of metformin with that of insulin for the treatment of gestational diabetes mellitus (GDM) and type 2 diabetes mellitus (T2DM) unresponsive to diet therapy.

Materials and Methods: In this prospective observational study, maternal glycemic control and perinatal outcome in diabetic pregnancies were compared between 2 obstetric units, one using insulin therapy and the other using metformin therapy. Baseline pretreatment glycemic profile was done and then repeated weekly throughout pregnancy. The outcome measures studied were glycemic control, maternal complications and perinatal outcome.

Results: Sixty women with gestational and type 2 diabetes were enrolled, 30 each for metformin and insulin. Both groups were comparable with respect to age, body mass index (BMI), parity and pretreatment plasma glucose levels. Glycemic control was better with metformin after 1 week of therapy and also throughout gestation ($P = 0.03-0.007$). There were no major complications or perinatal deaths in this study. Mean gestational age and birth weight (2.9 ± 0.4 kg versus 3.1 ± 0.4 kg, $P = 0.30$) were comparable. However, there was a significant increase in neonatal intensive care unit (NICU) admission and stay for babies born in the insulin group. The cost of treatment was tenfold higher in the insulin group. **Conclusion:** Metformin is clinically effective, cheap and a safe alternative to insulin therapy in pregnant diabetic women.

Keywords: Gestational diabetes, insulin, insulin resistance, metformin, type 2 diabetes in pregnancy

TREATMENT OF SEVERE FORMS OF THYROID EYE DISEASE

Nevenka Laban-Guceva, Slavica Stratova-Subevska, Irfan Ahmeti
Clinic for Endocrinology and metabolic diseases, Medical Faculty Skopje Associate
Professor of Ophthalmology Nevenka Laban-Guceva, Clinic for Endocrinology,
Metabolism and Diabetes, Medical Faculty Skopje

Background: Thyroid eye disease (TED) can be a hyperthyroid independent entity. Severe forms of TED can be a major challenge to treatment, with blindness as possible consequence. This malignant exophthalmos can be treated with several approaches: systemic corticosteroids, orbital/retro bulbar irradiation, and several types of surgical decompression. In addition, cytostatic drugs or tissue growth factors are under experimental and clinical evaluation for the treatment of TED.

Patients, methods, results: We evaluated 25 patients treated with systemic corticosteroids and/or cranial irradiation (mean age 48.4 ± 12.54 ; M/F=12/13). Visual evoked potentials were reduced in all of the patients. Magnetic Resonance Imaging (MRI) of the orbits showed a significant volume increase of recti muscles (Inferior, medial and lateral).

All 25 patients had significant reduction of TED signs and symptoms after 3 months of treatment (from Hertel: OD 24.25 ± 4.15 , OS 23.8 ± 3.22 to Hertel: OD 22.15 ± 2.9 , OS 23.1 ± 3.17 ; extraocular soft tissue decreased significantly on MRI. Only one patient had a relapse of TED, noted after 10 years after first disease manifestation. Treatment with CS induced no TED regression. Orbital irradiation with 30 Grays over 10 days induced a remission of 2 months (so far).

Conclusions: It is of note that most patients responded well when treated with CS. Nevertheless, a significant percentage of patients have been found to be CS treatment resistant. Orbital irradiation was effective in controlling the TED in all CS resistant patients. No patients were resistant to both CS and OI treatment.

DIABETES MELLITUS RELATED TO OXIDATIVE STRESS

Beti Dejanova MD, PhD, Suncica Petrovska MD, PhD, Petar Dejanov MD, PhD
Institute of Physiology, Medical Faculty, University of Ss. Cyril and Methodius,
Skopje, Macedonia

Background: Oxidative stress is a condition of increased free radicals as unpaired electrons which are highly reactive and may damage cell structure leading to its dysfunction or accelerated apoptosis. The aim of the study was to examine the level of oxidative stress in diabetes mellitus (DM) patients regarding their illness duration.

Methods: Patients with DM (n=125) were examined due to their illness duration: I group - < 1 year (n=34); II group - 2-5 years (n=56); III group - > 5 years (35). The following parameters were used: ROM - reactive oxidative metabolites as free radicals, AOS (antioxidative status) from Diacron, Italy and lipid peroxidation (LP) using the flourimetric method with end product malonyldialdehyde (MDA). The group of 35 volunteers as a control group was used.

Results: ROM showed increased value in II group – 410 ± 95 UCarr and in III group – 450 ± 101 UCarr, compared to the I group - 390 ± 70 UCarr ($p < 0.05$). The referent value was found in control group as 353 ± 68 UCarr. For AOS no statistical significance was found, while LP showed the highest value in the III group 4.8 ± 0.7 $\mu\text{mol/l}$ ($p < 0.01$), when compared to the control group 3.7 ± 0.3 $\mu\text{mol/l}$.

Conclusion: Due to obtained results we may conclude that oxidative stress increases with illness duration of DM which contributes to further endothelial dysfunction and to appearance of other related complications, respectively.

Key words: diabetes mellitus; oxidative stress; illness duration

CARDIOLOGY

MARKERS OF PRECLINICAL ATHEROSCLEROSIS AND THEIR CLINICAL RELEVANCE

Professor Pavel Poredoš, MD, PhD

Department of Vascular Disease, University Medical Centre Ljubljana, Slovenia

The estimation of risk for atherosclerotic and cardiovascular events based only on the presence of classical risk factors is often insufficient. Therefore, efforts have been made to find markers that indicate the presence of preclinical disease in individual subjects like blood markers of atherosclerosis and preclinical deterioration of the arterial wall.

Elevated levels of several inflammatory mediators have been found in subjects with atherosclerosis. Prospective epidemiological studies have found increased vascular risk in association with increased basal levels of cytokines, the cell adhesion molecules P-selectin and E-selectin; and acute-phase reactants such as high sensitive C-reactive protein (hsCRP), fibrinogen, and serum amyloid A. For clinical purposes, the most promising inflammatory biomarker appears to be hsCRP. In the last decade, markers of plaque stability and unstable coronary artery disease have been sought such as myeloperoxidase, soluble CD40 ligand, pregnancy-associated plasma protein A, free fatty acids and placental growth factor.

Further, markers of endothelial dysfunction (ED), like circulating molecules as well as indicators of functional deterioration of the arterial wall, that represent a common denominator of harmful effects of risk factors on the vessel wall were identified. It was shown that endothelial dysfunction is closely related to different risk factors of atherosclerosis, and to their intensity and duration.

Measurement of the intima-media thickness (IMT) using high resolution B-mode ultrasonography has emerged as one of the methods of choice for determining the anatomic extent of preclinical atherosclerosis and for assessing cardiovascular risk. A strong correlation between carotid IMT and several cardiovascular risk factors was shown and it has also been found to be associated with the extent of atherosclerosis and end-organ damage of high risk patients.

Determination of markers of preclinical atherosclerosis could influence the decision of a clinician to intervene with medication and to use more aggressive treatment of risk factors in primary prevention, and in patients with atherosclerotic disease.

INTERRELATIONSHIP BETWEEN ARTERIAL ATHEROSCLEROTIC AND VENOUS THROMBOEMBOLIC DISEASE

Mateja Kaja Jezovnik, MD, PhD,

Prof. Pavel Poredoš, MD, PhD

Department of Vascular Disease, University Medical Centre Ljubljana, Slovenia

Traditionally, the pathophysiology of thrombosis has been separated into venous and arterial thrombosis. The formation of arterial and venous thrombi has been explained by two distinct mechanisms influenced by different risk factors.

Over the last few decades, however, this notion has been partially challenged by the accumulation of evidence suggesting an association between arterial atherothrombotic disease and idiopathic venous thrombosis. Studies have indicated that patients with atherosclerosis may be at increased risk of venous thromboembolism and that thrombogenic factors are involved in the development of atherosclerosis. Further, recent basic and pathomorphological studies suggest similar etiopathogenetic mechanisms and risk factors for the two diseases. Similarities in etiopathogenetic mechanisms are also indicated by a resemblance in the appearance of atherosclerotic disease and venous thromboembolism.

During the last decade, the role of inflammation in the etiopathogenesis of arterial thrombosis has been elucidated. Inflammation has been accepted as a possible mechanism through which different risk factors trigger thrombus formation in veins. That inflammation is the basic etiopathogenetic process of venous thromboembolism is also supported by the relation of some risk factors to both arterial and venous thrombosis: age, increased body mass index, hypercholesterolemia, hypertension, lupus anticoagulant and hyperhomocysteinemia.

The identification and elucidation of markers relevant to both, arterial and venous thrombosis could provide targets for future prevention and therapy.

ОЦЕНКА РИСКА, СЛЕДОПЕРАТИВНА ГА МОРБИДНОСТ И ПРОГНОЗА ПРИ КАРДИОХИРУРГИЧНИ ПАЦИЕНТИ: SOFA СКОР

Царянски Г. Чолаков И. Абединов Ф. Тенев Б. Димитрова В, Манолова В, Начев Г, „Св. Екатерина" София, България

Увод: системата за оценка на риска при кардиохирургичните пациенти Euro Score. IS се използва рутинно в редица институции. Макар и добре валидирана спрямо изхода от лечението, тази система не позволява оценка на моментното състояние на виталните функции и следоперативния период. I (последното се описва добре със системата Sequential Organ Failure Assessment, SOFA. Цел: да се изследва информационната стойност на сборуваните системи ES и SOFA в периода на следоперативно лечение при ограничена група кардиохирургични пациенти.

Метод: изследването е проведено за времето 15.01.2011-30.06.2011 г. Включени са пациентите, оперирани и приети в интензивното следоперативно отделение на институцията. Пациентите, планови и спешни са приети за кардиохирургични операции с ES 6.34. I [Окрилите критериите за възстановяване напишеш и и преведени в следоперативното отделение до 72-ия следоперативен час са изключени от проучването. Изследвани са пациентите, които и след 72-ия час продължава! да се лекува! в ИО. I при тях е изчисляван SOFA скор до 21-ия следоперативен ден. Оценени са параметрите: смъртност, продължителност на престоя в ИО, продължителност на механичната вентилация МП настъпването и продължителността на бъбречно заместителната терапия, БЗТ и продължителност на хемодиализа и члнната подкрепа.

Резултати: I (ациентите, при които лечението е продължено в ИО и след 72-ия час са с ES 7.4. SOFA скор на 72-ия час е S.S. като при проследяване до 21-ия ден величината остава висока. Смъртността при пациентите лекувани в ИО

над 3 дни е 8.5%. Установихме различна тежест на изразеност на органните увреждания в периода след 3-ия следоперативен лей. Следоперативния престой в ИО при тези пациенти е 7 дни. МВ 3.3 дни. БЗТ е извършвана при 21 нациста, хемодинамична подкрепа е прилагана 5.1 дни а IIABI е използвана при 20 пациента.

Заклучение: при кардиохирургичните пациенти предоперативната оценка па риска по IS в значителна степен съответства на оценката по SOFA па 3-ия след оперативен ден. SOFA системата позволява сравнителна оценка на ви I алии ге функции.

РОЛЯ И МЯСТО НА КАРДИОХИРУРГИЯТА В ЛЕЧЕНИЕТО НА ОСТРИЯ МИОКАРДЕН ИНФАРКТ

Д. Кючуков д-р; Б. Баев д-р ДМ Доц.; Д. Петков д-р ДМ, Доц.; Г. Начев д-р ДМН Проф.СБАЛССЗ"Св. Екатерина" София

Острия миокарден инфаркт е водеща причина за смъртност и заболяемост в модерния свят. Терапевтични опции за реваскуларизация са перкутанните коронарни интервенции, тромболизата и хирургичната реваскуларизация. Особено важно за добрия резултат е времето от настъпването на инфаркта до реваскуларизацията. Подобрените резултати при пациенти подложени на перкутанни интервенции постепенно доведе до намаляване на интереса към хирургичната реваскуларизация в острия стадии на миокардния инфаркт. Въпреки това при пациенти с механични усложнения, неуспешни интервенции, кардиогенен шок- хирургичното лечение остава единствена опция.

Материали и методи: За периода 2001- 2011 в СБАЛССЗ"Св. Екатерина" общо 748 пациенти са били подложени на различни хирургични интервенции по повод остър миокарден инфаркт и неговите механични усложнения. Остър миокарден инфаркт- 185, остра руптура на междукамерния септум- 12, остра руптура на лява камера- 3, остра митрална регургитация- 5, лявокамерни аневризми – 312, исхемична митрална регургитация- 159, високорискови пациенти с исхемична болест и механични усложнения- 72. Средна възраст- 61,7 год. Мъже- 70.2 %.

Резултати: Общата болнична смъртност е 9,5 %, като варира от 6,4 % при пациентите реваскуларизирани по повод остър миокарден инфаркт и достига 42 % при оперираните с остра руптура на междукамерния септум.

Изводи: При лечение на острия миокарден инфаркт е задължително да се спазват утвърдените алгоритми за поведение. Избор на начина на лечение – интервенционално или хирургично се взема от интердисциплинарен екип и в съответствие със състоянието на пациента. Хирургичните интервенции на пациентите с механични усложнения на острия миокарден инфаркт са единствена опция за тяхното лечение.

ROLE OF ECHOCARDIOGRAPHY IN SELECTION HEART FAILURE PATIENTS FOR CRT

E. Srbinovska Kostovska, University Clinic of cardiology, Skopje, Macedonia

Heart failure can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissue. Left ventricular adverse remodeling after myocardial injury (myocardial infarction, left ventricular dilatation from other reason, idiopathic cardiomyopathy) has been shown to be a chronic progressive process that contribute for years after the initial faze. Adverse remodeling and gradual dilatation leading to increased LV volumes are major predictors of poor outcomes among heart failure patients. Several therapies were found to slow the process of adverse LV remodeling , including beta-blockers and blockers of the renin-angiotensin-aldosteron system. But, despite optimal therapy, left ventricular dyssynchrony in commonly present in heart failure patients, particularly in those with prolonged QRS complex duration. Cardiac resynchronization therapy with or without defibrillators, in several study showed reversal remodeling and significant improvements in LV volumes, reduction the risk of the heart failure progression and death in mildly and symptomatic patents with ischemic and non-ischemic cardiomyopathy. Cardiac resynchronization therapy (CRT) is currently indicated on top of optimal medical therapy for patients with moderate to severe left ventricular (LV) systolic dysfunction. But, up to 40% of patients do not respond to CRT, depending on which definition of response is used. One of the reasons of not responding on CRT and poor prognosis after CRT is minimal, or no dyssynchrony. The other reasons are ischemic deseases with too much scar especially lateral wall scar, suboptimal lead placement. But, dyssynchrony can be identified prospectively by echocardiographic Doppler methods.

Several data have suggested that the identification of echocardiographic markers of dyssynchrony before device implantation could predict response to CRT. The PROSPECT trial (Predictors of Response to Cardiac Resynchronization Therapy), a multicentre study from Europe, United States and Hong Kong, failed to identify an ideal echo measure of dyssynchrony that could easily and reproducibly predict response to CRT in patients selected based on current recommendations. The use of different echocardiographic platforms and equipment to collect and analyze images may have exacerbated variability in measurements, so conclusion of the PROSPECT trial was that future work is needed to improve reproducibility of dyssynchrony analysis.

Novel echocardiographic techniques, including tissue Doppler, color tissue Doppler analysis, srain, strain rate, 3-dimensional echocardiography, tissue synchronization imaging, and other echocardiographic dyssynchrony methods play very important role, especially in selection a patient (responder) for CRT therapy. American Association of Echocardiography issued expert consensus statement which defines different echocardiographic measurements that provide information about different types of dyssynchrony.

With Echocardiography measurements can assess abnormalities of the mechanical activation, known as dyssynchrony, determine the type of dyssynchrony, improve patient selection for CRT respond and can do AV optimization after CRT.

ANABOLICS ABUSE AND CARDIOMYOPATHY IN A BODYBUILDER : CASE REPORT

Chaparoska D ,Spirovska V. University Clinic of Urgent Internal Medicine¹,
University Clinic of Cardiology², Medical Faculty, Skopje, R.Macedonia
Professors on Medical Faculty in Skopje

Background: Anabolic-androgenic steroids are synthetic derivatives of testosterone that some athletes have used to enhance muscle mass and improve their athletic performance. Adverse cardiovascular events attributed to anabolic steroid use, such as arrhythmias, myocardial infarction, cardiomyopathy, and sudden death, are rarely reported. Bodybuilders also have used and γ -hydroxybutyrate, a potent secretagogue of growth hormone, to promote muscle development. Although dilated cardiomyopathy is a known complication of excess growth hormone levels, it has not been associated with use of γ -hydroxybutyrate.

Case report: A 39-year-old male bodybuilder was admitted to Intensive-Care Unit . The patient had a history of anabolic steroid abuse over the last 3 years, self-administered in cycles of 6-10 wk, with a 2-3 wk suspension period between cycles. The most frequently used anabolic steroids were: methandrostenolone, stanozolol and oxymetholone (oral); and nandrolone decanoate, testosterone enanthate and trenbolone enanthate (intramuscular). He used massive doses of all anabolic steroids. There was no history of alcohol abuse or acetaminophen intake. He had no family history or past personal history of cardiovascular diseases. The patient was in good physical condition until approximately three weeks prior to admission, when he experienced increasing fatigue, decreased exercise tolerance and general malaise. Although he stopped exercising and self-administering the drugs, these symptoms continued to progress and he subsequently developed anorexia, becoming short of breath during exertion and tiring easily, blood pressure was low .Laboratory testing: Free testosterone and delta 4-androstenedione concentrations were elevated. Acetaminophen level was undetectable and with the suspicion of anabolic steroid-induced toxic hepatitis. Chest X-ray also revealed cardiomegaly, despite no evident pulmonary congestion. Echocardiogram showed a dilated cardiomyopathy with an estimated ejection fraction of 35% . A diagnosis of severe toxic cardiomyopathy associated with anabolic steroids was made after ruling out other causes of non-ischemic dilated cardiomyopathy, including infectious, autoimmune and metabolic causes. Serial echocardiograms showed left ventricular function (the fractional shortening increased < 30%). After 18 days hospitalization, the patient was discharged with oral therapy. However, not enough time has elapsed since treatment to assess full recovery of pathological changes and heart performance.

Treatment: General treatment measures included avoiding stress, limiting salt in the diet, and having periods of rest, which help reduce strain on the heart, particularly when the cardiomyopathy is acute or severe. Drugs, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, beta-blockers, spironolactone were given. Antiarrhythmic drugs were given to prevent abnormal heart rhythms. These drugs were prescribed in small doses. Doses are increased in small

increments, because if the dose is too large, an antiarrhythmic drug may worsen heart rhythm abnormalities or depress pumping function.

Conclusions: Several years after chronic misuse of AAS, power bodybuilder show a clinical impairment myocardial function, strongly associated with mean dosage and duration of AAS use. The interval of interrupted of AAS abuse is relatively short, to be able to evaluate the improvement of left heart cavity function.

CORONARY HEART DISEASE IN MACEDONIA – CHALLENGE FOR HEALTH SECTOR AND COMMUNITY

Assoc.Prof. Elena Kosevska, MD, Ph.D.

Medical Faculty, University “Ss. Cyril and Methodius”, Skopje, Republic of
Macedonia

Introduction: It is considered that almost 23.6 million people will die from cardiovascular diseases (CVD), mainly from heart disease and brain stroke, by 2030. Almost 60% of burden of disease in Europe, according to DALY, is due to the 7 leading risk factors: high blood pressure (12.8%), tobacco (12.3%), alcohol (10.1%), increased cholesterol (8.7%), overweight (7.8%), little consumption of fruits and vegetables (4.4%) and physical inactivity (3.5%). The most common disease is coronary heart disease (CHD) that mostly occurs after 40 year of life and it's more common for men than for women.

Purpose of the paper is to present the state of CHD in the Republic of Macedonia and measures that are taken to improve and strengthen multidisciplinary approach for health promotion and prevention of diseases, to reduce the incidence of CHD and CVD.

Material and methods: The descriptive and analytical method has been used. There are used statistical data from morbidity and mortality statistics, research studies, professional materials from domestic and foreign literature.

Results and discussion: According to WHO, there are 16.7 million people dying from CVD each year in the world. According to some studies, CHD for men is most common in Finland, and most rare in the UK. CVD were major cause of death for people younger than 65 years of age in Europe, with 803.000 deaths each year. Before 65 years of age, 31% of death people were men and 29% were women. Circulatory diseases are chronic diseases that occur as a leading cause of death among people in Macedonia. In 2010, 57.9% of dead people or 11,069 people died from cardiovascular diseases, as compared with the previous period (in 1990 -7113 death cases or 48.6% from total deaths) and there is no trend in terms of reducing death from these diseases. 1/5 of them are deaths from acute heart attack. The rate of hospital morbidity by CVD in Republic of Macedonia is equal to 172.2 / 10000 in 2010, that's average of 35000 patients, mostly men. CVD accounted with 14.3% from the total number of hospital diseases. Essential hypertension (EH) was recorded even at the age of 14 years (2007 to 3 cases). EH contributed with 7.7% in the hospital morbidity from CVD. In Serbia, number of cases of hypertension is increasing; it is considered that there are over 2 million patients with high blood pressure. Also, the prevalence of hypertension in Croatia is about 37.5%. Republic of Macedonia follows the recommendations of WHO for comprehensive approach for CVD prevention with more active involvement of

doctors from primary health care; using a holistic approach in educating and informing the public and providing support for the implementation and monitoring of screening and other activities. Holders of the activities are the Ministry of Health, Health Insurance Fund, Institute of Public Health, 10 Public Health Centres, NGOs, Red Cross of Macedonia, Macedonian Doctor's Association, Association of Private Practitioners, Association of cardiologists and others.

Conclusion: CHD is a preventable condition. Although so far there are no signs of reduction in morbidity and mortality, in the future, it can be control thanks to the preventive measures that are taken so far. However, it's necessary to be made a special National program for prevention and control of CVD and CHD by the Government, in which target groups will be units from the local government, general population, especially over 35 years of age, mass media and others, in which there will be written a specific activities for the training of local leaders in management, to be prepared a Local action plan for health promotion and primary prevention of CHD, organizing social activities for free medical examination and more.

LEFT ATRIAL THROMBUS IN PATIENT WITH MITRAL VALVE DISEASE

Boshev Marjan, MD

Otljanska Magdalena, MD, PhD, assistant professor

Arnaudova-Dezhulovikj Frosina, MD

University Clinic Of Cardiology, Skopje, Macedonia

Background: Left atrial thrombus in patients with mitral valve disease is relatively frequent condition. Echocardiography is reliable and safe method in diagnosis and differential diagnosis of the intracardial masses.

Material, methods and results: We present a clinical case of 59 years old female patient who visited an Emergency Cardiology Department complaining in fatigue, dyspnea, and chest pressure associated with vertigo and nausea started couple of months ago. She was in atrial fibrillation on admission with unknown duration with symptoms and signs of advanced heart failure (NYHA III-IV). Echocardiography revealed normal LV dimensions, function and ejection fraction, but largely dilated right heart cavities. Left atrium was also dilated (62x96 mm from apical position) with visualized oval intracavitary mass, most likely thrombus, with dimensions 26x63 mm. Mitral valve apparatus had fibrocalcific changes on mitral cusps with high grade mitral stenosis (MVA 0,3 cm²) and moderate mitral regurgitation. Patient was treated with anticoagulants, diuretics and antibiotics. Echocardiography control showed non-significant reduction in thrombus dimensions. She was offered cardiosurgical treatment but she refused it, and conservative treatment with oral anticoagulants was continued.

Conclusion: Transthoracic echocardiography is a method of choice in diagnosis of intracavitary masses of the left atrium. Differential diagnosis between left atrial thrombus and myxoma may be difficult if the mass has a stalk. When differential diagnosis is difficult and probability of thrombus is high, oral anticoagulant therapy remain good alternative with echocardiographic follow-up.

Key words: left atrial thrombus, mitral valve disease, echocardiography.

CARDIAC VALVULAR CALCIFICATION AS A MARKER OF ARTERIAL CALCIFICATION IN END-STAGE RENAL DISEASE PATIENTS ON PERITONEAL DIALYSIS TREATMENT

M Rroji (Molla), MD¹, S Seferi, MD¹, M Cafka, PhD², N Zeneli, MD¹ and N Thereska, Prof¹.

¹Department of Nephrology-Dialysis-Transplantation, University Hospital Center "Mother Teresa", Tirana, Albania.

²Department of Cardiology, University Hospital Center "Mother Teresa", Tirana, Albania.

Introduction: Vascular and valvular calcifications are a common finding in chronic kidney disease (CKD) patients and are associated with increased morbidity and mortality. We investigated the hypothesis that calcification of the cardiac valve is a marker of carotid artery calcification (CAC) reflecting an excessive calcium phosphorus load in ESRD patients.

Methods: We conducted a cross-sectional, descriptive study during September 2011- March 2012, enrolling 38 stable patients (55.5 % males; mean age 55.7 +/-13.5 years and average duration of dialysis 27.7+/-17.5 months) that had been treated with Peritoneal dialysis more than 6 months. Demographic data, basic nephropathy and biochemical data were examined. Baseline echocardiography was performed to screen for calcification of the aortic valve, mitral valve, or both as an easy way to evaluate cardiovascular calcifications. B-mode ultrasonography was used to determine the occurrence of plaque and calcification in carotid artery.

Results: Valvular calcifications were found in 47.3% of patients; mitral valve calcifications in 37%, aortic valve calcifications in 23.6% and both valves calcifications in 21% of patients. Fifty percent of our patients had carotid artery calcification among which 21% had calcification detected in either one of the carotid arteries and 26.3% of patients had calcification present in both carotid arteries. Carotid artery calcification was present unilaterally and bilaterally in 19 % and 22% of patients with valvular calcification *versus* 2.7% and 8.1 % of patients with no valvular calcification respectively . Controlling for age, CaxP, PTH and Pulse pressure persons who have calcification of the valves have 16 times more likely to make the carotid calcification, versus those who didn't not had calcification of the valve (OD=16,23, CI 95%: 5.014-19.096).

Conclusions: The associations between valvular calcification ,and carotid calcification suggest that calcification of the aortic valve or mitral annulus not only reflects poor calcium phosphorus balance but is also a marker of arterial calcification in the ESRD population.

Keywords: Peritoneal dialysis; valvular calcification;vascular calcification; calcium phosphorus balance.

ONCOLOGY

CERVICAL CANCER SCREENING IN THE ERA OF HPV VACCINATION

Goran Dimitrov MD, MSc

University Clinic of Obstetrics and Gynaecology – Skopje, MACEDONIA

Worldwide 530,000 women were diagnosed and 275,000 women died from cervical cancer in 2008. Eighty six percent of all cervical cancer cases are found in less developed countries. [Arbyn et al, 2011] With the implementation of cervical cancer screening programs during the past four to five decades, cervical cancer incidence and mortality have declined dramatically in developed countries [Runowicz 2007]. The success of Pap (Papanicolaou) test (“historic gold standard for cervical screening”) to detect early stage cervical cancer and precancerous lesions is in part due to the natural history of the cervical cancer precursors, amenable to secondary prevention. [Solomon 2003] At the end of the 80’s and beginning of the 90’s a lot of authors “revisited” the Pap smear and even informed the public that “this complex detection system leading to the discovery and treatment of precancerous lesions and early cancer of the uterine cervix has potential failures”, calling it “a triumph and a tragedy”. [Koss 1989]

With the invention and development of liquid-based cytology (LBC), certain disadvantages of the conventional cytology has been tried to be overcome and some novelties added. [Chivukula et al, 2007]. Majority of randomized studies are not reporting of improved or even equivalent sensitivity in detecting cervical abnormalities in comparison with conventional cytology in contrary of nonrandomized studies, but in almost each of these the number of unsatisfactory samples is significantly reduced [Arbyn et al, 2008].

In the last years of the past century the HPV DNA testing of all molecular-based technologies has elicited greatest interest for cervical cancer screening. HPV testing has 25-35% higher sensitivity than cytology in absolute terms but somewhat lower specificity, 5-10% for detecting high grade lesions. [Cuzick et al, 2006].

Not only promising new screening tests but also very effective HPV vaccines emerged at the beginning of the 21st century as a tool for primary prevention of not only cervical carcinoma but HPV infections and related malignancies. [Bonati et al, 2009] The first recombinant vaccine against types 6,11,16 and 18 (the quadrivalent Gardasil®) was approved in 2006 by FDA and EMA for the prevention of high-grade cervical (CIN 2/3) and vulvar (VIN 2/3) dysplastic lesions, cervical cancer, vulvo-vaginal cancer and genital warts. Later a second cervical cancer vaccine (the bivalent Cervarix®) was granted marketing authorization limited to the prevention of cervical carcinoma and cervical intraepithelial neoplasia. [WHO Strategy paper, 2008]

When a static Markov model is used: follow of a hypothetical cohort of women with vaccination coverage of 70-100% in the target group – age of vaccination, 12 years; biennial screening starting at age of 24 – the results show an ICER of 24,300 \$US per QALY gained. [Goldie, 2004] A second similar study: vaccination at 12 years, biennial screening and vaccine booster doses every 10 years gave an ICER of 22,755 \$US per QALY gained compared with current practice [Sanders et al, 2005] When a Markov dynamic transmission model is used that means that several issues are taken into account: epidemiological changes in HPV types prevalence over the time, the impact of herd immunity and if only females should be vaccinated. In a study from year 2007, the vaccination (with 70% coverage) of 12-year-old girls would reduce the incidence of

cervical cancer by 78%, and with a strategy which included males – the ICER was 45,056 \$US and reduction of cervical cancer by 91% [Elbasha et al, 2007]

Several key points should be stressed: 1. Mathematical models suggest that population-wide Pap test screening (at three year intervals) reduces the rate of invasive cervical cancer by 91% and at five year intervals by 84% 2. A strategy is considered cost-effective if the ICER is in the range of 50,000 – 80,000 \$US per QALY saved 3. As the frequency of screening increases – the ICER increases (an annual screening is well over 100,000 \$US or more compared with biennial screening) [Dimitrov Go et al, 2011; Goldie et al, 2006]

The recent study with a calibrated Markov model [Accetta et al, 2010] showed that a current screening policy (Pap test every 3 years) is more costly and less effective than HPV DNA test and Pap test every five years. Their findings strongly support changing the Pap screening policy to the use of HPV DNA as a primary test with Pap test triage for both vaccinated and unvaccinated women. Having in mind that vaccinated girls will not reach the initial screening age (i.e. 30 years) until 2023, and millions of unvaccinated Dutch women born before 1993 will continue to be screened until they have reached the last screening age, van Rosmalen et al. in their most recent study (2012) conclude that: “increasing the interval between screening rounds and changing the primary test from cytology to HPV testing can improve the effectiveness and decrease the costs of cervical cancer screening in the Netherlands”.

With highly effective vaccines against infection with HPV types 16 and 18 as primary screening prevention and new technologies producing novel and improved screening tests as secondary prevention – cervical screening guidelines should change retaining balance between maximizing efficiency using more sensitive and specific tests at less frequent intervals, starting at later ages and in this way reducing incidence and mortality from this highly preventable malignancy.

THE CHANGING PRESENTATION OF GERM CELL TESTICULAR TUMORS BETWEEN 1976 AND 2005

Prof. PhD Đorđe Argirović, Aleksandar Argirović
Outpatient Clinic Argirović, Urology, Belgrade, Serbia

Background: To prospectively investigate the presentation of germ cell testicular tumors in terms of clinical stage or histology, as the incidence of this disease is increasing.

Methods: Information was collected from a prospective database initiated in 1966. Patients diagnosed with germ cell testicular tumors between 1976 and 2005 were categorized into 3 periods depending on date of diagnosis of the germ cell testicular tumors and presentation characteristics assessed. For purpose of analysis, patients were assigned to 1 of 3 similar groups in term of duration (10 years) (1976-1985, 1986-1995, 1996-2005). These 3 periods were compared statistically to indentify possible changes in the presentation of germ cell testicular tumors.

Results: Among 1935 patients, the number diagnosed in each period was 111 (6%), 695 (36%) and 1129 (58%), respectively. There was substantial arise in the percentage of patients with germ cell testicular tumors during the period of 30 years, particularly in 3rd vs. 2nd and 1st decade ($P < 0.0001$). The median (range) age of the

whole cohort was 34 (14-80) years. The median age for developing metastatic seminoma was 4 years more than in clinical stage I disease (38 vs. 42 years respectively), while the median age for the presentation of clinical stage I and metastatic nonseminoma was identical (31 years). Overall, 46% of patients were diagnosed with seminoma and 54% with nonseminoma. The proportion of seminoma increased significantly in time (48% vs. 55%), and this was accompanied by a significant decrease in nonseminoma (60% vs. 45%)($P<0.001$). The proportion of patients with clinical stage I disease also increased significantly with time (45% vs. 77%), while the proportion of patients with metastatic disease decreased (55% vs. 29%) ($P<0.001$). In the most recent period 77% had clinical stage I and 23% had metastatic disease. There was a significant rise in proportion of patients with clinical stage I seminoma (27% vs. 47%) and nonseminoma (18% vs. 30%), accompanied by a significant decrease in the proportion of patients presenting with metastatic nonseminoma (42% vs. 15%)($P<0.001$). However, the proportion of patients with metastatic seminoma remained largely unchanged (13% vs. 9%).

Conclusion: The present study shows an increase in the proportion of patients with germ cell testicular tumors in clinical stage I. This is good news for patients with germ cell testicular tumors, as it not only reduces the need for chemotherapy and/or cytoreductive surgery, but also is associated with better long-term survival. The other finding is that there has been an increase in the proportion of patients presenting with seminoma rather than nonseminoma. The reasons for these remains unclear and require further investigation.

КЪМ ВЪПРОСА ЗА ЛИМФНА ДИСЕКЦИЯ ПРИ ТИРЕОИДЕН КАРЦИНОМ

Проф.д.м.н. Р.Петков, проф.д.м.н.Ал.Атанасов, В.Младеновски УМБАЛ
"Александровска" София, МБАЛ "Св.Ив.Рилски 2003" Дупница

Карциномът на щитовидната жлеза е чест сред туморите на ендокринните жлези и заема 1 % от всички тумори. За 2001 г. във Франция / по М.Матенот / е представлявал 0.5 - 10/100.000% от население, като боледуват по-често жени.

Проследени са 800 болни, 593 жени = 74.12 % и 207 мъже = 25.87%. С папилиферен карцином са били 657 болни = 82.12%, с фоликуларен - 120 болни = 15.0 % и недиференциран карцином - 23 болни = 2.87%. Предоперативно чрез КАТ / скенер / и сонография са открити паратрахеални лимфни метастази при 27 изследвани болни, предоперативно суспектни за карцином. Интраоперативно се проследяват визуално и палпаторно лимфните групи около щитовидната жлеза и дистално от нея - югуларната ямка. При всички суспектни и дакозани болни с лимфни метастази е осъществена веназширена шийна лимфна дисекция,

Наблюденията показват, че при всеки болен опериран за карцином на щитовидната жлеза, независимо от неговия хистологичен вид е необходима визуална и палпаторна преценка, последвана от експрес-хистологично изследване на взети лимфни възли / гефрир / и преценка за различен обем на шийна лимфна дисекция. Болните подлежат на диспансерно наблюдение. За ориентацията относно сложността на проблема показва топографската анатомия на шийната лимфна верига / система / .

ПРОБЛЕМИ НА КОЛОРЕКТАЛНИЯ КАРЦИНОМ В СТАРЧЕСКА ВЪЗРАСТ

В. Василев, Е. Лефтеров, Доц. А. Кехайов, проф.д.м.н.Ал.Атанасов
МБАЛ - Бургас ,МБАЛ "Св.Ив .Рилски 2003 " Дупница МБАЛ ¹¹ Д-р Бр.
Шукеров" Смолян

По литературни данни в последните десетилетия се наблюдава тенденция към постоянна нарастване на колоректалния карцином.Анализирани са истории на заболяване при 254 болни, 141 мъже = 55.5 % и 113 жени = 44.09 % на възраст 71 - 86 г.,опирани за периода 1998 - 2009 г. По локализация,карциномът е бил:

-на колона ,на различни нива - 39 болни = 15.3%

-на сигмата - 97 болни = 30.8 %

-на ректума - 118 болни = 46.8%

При всички болни са отчетени рискови фактори: възраст - в 100%,ИБС - 100%, ХОББ - 27.1 %, диабет - 47.2 %,високо артериално налягане - 90.9 %.С висок оперативен риск са били 43 болни = 16.9 %/оперирани заради развит механичен илеус /, с оперативен риск от средна степен - 71.2%;останалите са били с нисък оперативен риск.Карциномът е установен с комплесна диагностична програма:общ и локален статус,ендоскопия,КАТ,ехография на корем и коремни органи.При всички болни са установени авансирани форми.Предоперативни усложнение: механичен илеус - 38.2 %.При всички болни е осъществена палиативна операция ,поради авансирания карцином.

Наблюденията посочват, че при сегашните условия в старческата възраст преобладават авансирани форми да карцином с наличие на сериозен оперативен риск.В тези групи заболяването се открива късно,поради нежелание за преглед от самите болни и късно появяване на обективната симптоматика.Анализът посочва че заболяването в старческа възраст поставя сеиозни проблеми пред личните лекари,гастроентеролози и хирурзи.

CURRENT SURGICAL MANAGEMENT OF THE PANCREATIC CANCER

Radoslav Gaydarski, N.N. Katev, V. Marinov, K. Draganov
HBP Surgery , Tokuda hospital – Sofia, Bulgaria

Worldwide, over 200,000 people die annually of pancreatic cancer. In Europe , pancreatic cancer is the 6th leading cause of cancer death, and in United States it is the 4th. Great majority of patients present with locally advanced or metastatic disease. Surgical resection remains the only potentially curative intervention for select patients who present with localized disease.

With advances in surgical techniques and perioperative care, more extensive resections of the pancreas are possible, the mortality rates associated with the procedure has reduced to less than 5%, (40 % last decades) but the morbidity rate is still up to 40 % even in high-volume centers.

Approximately 15-20% of patients initially diagnosed with pancreatic cancer are amenable to resection . Great majority of pancreatic cancer (90%) are ductal in origin located predominantly in the head of the gland (>75%). Unresectable lesions are those involving SMA or celiac trunk (T4) or those with distant metastases (M1).

Controversy exists regarding the definition of borderline resectable lesions. Generally, tumor abutment of visceral arteries or short-segment occlusion of the superior mesenteric vein is considered anatomically borderline resectable lesion

The operative techniques for pancreatic cancer can be divided to Potentially curative techniques (Pancreatoduodenectomy, Distal Pancreatectomy, Total pancreatectomy) and palliative procedures (Gastro intestinal, Biliary and Pancreatic bypass(decompression) operations and pain reducing opeations (gangliectomy – left, right, billateral)

From January 2000 to August 2012 , we have 1216 pancreatic cancer procedures. Duodenopancreatectomies 276 (246 Whipple, 30 Traverso- Long.), Distal Pancreatectomies 176 (121 hemipancreatectomies, 55 subtotal), Gangliectomies 102 (74 right, 10 left abd 18 billateral). Decompressive bypass operations of GI, Biliary and pancreatic duct – 662.

ОЦЕНКА КАЧЕСТВОТО НА ЖИВОТА ПРИ БОЛНИ ,ОПЕРИРАНИ ЗА ДЕБЕЛОЧРЕВЕН КАРЦИНОМ

Проф. А. Атанасов ,Е.Лефтеров ,В Василев , А. Кехайов , М. Савов, В.Пенчев,
Б.Полянов

МБАЛ "Св.Ив .Рилски 2003 "-Дупница, МБАЛ - Бургас , МБАЛ "Д-р Бр.
Шукеров " – Смолян

Терминът "Качество на живот " е въведен от J.Erkinton през 1966 г. и утвърден окончателно през 1977 г.Според експертите на СЗО включва " пълно физическо,психично и социално благополучие" на отделния индивид".

Чрез анкетни карти и въпросник ,основан на принципите на *Quality of life index* в 5 направления :

- наличие на болков синдром след операцията,
- състояние на физическата активност,
- наличие на психологични неудобства и нарушения
- социална активност на индивида и връзки със семейството
- самооценка на здравното състояние.

По възрастови групи анкетираните болни/ или анкети в семейството / болните са били 98 мъже - 63.2 % и 57 жени - 36.7 % ,общо 155 болни на възраст от 75 до 86 години като във възрастова група 75-78 г.са били 31%,група 79-82 г.- 22.2 %,група 83 - 86 г. -69.5 %.Освен различни типове чревни резекции при 12.2 % от оперираните е наложен дефинитивен анус претернатуралис.При дурги 874 болни оперирани през периода 2000 - 2010 г. преживяемостта след операцията при радикални оперативни намеси е била средно 11 месеца и 13 дни.При палиативни операции с чревни анастомози -9 f месеца и J4 дни,при болни с анус претернатуралис - 8 месеца и 15

Заключение: Въз основа на проведената анкета могат да се направят следните изводи:

а)При болни с дебелочревен карцином в старческа възраст, оперирани по спешност настпвът често сериозни следооперативни усложнения и рязко влошаване качеството на живота ;

b) Всички болни с диагностициран дебелочревен карцином, независимо от предвиждани палиативни или радикални операции, следва да бъдат оперирани, което осигурява минимално влошаване на качеството на живот при болните с чревни анастомози и по-значително при наложен ануспретенатуралис, при почти еднакъв срок на следоперативна преживяемост.

LONG-TERM TRASTUZUMAB IN THE METASTATIC SETTING OF PATIENTS WITH HER2 OVEREXPRESSED BREAST CANCER

Snezhana Smichkoska, MD, PhD, Deva Petrova, MD, Valentina Krstevska, MD, PhD,
Igor Stojkovski MD, Emilija Lazarova MD

University Clinic of Radiotherapy and Oncology, Skopje, Macedonia

Background: Empirically, trastuzumab has been continued in many patients with disease progression, mainly due to its favorable safety profile and the assumption that progression was due to resistance to the co-administered chemotherapeutic agent but not trastuzumab itself. Retrospective analyses provided some support for this treatment approach, at a weak level of evidence.

Patients and methods: We retrospectively analyzed records of 11 patients with relapsing HER2 overexpressed breast cancer exposed to long-term trastuzumab therapy concurrently with multiple lines of chemotherapy or hormonotherapy according to the subsequent relapse of the disease in the period from 28/07/2004 to 20/01/2010. July 2004 was starting point because since then trastuzumab was available for the treatment of metastatic HER2 overexpressed breast cancer. At a cut-off point (June 2012) 10 patients were still alive. We evaluated the initial stage of the disease, site of relapse, median time to progression (TTP), median duration of response to first line therapy for metastatic disease, overall survival (OS) and duration and toxicity of long term trastuzumab. The starting points were the date of initial diagnosis of breast cancer and the date in which trastuzumab-based therapy started as a result of distant relapse of the disease. The dates of tumor relapse and tumor progression were used to calculate median TTP, whereas that of death for any cause was used to calculate OS. Surviving patients were censored at the date of the cut-off point (June 2012). LVEF was measured in 3 monthly intervals after rechallenge of trastuzumab because of the metastatic disease and the results were presented in 3 cut-off points (**initial** at the time of rechallenge of trastuzumab, **median** in the middle of the treatment period for each individual patient and **final** that was last measurement for each individual patient).

Results: Eleven women with median age of 44.0 years (range 38-57) were included. 45.5% were pretreated with trastuzumab-based therapy in adjuvant setting. Visceral metastases were identified in 7 patients (64%) and bone/soft tissue in 4 (36%). Median time to progression (TTP) was 43 months (range 13-115 months). Median duration of response to first line therapy concurrently with trastuzumab was 20 months (range 8-45 months). Overall median survival was not reached. Median duration of trastuzumab therapy was 44 months (range 15-93 months). No unexpected toxic effects occurred. Trastuzumab was temporally stopped in only 1 patient for a period of 2 months. There was no statistically significant decrease of left ventricular ejection fraction (EF%) during three measurement cut-off points with 67.8%, 68.6% and 64.5% respectively ($p < 0.05$). At a median follow-up of 37 months (range 15–93 months) from

the start of rechallenge with trastuzumab-based first line therapy, 1 patient had died and 10 are still on trastuzumab therapy

Conclusion: Trastuzumab paired with a standard chemotherapy as starting treatment can also be continued alone, with subsequent chemotherapy or with hormone-blocking medications, such as an aromatase inhibitor or tamoxifen. Long-term trastuzumab-based therapy showed clinical benefit (CB) and 50% of patients survive more than 122 months. In women at higher risk of recurrence and with no signs of a weak heart, long term trastuzumab offers far more benefits than risks.

TOBACCO USE AND SECONDHAND SMOKE AS RISK FACTORS FOR LUNG CANCER

I. Pavlovska¹ Ph.D., N. Orovcanec¹ Ph.D., B. Tausanova¹ Ph.D., B. Zafirova¹ Ph.D.

¹ Institute of Epidemiology and Biostatistics with Medical Informatics, Medical faculty,
Skopje, Republic of Macedonia

Background: Cancer represents a particular problem in highly developed industrial countries. In these countries, a great percent of general population belongs to older age categories, in which the risk of occurrence of this disorder is higher. Lung cancer (LC) is the most frequent disease in the world. Worldwide, about 80% of LC cases in men and 50% in women are caused by tobacco smoking. Other risk factors include secondhand smoke and exposure to asbestos, radon, arsenic, and air pollution. Tobacco also causes deaths among non-smokers. Exposure to secondhand smoke in the home, workplace, and public areas also kills tens of thousands of non-smokers every year. Our specific **objective** was to analyze the role of active and passive smoking in lung cancer risk.

Method: The investigation was an analytical type of case-control study. It elaborated 185 patients diseased of lung cancer (investigated group-IG), and the same number of persons without malignant disease (control group-CG). Both group members were interviewed during the initial 18-month period of the study. Risk analyses were done using unconditional logistic regression, which provides results in the form of crude odds ratio. The odds ratios and their 95% confidence intervals (CI) were computed.

Results: Among patients were 67% of current smokers (CS), 23.8% of former smokers (FS) and 9.2% of never smokers (NS), compared to 40.5% of CS, 28.7% of FS and 30.8% of NS among controls. The greatest percent of the diseased (44.4%), started smoking up to the age of 15-years. LC patients, in average, smoked almost 29.95 ± 11.03 cigarettes per day (c/day), compared to the controls, in whom the average was 21.35 ± 9.50 c/day. Most of the members in both groups consumed cigarettes with filter (LC-87.1%; CG-97.4%). In the group with LC 33% tried to stop smoking, and their stoppage period, in average, was 9.48 ± 13.04 months. CS and FS, together, had 4.40 (95%CI, 2.44-7.93), times as great risk to become ill from LC in relation to the NS. CS who smoked >40 c/day had 3.56 times (95%CI, 1.23-12.64), significantly greater risk to get LC, compared to those who smoked <40 c/day. CS whose length of the smoking period was >40 years (y), had 3.94 (95%CI, 2.11-7.35), times greater risk to become ill compared to those who smoked <40 y. Exposition to passive smoking was registered in 82.4% from the members of the IG, i.e. 63.2% members of CG. In addition, 42.8% of

the diseased non-smokers inspired the cigarettes smoke at the working place and at home. Exposition to passive smoking lasted >16y in almost all diseased persons (92.9%). The risk of developing LC is 2.72 (95%CI, 0.7-10.59), times greater in the exposed to passive smoking, compared to the non-exposed.

Conclusion: Lung and other cancers caused by tobacco are often untreatable at the time of diagnosis. The key to reducing these cancers is to prevent initiation of smoking in young people, and to encourage smokers to quit. Quitting smoking substantially reduces cancer risk.

PSEUDOPAPILLAR PANCREATIC CANCER-FRANZ TUMOR -CASE REPORT

Dr. Ljubica Nožinić-Vilus, dr Miroslav Milješić
Primary Health Center Sabac, Serbia

Background: Pseudopapillar 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 hemato-peritoneum 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, pseudopapillar 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

Dr. Ljubica Nožinić-Vilus, dr Miroslav Milješić

Primary Health Center Sabac, Serbia

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 confirmed :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.

IMMUNIZATION

CURRENT AND FUTURE TRENDS IN IMMUNIZATIONS

Bernardus Ganter, former Senior Adviser, Communicable Diseases Health Security and Environment, WHO, Regional Office for Europe

Immunizations is considered to be one of the most cost-effective interventions in infectious disease control, and during the last 20 years tremendous success has been made globally in reducing those diseases which are preventable by immunizations. In 1988 over 300.000 children were estimated to suffer from poliomyelitis each year leaving most of those crippled and disabled for life. Over 125 countries were considered endemic for the wild poliovirus. In 2012 less than 500 cases of poliomyelitis were reported and these occurred in only 4 countries, Chad, Nigeria, Afghanistan and Pakistan. The eradication of this disease is imminent. However there is no reason for complacency. An outbreak of over 60 cases in Tajikistan in 2010 caused by low levels of vaccination during several years, highlights the importance to maintain high levels of immunization and surveillance of suspected cases at all times.

Similar success stories can be told for other infectious diseases which are preventable by immunization and WHO estimates that between 2 and 3 million deaths are now prevented by vaccination against diphtheria, tetanus, pertussis (whooping cough) and measles. In 2010 around 109 million children received 3 doses of the diphtheria, tetanus, pertussis (DPT3) vaccine. 130 countries achieved immunization coverage of over 90% with DPT3 in 2010.

Increasingly new vaccines are added to the existing national immunization schedules. In 2010 Hepatitis-B vaccine is used in 179 countries, Haemophilus influenzae type B (Hib) in 169 and global coverage of this vaccine is estimated to be 42% Rubella vaccine, usually in combination with measles vaccine was introduced in 130 countries, mumps vaccine in 118 countries, pneumococcal vaccine in 56, rotavirus vaccine in 28 and human papilloma virus vaccine (HPV) in 37 countries. Other older vaccines are more widely used such as yellow fever vaccines in at risk areas and groups and tetanus vaccine in mothers (MNT).

As result of these achievements and continuous increase of immunization coverage many diseases become more rare and people, parents are less inclined to actively look for the vaccination of their children or themselves. Vaccination refusal is a common problem in many countries as parents do not recognize the benefits of the vaccines in the absence of apparent disease. A breach in herd immunity easily leads to outbreaks of disease and this is observed especially for measles, rubella and pertussis.

A good example is the situation with measles and rubella, currently targeted by WHO for elimination in 2015 and reduction of deaths by 95% compared to the situation in 2000 when an estimated 535 000 children died of measles. In 2010 over 139000 children died of measles most of them in countries with poor health care systems, poverty and malnutrition. In 2010 for the first time since 2006 the global number of reported measles cases increased and perhaps surprisingly most of this increase was caused by large outbreaks occurring in the European Region. This continued in 2011 showing outbreaks especially in West European countries. On average over 75% of the cases were unvaccinated children.

Vaccine are considered one of the most effective and safe public health interventions and adverse events to vaccine are usually limited to local reactions and fever. Serious adverse events are extremely rare. Scientific evidence of the association

of measles vaccine to the occurrence of Crohns disease, Guillain Barre syndrome and autism are now considered extremely weak, if not absent. WHO considers that severe neurological adverse events after measles vaccination are less then one in 1 million vaccinations, and there causative association to vaccination is still doubtful. Contra indications for vaccination are very few and are mainly related to a severe anaphylactic reaction to a previous dose. Never the less, parents concern about the safety of vaccines is the main reason for under vaccination in Europe. There is a growing number of people who distrust vaccinations, in the United Kingdom a recent study showed that 28% of parents interviewed expressed concern on the safety and benefits of vaccination.

The role of medical staff and the media cannot be under estimated. In the US a direct relation could be established between the positive influence of the general practitioner on the est parents believes about vaccine safety.

On the other hand many more children could be vaccinated if all opportunities to do so would be used. Population studies and exit screening studies at health facilities show that on average 30% of children eligible for vaccination miss that opportunity. Many of these missed opportunities for immunization are related to health care related procedures, such as not applying several vaccines at the same time, false contra-indications indicated by health care staff, timing of vaccinations on a specific day or hour, lack of vaccines among and other reasons.

Despite the tremendous impact that immunizations has made on child survival and the increasing availability of new vaccines to combat infectious diseases and other conditions, vaccine uptake is stalling. Refusals of vaccination and missed opportunities to administer vaccines in eligible children are of increasing concern in the world, specially when parents are not fully informed about safety and benefits of vaccines. Medical personal should be further made aware of the safety of vaccines and missed opportunity studies in health care settings can provide additional and useful information were and how vaccine uptake can be improved, leading to higher coverage rates and ultimately improved disease control and reduced mortality and disability. On the other hand national surveillance systems to notify adverse events after vaccinations would further provide information that serious events are rare, but that these events are carefully monitored. This would further provide confidence to parents and caretakers.

MANTOUX TEST IN VARIOUS FORMS OF CHILDHOOD TUBERCULOSIS AND CONTACT POSITIVITY

Taushanova B, Orovcanec N, Zafirova-Ivanovska B, Pavlovska I

Medical Faculty, Institute of Epidemiology and Biostatistics, Ss.Cyril and Methodius University Skopje, R. Macedonia

Objective: To study the role of the Mantoux test and contact history in various forms of childhood tuberculosis.

Methods: A retrospective and descriptive study was carried out in Pediatric Tuberculosis Department at the Kozle Institute for Respiratory Diseases in Children, Skopje, Macedonia. 314 children with diagnosed various forms of tuberculosis, treated during the period of 2003-2007 were object of the investigation. Clinical examination findings, basic investigations, chest skiagrams, computeriazied tomography (CT),

wherever warranted, sputum or gastric aspirates for AFB smear, conventional (L-J) culture, histopathology wherever possible were analyzed.

Results: Out of 260 children with positive Mantoux test, the distribution among various forms of tuberculosis was: Mantoux positivity in 147 (56,4%) children with TBC pulmonum primaria, 45 (17,3%) children with TBC pulmonum primaria complicata, 27 (10,45) children with TBC lymphadenitis, 37 (14,2%) children with primoinfectio specifica, 2 (0,8%) children with complexus primarius, in 1 (0,4%) child with TBC meningitis and in 1 (0,4%) with TBC fibrocavosa.

Out of 187 confirmed cases with contact positivity, 112 (59,9%) children have TBC pulmonum primaria, 33 (17,6%) children have TBC pulmonum primaria complicata, 18 (9,6%) have TBC lymphadenitis, 22 (11,8%) have primoinfectio specifica, 1 (0,5%) was child with complexus primarius, 1 (0,5%) child has TBC meningitis.

Mantoux positivity was 82,8%, contact positivity was 59,56%.

OR=2 was calculated for all forms of tuberculosis in children. OR was 8,57 for TBC pulmonum primaria, which means that the chances of resulting with the Mantoux positive test are almost eight times higher in children under the risk of positive contact with TB infection.

The sensitivity of the Mantoux test for all forms of tuberculosis was 62%, the specificity was 52%. The sensitivity of the Mantoux test for TBC pulmonum primaria was 71,43%, the specificity was 77,41%. The positive predictive value was 93,75% for TBC pulmonum primaria.

Conclusion: The chances of resulting with the Mantoux positive test are almost eight times higher in children under the risk of positive contact with TB infection. Sensitivity of the Mantoux test for TBC pulmonum primaria was 71,43%, which was higher than the sensitivity of 62% for the Mantoux test calculated for all forms of tuberculosis. Specificity of the Mantoux test was 77,41% for TBC pulmonum primaria, which was also higher than the specificity of 52% for all forms of tuberculosis. Mantoux test is still important for diagnosing TBC pulmonum primaria. There is a need of providing a new test for screening and diagnosing all other forms of tuberculosis.

Key words: Mantoux test, Childhood tuberculosis, contact history

THE DEVELOPMENT TENDENCY OF VACCINATIONS COVERAGE IN THE WEST PART OF R.MACEDONIA

Isjanovska Rozalinda, MD.PhD, professor, Stefanovska V.V, MD.PhD, professor, Zafirovska B, MD.PhD, professor, Tausanova B., MD.PhD, professor, Pavlovska I., MD.PhD,

Institute of epidemiology, Medical faculty, University St.Ciril Metodij, Skopje, RMacedonia

Vaccines are one of the greatest achievements of biomedical science and public health. Vaccines are valuable, cost-effective tools for preventing disease and improving community health. Despite the importance and ubiquity of vaccinations childhood immunization coverage rates vary widely by geography, race and ethnicity. Healthy People 2010 objectives include increasing vaccination coverage among children. For the children, the target is $\geq 90\%$ vaccination coverage for the following: Hepatitis B

vaccine; diphtheria, tetanus toxoids, pertussis vaccine, poliovirus vaccine; measles, mumps, rubella, haemophilis influenza tip B, TBC. The data were analyzed from reports submitted for ten years-2001-2010 for 5 communities –Kicevo, Vranstica, Drugovo, Zajaz and Oslomej, the data were obtained from health records , immunization records. Vaccination coverage was calculated by comparing the number of children eligible for immunization with the number of vaccinated children. This study summarizes findings from the retrospective analysis which indicate that approximately 5 communities have reached the 2010 objectives of at least 90% coverage for all of the vaccines recommended with some exceptions of some community with lower coverage rates for some vaccinations. The linear trend show the development tendency decrease for Macedonian and Roma national children vaccination coverage, but for Albanian and Turkey children the development tendency increase. Rubella vaccination, DeTePer 3 , polio3, measles, were significantly lower in rural community Zajas and Oslomej in the first five years, lower than 90% vaccine coverage. To achieve the full potential of vaccines, parents must recognize vaccines as a means of mobilizing the body's natural defenses and be better prepared to seek vaccinations for their children; health-care providers must be aware of the latest developments and recommendations; vaccine supplies and financing must be made more secure, especially for new vaccines; researchers must address increasingly complex questions about safety, efficacy, and vaccine delivery and pursue new approaches to vaccine administration more aggressively; and information technology to support timely vaccinations must be harnessed more effectively.

ROUND TABLE

РЕЗУЛТАТИ ОТ АНКЕТНО ПРОУЧВАНЕ

Доц. д-р Андрей Кехайов, дм

Президент на Сдружение Югоизточно-европейски медицински форум

71% от лекарите в България са неудовлетворени професионално и 69% не се чувстват защитени от съсловната си организация - това сочат резултатите от национално изследване, проведено сред 720 лекари от 94 населени места от страната през февруари-март тази година. Изследването извърши екип от професионалисти на Сдружение „Български лекар” под формата на анкета сред лекарите, с цел да се установят основните фактори, които влияят върху тяхната удовлетвореност.

Изследването се проведе електронно с помощта на изследователски инструмент-въпросник. При съставянето на въпросите се ползва опит от подобни изследвания, проведени сред лекарите в Швейцария, САЩ и Англия, както и в Македония (HEALTHGROUPER). Финалният въпросник е адаптиран към целта на изследването и ситуацията в страната. Съставен е от 22 въпроса.

Анализирани са факторите, определящи удовлетвореността на лекарите от приходите, сигурността на работното място, сътрудничеството с колеги и работната атмосфера, имиджа в обществото, в семейството и сред приятелите, както и сред пациентите. Тук са включени и въпроси, свързани с условията на труд и качеството на здравното обслужване; евентуален интерес за промяна на работното място и общото удовлетворение от работата като лекар в България.

Отделна група въпроси се отнася до удовлетвореността от реформите, които се провеждат в здравеопазването, Националния рамков договор и ръководството на съсловната организация.

Имаше и два открити въпроса с възможност да се коментира, а именно: Какви препоръки имате към БЛС и неговата дейност?

Какво най-много НЕ ви харесва в работата ви като лекар в България?

Основни изводи

1. 60% от лекарите не са доволни от заплатата, която получават.
2. 50% от лекарите не са доволни от статута си на лекар в обществото.
3. 79% от лекарите се оплакват от стреса в работата си.
4. 90% не са доволни от реформите в сектора.
5. 69% смятат, че ръководството на съсловната организация не изпълнява функциите си
6. 75% не са удовлетворени от НРД 2012
7. Почти половината лекари не биха препоръчали професията си на младите.
8. Общата неудовлетвореност от работата като лекар е 71 %
9. 56% от търсещите промяна желаят да напуснат страната.

THE INFLUENCE OF POLITICAL AND LEGAL ENVIRONMENT ON THE ACCESS TO MEDICINES AND PHARMACEUTICAL SERVICES

M. Nenchev¹, A. Stoimenova², G. Petrova²

¹ Bulgarian Pharmaceutical Union

² Department of social pharmacy and pharmacoeconomics, Faculty of pharmacy,
Medical University-Sofia

Address for correspondence:

Assoc. Prof. Assena Stoimenova

Introduction: The effective health care system should provide to every individual access to medicines, medical care and pharmaceutical services. Facilitating access is concerned with helping people to command appropriate health care resources in order to preserve or improve their health and it is one of the priorities in the health care sector state policy. The extent to which a population 'gains access' depends on financial, organizational and social or cultural barriers that limit the utilization of services. Thus access is dependent on the affordability, physical accessibility and acceptability of services. However, the importance of political and legal environment on these aspects of the access is undisputed especially in the light of liberalization of pharmaceutical sector in Bulgaria which resulted in vertical and horizontal integration in the various segments of the sector, oligopoly, impaired drug supply in rural areas, violations of regulatory requirements for dispensing of medicines etc. Policy makers and health specialists in Bulgaria are called to improve the health care system as regards to ensuring better access to medicinal products and related services in the pharmacies. Every strategy for achieving these particular goals must be based on a deep analysis of the current situation and precise across the country data is needed to establish measures for ensuring better access to medicines and pharmaceutical services.

The aim: of this publication is to present the results of the survey performed amongst Bulgarian pharmacists, members of Bulgarian Pharmaceutical Union, on various aspects of retailing pharmaceutical sector ensuring access for people to medicines.

Materials and methods: Inquiry survey was performed among pharmacists, working in retail sector. The inquiry includes questions related to ownership of pharmacies; the allocation of pharmacy; vertical integration; introduction of fixed medicines' prices; restrictions on opening of new pharmacies, availability of over-the-counter (OTC) medicines in drugstores; relations with National HealthCare Insurance Fund (NHIF); etc. 487 pharmacists (406 females/81 males) from 9 districts were included in the study and 100% response rate was achieved due to the methodology for collecting the data (questionnaires were provided and collected during educational events). 162 (33.26%) of the respondents were pharmacy owners (pharmacists), 159 (32.65%) were employees in pharmacies owned by pharmacists and 140 (28.75%) were hired by non-pharmacists' owners.

Results: 455 (92.43%) of the respondents approved the re-introduction of so called "ethical model" of pharmacy ownership (only pharmacist to be eligible to pharmacy ownership and establishment). 369 (75.77%) pharmacists considered there must be a restriction on the number of pharmacies/per pharmacist. Only 160 (32.85%) of the respondents considered that "one pharmacist-one pharmacy" rule should be implemented. 350 (71.87%) of the respondents approved 100% ownership of the

establishment capital by the pharmacist-owner. Various measures against the uncontrolled increase of the number of pharmacies in Bulgaria, seen in the last 20 years were proposed by the respondents: e.g. 2 pharmacies/per pharmacist-owner; obligatory 24 h. coverage of every second established pharmacy (to improve the physical access to medicines in rural areas); 1 pharmacy/5000 inhabitants; introduction of minimal distance between pharmacies etc. 336 (69%) do not approve the existing vertical integration in the pharmaceutical sector and only 0.61% of the respondents considered that the medicines prices should not be fixed. Only 9% of the respondents were against restriction of the type of OTC medicines sold in the drugstores outside the pharmacies. The pharmacists proposed various measures that could improve the access to medicines in rural areas in Bulgaria (obligation for establishment of certain number of pharmacies in rural areas and 24 hours service) as well as the access to pharmaceutical services (fixing of medicines prices will move the patient focus from price to the counseling role of the pharmacists).

Conclusions: The liberalization of the pharmaceutical sector did lead neither to price decrease nor to improved services available in the pharmacy. Pharmacists' opinion and proposed measures based on their daily experience with patients, the system and National HealthCare Insurance Fund should be taken into consideration by the policy makers who are called to improve the health care system.

PROFESSIONAL CAREER OF YOUNG DOCTORS – UNDERESTIMATED PRIORITY ISSUE OF HEALTH REFORM

Veselin Borisov

Professor, Doctor of Medical Sciences

Faculty of Public Health, Medical University, Sofia

Career development of young doctors are increasingly important for health systems worldwide. The problem of young doctors is part of the general problem of management of human resources in the healthcare. Basic key aspect of this problem is the professional motivation of graduating physicians. But special studies on the motivation of new graduates and young doctors are few.

Some studies of Bulgarian authors showed that the problem of young doctors standing outside the attention of both health policy makers and the professional organization of physicians (Bulgarian Medical Association). According to S.Vasilev significant percentage (41.1%) of young doctors do not see a clear perspective and opportunities for future permanent career in public hospitals. In the 2010 survey identified a number of young physicians difficulties and problems in their daily activities. These hardships are mainly organizational (scheduling, congestion), socio-psychological (communication, peer), great documentation and financial difficulties. Impressive low percentage of reported financial difficulties and the relatively high proportion of socio-psychological difficulties – difficulties of communicating with patients, difficult interactions with older peers and others.

There is actual or potential turnover, which indicates a weak integration of young doctors to this team and the conditions of the hospital. This report concludes that the professional implementation of the new generation of doctors is at risk and many

random factors. It is needed overall system strategic approach to planning and managing their career development and development.

ЧАСТНОТО БОЛНИЧНО ЗДРАВЕОПАЗВАНЕ В БЪЛГАРИЯ – МИНАЛО, НАСТОЯЩЕ, БЪДЕЩЕ

Доц. д-р Стайко Спиридонов, д.м.

Председател на Националната асоциация на частните болници, България

Болницата е най-сложната институция в съвременната здравеопазна система. За нейното функциониране са необходими огромни ресурси. В статията авторът проследява развитието на частното болнично здравеопазване в България, като го разделя на три периода: минало – 1991 г. – 1998 г.; прави анализ на настоящето; поставя цели за развитието на сектора в бъдеще.

В края на XX в. в България бе поставено началото на реформата в управленската структура на здравната система.

През 1991 г. промени в Конституцията на Република България разрешиха частното здравеопазване. Една година по-късно в България има 3 частни болници. Характерни белези за периода са неравнопоставеността на частните болници спрямо публичния сектор и липсата на банково кредитиране.

След 1998 г. е налице политическа воля за цялостна реформа в сектор „Здравеопазване“. Закон за лечебните заведения регламентира равнопоставеността на частните и държавните лечебни заведения и защитава конституционното право за избор на пациента. Приети са Закон за здравното осигуряване и Закон за съсловните организации.

Към днешна дата броят на частните болници в България е нараснал на 102. Повечето от тях са членове на Националната асоциация на частните болници - правоприемник от Сдружението на болниците с частно участие, учредено на 14 септември 1994 г. Годишно частните болници извършват 9% от цялата медицинска дейност в страната.

Проект за дългосрочна здравна стратегия на България може да предвижда приватизация на всяка 5-та болница от публичния сектор. Очаквания за бъдещето: разрастване на частния сектор, повишаване на качеството при диагностиката и лечението, равнопоставеност при финансирането на публичния и частния сектор.

NATIONAL MEDICAL ASSOCIATIONS AND CHAMBERS IN SOUTHEAST EUROPE - ROLE FOR THE PROFESSIONAL SELF- REGULATION

STAGES OF DEVELOPMENT, ACHIEVEMENT, PRESENT AND ROLE OF ORGANIZATIONS OF PROFESSIONAL MEDICAL SELF-GOVERNANCE

Oleg Musii, MD

President of the Ukrainian Medical Association, Kyiv, Ukraine

World history of unite of doctors-professionals in their own organizations to defend corporate rights is over 200 years old. With the development of the medical profession, these organizations reach a higher structural and organizational

development. Becoming of organizations of physicians can be divided into several periods of their development.

More than 100 years ago, in many European countries, organizations of doctors began to move to a new level of influence and participation in the health systems of their countries. States, realizing advanced and progressive role of organizations of professionals on law level regulated their status and authority by transferring for corporate organizations of physicians a number of important public functions. This time can be described as 1st period of develop of the relationship between the state and doctors-professionals - the period of self-regulation of professional medical organizations.

Next, the 2nd period of development, the period of transition to self-government, within the time around from the end of II World War a long for 20-30 years, can be set as qualitative growth self-regulation and moving to self-government of physicians organizations. During this period, established a number of international medical organizations and structures that summarized the experience, activity and status of medical corporation's organizations in each of the participating countries. Most effective of these organizations is the World Medical Association (WMA).

Last present, 3th, the period of formation and development of medical self-governance, began about 30 years ago. This transition from the existing self-government to quality higher functions, powers and responsibilities - medical self-governance. At this period of development occurred with the adoption of relevant legislation about self-regulation medical professions in almost all 12 countries of Central and Eastern Europe.

Despite the success in obtaining professional and clinical autonomy, over the last few years we have witnessed how the governments of several countries, contrary to the established international practice, trying every way affect the independence of the medical profession, to put it under control, limiting and reducing the existing powers of medical organizations. These negative processes we see in Slovakia, Bulgaria, Turkey, Western Africa, attempts in Poland, some countries of the former Soviet Union. Instead achievements that are in the countries of former Yugoslavia, can serve as an example of understanding of the importance of principles that are declared in the documents of the WMA concerning professional autonomy and freedom, and clinical independence of medical professionals.

I think that one of the important tasks of organizations of doctors in the world are explaining to governments and popularization among the medical community and introducing in their countries key principles embodied in these documents of the WMA, namely:

WMA Statement on the Twelve Principles of Provision of Health Care in any National Health Care System (New York, 1963),

WMA Declaration of Lisbon (1981),

WMA Declaration on Physician Independence and Professional Freedom (Rancho Mirage, CA, USA, 1986),

WMA Statement on Physicians and Public Health (Bali, 1995),

WMA Resolution on Medical Workforce (Ottawa, 1998),

WMA Declaration of Seoul on Professional Autonomy and Clinical Independence (Seoul, 2008),

WMA Declaration of Madrid on Professionally-led Regulation (New Delhi, 2009),

WMA Resolution on the Independence of National Medical Associations (Montevideo, 2011),

WMA Council Resolution on the Autonomy of Professional Orders in West Africa (Prague, 2012),

WMA Council Resolution on Threats to Professional Autonomy and Self-Regulation in Turkey (Prague, 2012).

For deepen understanding of basic principles, on which work the now a associations of doctors in world and acts advanced of global medical thought, appropriate to cite a few quotations from the above documents:

“By providing independence and professional freedom for physicians to practice medicine, a community assures the best possible health care for its citizens, which in turn contributes to a strong and secure society”.

“The World Medical Association reaffirms the importance of professional autonomy and clinical independence not only as an essential component of high quality medical care and therefore a benefit to the patient that must be preserved, but also as an essential principle of medical professionalism”.

“The WMA demands that no government interferes with the independent functioning of national medical associations”.

Conclusions for our future activities shall include:

- need to active advocacy and implementation of the modern principles of interaction between our national medical associations and governments of our countries, constructed on basis of the above principles;

- protecting and defending the interests of physicians and patients on the national and international level;

- exchange of experience of activity of national medical associations in their countries and internationally;

- support and ensure the functioning of international medical organizations (WMA, CPME, SEEMF, EFMA, ZEVA, WFUMA, UEMO, UEMS, EMSA etc.), like structures that impact on the formation of professional independence and autonomy of doctors in the world;

- develop joint tactics of counteraction for governments that seek to limit or cancel the influence and independence of our organizations.

Only joint our efforts will be able to provide for our organizations, our doctors, our patients, our citizens, our countries - force, power, safety, highs quality of healthcare and welfare, prosperity to.

ТРАВМИ, ИКОНОМИКА, ФИНАНСИРАНЕ, МИЗЕРИЯ

Проф.М.Миланов, Ст.Миланов

УМБАЛСМ „Пирогов”

Разглежда се сегашното състояние или по-скоро липсата на ТРАВМА в системата на Република България.Посочва се значението на ТРАВМАТА относно морбидитета, морбилитета, разпределени по възрастови групи и загубата на

години потенциален живот.Посочени са основните физиологични и патофизиологични механизми на травматичното състояние.Предлага се нова структура, функция и финансиране на ТРАВМАТА в системата.

THE ASSESSMENT OF QUALITY AS AN APPROACH FOR SWOT-ANALYSIS IN HOSPITALS

Darina Mineva, Boriana Borisova

Faculty of Public Health, Medical University, Sofia

The study refers to new approaches for quality assessment in health care sector. The methods SERVQUAL is used. It measure quality of service by quantitative index “Service Quality Index”, that reflects the correlation between expected quality and perceptions of quality on the basis of five measurements of perfect service: tangibles, reliability, responsiveness, assurance and empathy.

503 patients are investigated in two Bulgarian hospitals – SBALBB “Pencho Semov” JSC - Gabrovo and MBAL “D-r Tota Venkova” JSC - Gabrovo, from February 2012 until March 2012. The methods of statistics, graphic and correlation analysis are used.

It was found that private quality coefficients may be criteria for determination of strengths and weaknesses of organization activities. These of them, which meaning are positive or negative, but nearby zero meaning, define strengths of organization. The negative meaning of private quality coefficients, inclining to one, define weaknesses of organization. The opportunities are the factors of external origin, that are able to change private quality coefficients to positive meaning (to a higher level). Threats are the factors of external origin that are able to change private quality coefficients to negative meaning (to a lower level). The change of customer needs, new products and technologies, drugs, approaches of diagnostics and treatment, changes of public health care politics and legislation, the change of value of society and quality of life. For SBALBB strengths are formed from criteria responsiveness and empathy, but weaknesses – from tangibles. For MBAL strengths are formed from criterion empathy, but weaknesses – from reliability and assurance.

In the paper, it is based on that methods SERVQUAL may be a tool for SWOT analysis by private quality coefficients, as a factors for determination of strengths and weaknesses of organization activities. The system variances (that belongs of process like as: equipment, skills, time of service performance) may be measured by private quality coefficients of methods SERVQUAL. Quality criteria, service quality index and private quality coefficients of less value zero and negative may consider as an equivalent of nominal of process and corresponding of process stability. This is a balance between expectations and perceptions. This analysis may be use as a part of PDCA cycle at the stage of identification of aims of improvements. The methods SERVQUAL is an indirect and qualitative measurer of unsalable additional value of product/service. This measurement is qualitative and prove whether there are or there aren't costs of poorly quality. And relationship of this costs with criteria and quality aspects. This conclusions define the meaning of methods SERVQUAL as a tool for measurement of total quality of services, also.

СЪСТОЯНИЕ НА ОБЩИНСКОТО ЗДРАВЕОПАЗВАНЕ В БЪЛГАРИЯ

Д-р Атанас Атанасов – управител на „МБАЛ Д-р Добри Беров” ЕООД

Общинското здравеопазване в Република България се осъществява от лечебните заведения за първична и специализирана извънболнична медицинска помощ, лечебните заведения за болнична помощ, филиалите на ЦСМП, здравните кабинети в училищата и детските градини и общинските служби, които провеждат местната здравна политика.

Общият брой на лечебните заведения за болнична помощ към 30.12.2011г. е 293. Броят на многопрофилните общински болници за активно лечение е бил 57 от общо около 130 болници за активно лечение в страната. Специализираните болници са 70, а държавните психиатрични болници - 11. Общинските болници за активно лечение са регистрирани по ТЗ като търговски дружества. Повечето от тях са създадени в края на 18-ти и началото на 20-ти век в резултат на исторически възникнали обективни потребности. Към днешна дата тези лечебни заведения са различни по мащаб, обслужват различен брой население и функционират при различни условия, поради което можем условно да ги разделим на няколко групи: големи – с обслужвано население над 80 000 души; средни – с обслужвано население от 50 000 до 80 000 души; малки – с обслужвано население от 20 000 до 50 000 души и много малки – с обслужвано население под 20 000 души.

Към настоящият момент общинското болнично здравеопазване в България е пред пълен срив. Налице са противоречиви управленски действия, на фона на липсваща ясна концепция и национална здравна стратегия, което води здравеопазването и особено общинското към дестабилизация и криза. Част от българските граждани, живеещи в периферните райони на страната са поставени в дискриминационно положение по отношение на достъпа до болнична медицинска помощ. В общините със закрити вече болници е затруднена функцията и на ЛЗ за ИБП и на филиалите на ЦСМП. Функциониращите все още общински болници са лишени от субсидии за оказаната спешна помощ на лица, които не са хоспитализирани, както и за интензивното лечение на хоспитализирани лица, което ги прави неравнопоставени по отношение на финансирането спрямо държавните болници. Липсата на здравна сигурност е допълнителна предпоставка за обезлюдяване на определени региони и засилване процесите на свръхурбанизация.

Необходима е пълна преоценка на посоката, в която се тласка здравната система в България. Реформата трябва да води до по-добро състояние на здравеопазването, а не до по-лошо. Състоянието на здравето се измерва със здравните показатели, които за съжаление в България все повече се влошават. Трябва да се стремим да постигнем показателите на страните от европейския съюз, а това не може да стане със закриването на болници и то точно на тези, които работят с най-малко средства. Институциите следва да имат категорична яснота дали ще продължат да развиват здравно осигурителния модел основан на принципите на солидарност, равнопоставеност, договаряне, свободна конкуренция и пазарни елементи във финансирането или ще върнат здравеопазването към административното регулиране, бюджетното финансиране на остатъчен принцип и петилетните планове.

VARIA

THE BALKAN ANTIOXIDATIVE DIET IN THE PREVENTION OF THE METABOLIC SYNDROME

Sv. Handjiev, T. Handjieva-Darlenska
Medical University, Sofia

Our recent studies have shown that the traditional Balkan cooking from the end of the 19th and the first half of the 20th century is much similar to the Mediterranean diet. Furthermore, the nutritional habits in all of the Balkan countries are stressing on an exclusive closeness. This fact is giving the right to define the Balkan healthy food or the Balkan diet. The traditional nutrition in the Balkan countries is responding to many of the major aspects of healthy food. From the nutritional prevention point of view, the results, related to the risks of developing a disease and their connection to the dietetic models, seem to be promising. The healthy effects of the integral dietetic models are of extreme importance in the nutritional prevention. The statement that the traditional Balkan nutrition from the past century has many beneficial effects regarding many diseases, including metabolic syndrome and the coronary heart disease, is gaining more and more supporters. The traditional Balkan nutrition is rich in antioxidants. The Balkan healthy food contains the highly active antioxidants resveratrole and pycnogenol. The diet is rich in alpha-tocopherol, ascorbic acid, beta-carotene, selenium, bioflavonoids, and many other biologically-active substances.

The traditional for the Balkan cuisine meals are distinguished with various and rich content of biologically active components. Besides the Bulgarian yoghurt and the typical kinds of cheese, here belong the traditional vegetables – a rich source of various flavonoids and carotenoids. The specific character of the culinary treatment preserves the biological activity of the contents. The so called BALKAN HEALTHY FOOD (resp. Balkan diet) has the positive properties and all of the elements of the healthy nutrition. With its rich content of healthy food ingredients the Balkan diet is a circumstance for developing of various preventative and curative diet regimens.

DIAGNOSTIC VALUE OF P SMALL ROUND OPACITIES ON CHEST RADIOGRAPHY AND P' OPACITIES ON HRCT IN EARLY DETECTION OF NODULAR PNEUMOCONIOSIS

Prof. Elisaveta Petrova, MD, PhD, DSC

Head of Section on Preventive Medicine, Tokuda Medical Center, Sofia, Bulgaria

Aim: To perform a comparison between radiological perfusion of p small round opacities (p) on conventional chest radiograph (CCR) and p' opacities on chest HRCT (HRCT) and to assess the diagnostic value of HRCT in patients suspected for nodular pneumoconiosis.

Material and Methods: 84 quartz exposed workers, endangered by pneumoconiosis and patients with reticular, and micro - nodular pneumoconiosis were studied. A comparison between mean profusion of p' - small round opacities on CHRCT with mean profusion of p - small round opacities on CCR was done. A multiple regression analysis was performed.

Results The mean profusion of the p' - small opacities on CHRCT was more intensive in comparison to mean profusion of the p – opacities on CCR. A statistically significant correlation between p' - and p - opacities was found ($R=0.36337$; $P \leq 0.001$).

Conclusion: CHRCT is more sensitive image method for detection of p small round opacities. We recommend CHRCT for early diagnosis of reticular, reticular nodular and nodular pneumoconiosis.

Key words: p small opacities, CCR, HRCT, nodular pneumoconiosis

ЕДИНСТВО НА МАТЕРИЯ И ИНФОРМАЦИЯ – ФИЛОСОФИЯ НА ПСИХО-ФИЗИЧНАТА ОБЕКТИВНА ИСТИНА

Акад. проф. д-р Никола К. Узунов, дмн

Философията е наука за истината и изследване причините и принципите на нещата. Аристотел (IV в. пр. н. е.)

Този абстракт е кратко допълнение към философията на моята книга “ПСИХОЛОГИЯ НА ИСТИНАТА” за мислещия човек, (Изд. “Знание”, 2010 г.)

Мнозина философи са посветили изследвания на проблема за ИСТИНАТА. Философите са се опитвали да съберат отделните части на истината за да може ОБЕКТИВНАТА ИСТИНА да стане пътеводител в живота на хората.

От незапомнени времена философите са се стремели да обяснят какво е истина, защото тя може да служи, като сигурно средство за адекватно поведение на човека спрямо заобикалящата го действителност. Освен това философите са искали да е ясна разликата между истината и заблудата. Цитирано по “Сборник Теории на истината” Съставител Л. Сивилов, 1991 г.

Проблемът ЩО Е ИСТИНА е забелязан още от преди 25 века, от времето на световните мислител и особено от великия учен-философ Аристотел, обявил, че “действителността е познаваема реалност и, че нашето знание е истинско знание”. Аристотел създава първата дефиниция за “Истината като съответствие на мисълта с действителността”, която като, че ли за съжаление остава неразбрана. За Платон истината е една и е система от съответствия.

Арабския лекар КИНДИ, (Абу-Юсуф, Исак, 800-870 г.), основател на арабско-еврейската философия, обявява, че цел на философията е истината.

Рене Декарт (1596-1650 г.), търсейки истината, написа: “Мисля следователно съм”, или “действам, вярвам, следователно съществувам”, съм действителен. Известно е също твърдението му, че поне веднъж в живота си, човек трябва да подложи всичко на радикално съмнение за да открие истината.

Според великия немски философ Хегел (1770-1831 г.), ЗАДАЧА на науката е да ни казва ИСТИНАТА за това което е, и каквото е. Според нас, науката, познанието, училището, журналистиката, политиките, институциите трябва да ни казват задължително ЦЯЛАТА двузначна - духовна и материална - ОБЕКТИВНА ИСТИНА за човека, което и каквото е съществувало, съществува, е общовалидно, има смисъл и значение, е действително, действа и понася въздействие, носи радост или мъка съответно, създава верни повторями резултати и последици. Освен това познанието следва ясно и точно да дефинира, какво е закон, морал,, заблуда, лъжа, измама, посегателство. В противен случай няма необходимост от НАУКА, академии, университети, образование,

правосъдие, щом те не изпълняват своята основна задача да казват истината за нещата и съществата

Науката сравнявам с една огромна тъмна пещера. Естествените науки: медицина, математика, физика, химия и пр., изучават пряко реалността и истината и осветляват добре едната половина на пещерата Другата половина на пещерата е заета от хуманитерните науки. Тук са създадени толкова философии, психологии, журналистики, обществени и пр. науки, колкото са и техните автори. В тази половина на пещерата са нахвърлени най-безразборно различни верни, полуверни и неверни теории, лични гледни точки, митове, заблуди, несъществуващи “форми и закони на мисленето”, абстрактно мислене, диалектизми, изречения “в интерес на истината”, което е абсолютен нон сенс и пр. Очудващо е как лекарите могат да достигат до истината и точните диагнози за минути и часове, а на съдът са необходими месеци и години за решение понякога на елементарни дела. Защото всичко в естествената природа е истина, нормално, смислено, хармония. Извън словесната истина-симетрична на реалността - както и на моралната философия, всичко останало е неистини, полуистини, заблуди.

За Фойербах (1804–1872 г.) най-висшата задача на философията е постигането на обективната истина в познанието на “нещата и съществата такива, каквито те са”.

За Андре Мороа, материя, материално и духовно, култура са двете страни на действителността. Д. Михалчев (1952 г.) отбелязва: “Душевният живот на човека е така действителен, както и телесният”.

Русо, Жан Жак (1712-1778 г.) счита, че ”Във вселената има ред и целесъобразност, а в живота на хората – “хаос”, “бъркотия” и ”безредие”. Творец на злото не е Бог, а самият човек. За Достоевски “Ако няма Бог, всичко е позволено”. Няма ценностна система без ИСТИНА, вяра, религия, справедливост, БЕЗ МОРАЛНА ФИЛОСОФИЯ. Без тези ориентирни няма и не може да има съгласие, солидарност, справедливост, **ОСЪЗНАВАНЕ** на нещата и адекватни действия според действителността и истината.

Според Ж. Моно, ако математиката откаже да търси истината, ще изпадне в противоречие de facto с етиката.

Според видния ютослевски, общественик и политик, Милован Джилас, Енгелс греши прилагайки диалектиката и към природата .

Известният Български философ, психолог, общественик проф. Димитър Михалчев (1880-1967 г.), последовател на немския философ Йоханес Ремке, счита, че “Истината е надиндивидуално, общовалидно, вярно, действително твърдение, което има смисъл и значение, действа и понася въздействие”. Мисленето е пряко свързано с проблема за истината. Истината се изразява чрез верни смислени изречения, както и с т.н. логически закони. Изреченията биват верни и неверни, смислени и безсмислени, действителни и недействителни, положителни и отрицателни. Вярно е смисленото, а невярно е безсмисленото изречение. За Д. Михалчев, съждението винаги утвърждава нещо действително”. Последователите на Й. Ремке учат, че за познанието няма граници, че истината може да е обективна и в хиляди случаи тя е окончателна и абсолютна. (Д. Михалчев, 1998 г.) Според Д. Михалчев, непризнаването на истината от мнозина не означава, че тя не съществува.

Според нас, световните проблеми са: 1. Собствеността 2. Властта 3. Религиите 4. Етническият проблем. Всички те са проблеми на човека и очакват решение от него. Етническият проблем не може да се решава чрез толерантност а чрез истината. Крайно време е той да бъде решен от ООН. Известно е, че често доброто става мост по който минава злото. Според нас човекът е съзнателен, но преди всичко, несъзнателен, пристрастен (любов и омраза). Затова Хедонизмът и Алчността ще затрият света.

Причините да не се осъзнава и признава истината са преди всичко неинформираността, пристрастието, егоизма, егото, алчността, неосъзнаването и, които пречат на човека да разбира истината, като действително, вярно знание и название на нещата с истинските им думи, имена. Важно е още, че много хора нямат интерес от признаване на истината. И днес мнозина искат да няма обективна истина, адекватна на действителността, да няма съд, да сме безотговорни, да не бъдем санкционирани за нашите посегателства, престъпления.

Само с историческо мислене, за ясно минало, сегашно и предвидимо бъдеще, които повеляват, с реална ОЦЕНКА и ОСТОЙНОСТЯВАНЕ, ЦЕНА на социално-икономическото развитие на народите,- адекватно на текущата действителност,- човек може да има нормално речево и дейностно поведение. Ето защо пазарът и държавата следва да работят с единствените мерки “ЛЕВЪТ (цената) и ИСТИНАТА” а не чрез измислени политически догми. Наложителен е също строг кантрол над банките.

Според нашата философия за Единство на материя и информация-философия на обективната истина-

Материята, действителността, реалните живи и неживи неща, с тяхните качества и количества е материалното начало.

Информацията, паметта психиката, психичното, духът на човека, знанието, силата и въображението на мисълта, вярата, идеите, преживяванията, емоциите, чувствата, радостта, мъката назовани с думи, със смисъл, значение е духовното начало. Човешкият дух, знанието за Бога е ОСНОВА НА ДУХОВНАТА КУЛТУРА. Всички неща и същества в света са назовани с верни или неверни, смислени или безсмислени, действителни или недействителни думи. Материя и информация винаги са дадени в единство, макар, че двете са коренно различни, но са действителни неща. Материалните неща имат място, форма, големина, тежест, граници. Духовните неща, са несетивни, невидими с обективно око. Идеите, човешкият дух, знанието, преживяванията, емоциите нямат място, форма, тежест, големина, граници. Те са безгранични, Проблемът за взаимодействието на тялото и душата, психичното и материалното, субектът и обектът, все още не е решен окончателно. Виж ПСИХОЛОГИЯ НА ИСТИНАТА Н.Узунов, 2010 г.

Нашата тези е: ЕДНА, но двузначна е душевно-телесната действителност на човека и ЕДНА, но двузначна е обективната истина за него (материална и духовна, обща и конкретна, добра и лоша, радост и мъка, любов и омраза, материя и информация, човек и среда, начало и край на живите неща, живот и смърт и пр.), защото всичко у човека, обществото и природата е двустранно и повтарящо се. Истината се доказва само чрез истината. Истината подлежи на степенуване. За

истината са дадени много свидни жертви през всички времена. За истината не може да има давност.

Обективната истина няма никакви недостатъци. Тя способства за нормално мислене и поведение. Тя не пречи на въображението, на хората да се обичат. Истината често е ледена, студена. Да, при смъртта тя е такава. При нея няма, ако, дали, защото е обсолютна и окончателна истина.. Справедливост без истина не може да има. Справедливостта е конкретна човешка морална категория, която трудно се дефинира като общовалидно нещо. За нея няма мярка. Справедливостта не може да предотвратява пожари, наводнения, бедствия, беди и пр. Когато еднозначната и двузначната истина се знаят, тогава те могат да предвиждат. Истината може да се облагородява, лекува, облекчава, подкрепя, подпомага от истината, религията, поезията, театъра, от справедливостта, от хората. Обективната истина е **НАЙ-ОСТРОТО ОРЪЖИЕ**, което разумът на човека е измислил за борба с хаоса, посегателствата. **МОРАЛЪТ**, моралната философия, моралното съзнание, като 10-те Божии заповеди (не кради, не лъжи, не прави това което не искаш да правят на тебе), също следва да изпълнява важна роля. Светът не започва от нас и от днес. Светът има минало, което задължава, сегашно, което изисква и бъдеще, което повелява, според проф. А. Клисарова, лекар. За бъдещто следва да мислим от днес, защото ще има живот и след нас.

VITAMIN D- RECOMENDATIONS FOR OLDER ADULTS

prof.dr. Snezana Markovic Temelkova

Clinic of endocrinology and metabolic disorders, Clinical center Skopje, Macedonia

Cholecalciferol (D3) is the naturally occurring form of Vitamin D in the skin and in food. It is converted in the liver to: calcidiol (25-hydroxy Vitamin D), which is considered a “prehormone.” The calcidiol blood level is measured to assess Vitamin D stores in the body. Calcidiol is converted in the kidneys, breast, prostate, ovary, pituitary, brain, etc to calcitriol (1,25 hydroxy Vitamin D), which maintains calcium in the blood and has an array of effects in the body’s organs. (1)

Vitamin D functions as a steroid hormone. Cells containing 25OH-VitD3-1-alpha-OHase are: Breast, prostate, lung, skin, lymph nodes, colon, pancreas, adrenal medulla, brain, placenta (2,3)

There are a lot of cells which contain Nuclear VDR(vitamin D receptors) like: pancreatic islet cells, monocytes, transformed B cells, activated T cells, neurons, prostate, ovaries, pituitary, aortic endothelium, placenta, skeletal muscle cells.(4,5).

Vitamin D has few effects: on fracture risk, effects on neuromuscular function and falls, effects on calcium metabolism and effects on other health parameters.

Effects on fractures: A recent meta- analysis revealed that vitamin D in doses in the range more than 400-800IU/day(10-20mcg/day) reduces the risk of nonvertebral and hip fractures approximately 20%(6). Study of Osteoporotic Fractures: low 1,25(OH)2D - associated with ↑ hip fractures. Vit D intake < 100 IU/d - ↑ risk of hip fracture (7) . Vitamin D reduced incidence of vertebral fractures by 33% (8)

Vitamin acts on myocyte vitamin D receptors to exert its effects on muscle tissue. In prospective studies, lower serum 25HD levels have been associated with decrease grip strength and appendicular muscles mass in the older men and women

(9,10). Supplementation with vitamin D has improved lower extremity muscle performance and reduced risk of falling in several high quality double blind RCTs (11). Test which we should be ordered are: serum 25 OH Vit D (calcidiol) . Normal cluster 30-32 ng/ml(75-80nmol/L) “levels of 28-40 may lower the fracture risk” . No consensus on optimal 25OHD concentration for skeletal health. Several factors influence the increment in serum 25OHD in response to a given dose of Vit D3. : starting level of OHD, varies with a body size (smaller in subjects with high BMI than in individuals with normal BMI, OHD3 levels decline with aging, serum OHD very across commonly used assays) If we have supplementation in high-risk individuals, the serum 25OHD levels should be retested after about 3 months of supplementation to confirm that the target 25OHD level has been reached .

The required dose to reach 75 nmol/L can be estimated from the measured level. Each 2.5 µg (100 IU) of added vitamin D will increase the serum 25OHD level by about 2.5 nmol/L (range 1.75–2.75 nmol/L) or 1.0 ng/ml (range 0.7 to 1.1 ng/ml)(12)

Concerning hearth disease, MI risk doubles in pts with 25OHvitD levels <34ngr/ml (13). CHF pts have much lower 25OHVitD levels than controls (14) Deaths from CAD are more common in winter (15). Vitamin D deficiency is positively correlated with incident cardiovascular disease.

Concerning blood pressure: BP is higher in winter, BP higher with increasing latitude , BP higher with darker skin pigmentation(16).

Concerning cancers: Analyzed in terms of reviews, controlled and epidemiological studies relationship exists between sunshine exposure and overall cancer mortality (colon, prostate, breast). Exposure positively correlated with a lower risk of overall mortality due to organ cancer. (17)

Conclusion: vitamin D3 should be used as substitution (its active metabolites are not substitute for adequate vit D intake.

IOF estimates that vit D requirements for older adults to reach a serum 25OHD level of 30 ng/ml is 800-100IU/day(20-25mcg/day). The repletion need to be adjusted upward to as much as 50 mcg/day(2000 IU/day) in individuals who are obese, with osteoporosis, limited sun exposure with malabsorbtion (18)

ПУТЬК МЕМБРАННОМУ ПЛАЗМАФЕРЕЗУ

Prof. Valery A. Voinov, MD, PhD.

1961-1985г:В этот период шло освоение аппаратуры и методов экстракорпорального кровообращения при операциях на открытом сердце. Наличие частых осложнений после этих операций, главным образом лёгочных, заставили искать причины их возникновения. Многочисленные эксперименты (всего – более 2000 на собаках) позволили придти к выводу, что они являются следствием травмы крови во время экстракорпорального кровообращения. С этой целью участвовал в разработке первых Российских мембранных оксигенаторов «Север». Докторская диссертация «Постперфузионный лёгочный синдром» явилась результатом этих разработок.

Работая над этой проблемой не мог пройти мимо острых поражений лёгких, возникающих при острых пневмониях, панкреатитах, перитоните, тяжёлых травмах и ожогах, эклампсии беременных, септическом шоке.

Эксперименты на животных позволили установить, что эти поражения лёгких, объединённые понятием «Острый респираторный дистресс синдром», являются токсическим отёком лёгких вследствие эндотоксикоза и только детоксикация может восстановить их нормальную функцию. При этом экстракорпоральная мембранная оксигенация может компенсировать газообмен, но не в состоянии ликвидировать эти поражения лёгких. Только включение в экстракорпоральный контур гемосорбционных колонок позволили в течение 24-40 часов восстановить воздушность лёгких и нормализовать их газообменную функцию, в то время как и до сих пор при использовании только экстракорпоральной мембранной оксигенации (без детоксикации) для этого требуется от 2-х до 3-х недель.

1985-2000гг. В этот период встала задача лечения аутоиммунных диссеминированных заболеваний лёгких (фиброзирующие альвеолиты, саркоидоз). Оказалось, что с помощью гемосорбции невозможно достаточно эффективно удалить из организма аутоантитела и циркулирующие иммунные комплексы. Для этого требуется их удалять вместе с жидкой частью крови – плазмой и такая процедура носит название плазмаферез (аферезис по гречески – удаление). Однако в нашем распоряжении были только громоздкие центрифуги, в которых можно было отделять плазму от клеток крови. Но для этого требовались большие объёмы крови (до 500 мл), которые необходимо было забирать и для тяжёлых больных это создавало порой непреодолимые трудности. Поэтому было принято решение разработать собственные мембранные плазмодильтры. После целого ряда экспериментов такой плазмодильтр ПФМ-800 был создан и в 1992 году Минздравом России он был допущен для клинического применения.

2000-2011гг. Мембранный плазмаферез стал активно внедряться в медицинскую практику, однако стали видны и недостатки плазмодильтра ПФМ-800, чему способствовали некоторые конструктивные просчёты, а мягкий корпус позволял нарушать целостность его при транспортировке, хранении и сборке. Были ясными и недостатки аппарата «Гемос», который использовался при мембранном плазмаферезе. Поэтому перед вновь созданной компанией «Трекпор Технолоджи» была поставлена задача модернизировать и плазмодильтр и аппарат, что и было завершено к 2002-му году. Вновь созданный мембранный плазмодильтр показал высокую надёжность в работе, позволяя отделять все компоненты жидкой части крови и предотвращать попадание в отфильтрованную плазму клеток крови, что позволило Минздраву России разрешить его применение не только для лечебного, но и донорского плазмафереза. То же самое можно сказать и о новом аппарате «Гемофеникс», который позволяет проводить мембранный плазмаферез в автоматическом режиме, поддерживая дозу антикоагулянта и надёжно предотвращая попадание воздушных пузырьков в циркуляцию пациента. Простота и безопасность мембранного плазмафереза позволяют его использовать в любом медицинском учреждении, даже муниципального их звена, в том числе и в амбулаторных условиях.

С другой стороны, малый объём заполнения аппарата «Гемофеникс» даёт возможность его использовать при полиорганной недостаточности в критических состояниях пациентов, даже при нестабильной гемодинамике. При септических осложнениях, развивающихся на фоне иммунодепрессии, только с помощью

массивного плазмафереза с замещением удаляемой плазмы свежезамороженной донорской плазмой можно достичь не только детоксикации, но и восстановление нормальной иммунной защиты с более быстрым выздоровлением. Такой же плазмообмен (plasmaexchange) показал свою эффективность и при кровотечениях на фоне синдрома внутрисосудистого свёртывания крови (disseminated intravascular clotting syndrome).

Накопленный опыт позволил значительно расширить ареал заболеваний, при которых мембранный плазмаферез показывал свои преимущества. В неврологии – это острые и хронические demyelinating diseases (systemic sclerosis, multiple sclerosis, polineuropathy), в ревматологии – systemic lupus erythematosus и многие другие, представленные в прилагаемом списке аутоиммунных заболеваний. Следует отметить и работы по применению мембранного плазмафереза в онкологии, эндокринологии (сахарный диабет и аутоиммунный тиреоидит), в лечении хронических вирусных гепатитов и даже в геронтологии.

Кроме того, были показаны преимущества мембранного плазмафереза в профилактике и лечении ряда осложнений беременности – раннего и позднего токсикоза (преэклампсии), резус-конфликтов, генитальных хроникоинфекций (герпес, цитомегаловирус, хламидии, микоплазма и др.), привычных выкидышей в результате антифосфолипидного синдрома, холестатического гепатоза и HELLP-syndrome.

Малый объём заполнения мембранного плазмофильтра «Роса» позволил успешно его использовать при мембранном плазмаферезе у новорождённых и даже недоношенных младенцев с массой тела от 700 г. Для этого, помимо плазмофильтра, необходим один лишь шприц и небольшой комплект магистралей общим объёмом до 35 мл. Такая методика была одобрена Минздравом России ещё в 1996 году.

CLINICAL USAGE OF EXTRACORPOREAL METHODS OF TREATMENT: EFFERENT THERAPY. PLASMAPHERESIS IN A WIDE RANGE OF DISEASES.

V.A.Voinov

Research Institute of Pulmonology, Saint-Petersburg State I.P.Pavlov University of Medicine.

Efferent therapy finds more and more wide application in clinical practice. Many human diseases are accompanied by disturbances of structure of the internal environment which define the severity of a clinical course in many aspects and even may become principal reasons of failure, despite the usage of advanced modern medicamentous means or surgical treatment. Such problems arise during sharp inflammatory diseases of thoracic and abdominal cavity organs, serious traumas and burns injuries, poisonings and infectious diseases when the syndrome of endogenous intoxications with postprimary suppression of system of immune protection starts to develop. Some kind of «immune distress syndrome» starts to be developed

In this situation detoxication both with toxins extraction and other pathology process products allows to achieve crisis in the course of the illness.

The leading role belongs to plasmapheresis procedure performance, what allows together with endotoxins extraction to remove all incompetent components of humoral immunity. The replacement of the removed plasma volume by donor plasma promotes more effective restoration of protection system together with faster and absolute recovery. The period of patients' stay in medical intensive care units is considerably reduced together with the general treatment length and mortality decreases.

However during the different chronic human illnesses are accompanied by disturbances of structure of its internal environment, frustration of a biochemical and immune condition define the severity and irreversibility of their course. It is possible to remove autoantibodies, allergens, and immune complexes during allergies and autoimmune diseases only with the help of plasmapheresis procedure performance. There are possibilities opened to perform both symptomatic and pathogenetic therapy. Introduction of plasmapheresis in the scheme of complex therapy of autoimmune disseminated lung diseases has allowed to achieving more sustained response at 40% of volume reduction of hormonal therapy and full refusal from cytostatics, to double practically life time for this category of patients.

Elimination of products of lipidic exchange disturbance allows to control atherosclerosis course and its complications. Plasmapheresis eliminates serious toxic effects caused by radio- and chemotherapy in oncology. Its high efficiency shown during chronic intoxication, including drug addiction and alcoholism has not only medical, but also the high social significance.

Big perspectives are opened during the treatment process of pregnancy toxemia, the Rhesus incompatibility, "hidden" urogenital infections, antiphospholipidic syndrome with recurrent pregnancy loss and reliably help to prevent the disturbances of pre-natal fetation, to reduce the perinatal lethal level, to restore demographic balance.

After viral hepatitis, especially HCV, autoimmune chronic hepatitis is being inevitably formed with next follow-up into nonreversible hepatic cirrhosis and even into primary liver cancer. With the help of plasmapheresis procedure performance it is possible to remove autoantibodies and pathological metabolites with the result of which the progression of liver injury can be suspended. Considering a large quantity of people infected with these viruses of hepatitis, this problem also has a big social importance.

At first sight the diabetes does not carry any serious threat because insulin or tablets help to support sugar level at the supportable level. However, during such treatment it is not possible to prevent the secondary exchange disturbances and vascular disorders with next irreversible sight loss, infringement of vascular permeability of the low limbs, heart and brain can start. All these disorders reduce general life time. With the help of plasmapheresis it is possible to reduce considerably the potential risk of these secondary diabetes implications.

There is a long list of human diseases in which the efferent therapy can considerably raise the treatment efficiency, and really find more and more wide application in clinical practice.

The expensive and special equipment is not needed for small-sized and universal plasma filters with "ROSA" brand name (The manufacturer is "Trackpore Technology holding corporation" company, Russia). The simplicity and safety of membranous plasmapheresis techniques will allow to apply these methods in the widest network of medical institutions. The specialized efferent therapy units are being formed in many clinics and in most ordinary hospitals, even the municipal ones. There are no

analogues in world practice to use these plasma filters with small filling volume in pediatrics, even during the treatment of premature babies with weight of a body from 700 gr, having no analogues in world practice.

Quality of the received plasma has appeared so high, that there are new possibilities of “ROSA” plasma filters to be used in blood banking for receiving both whole donor plasma, and various blood preparations.

OUR EXPERIENCE IN USE OF PROHERBIS DROPS IN TREATMENT AND PREVENTION OF HELICOBACTER PYLORI

Rosoklija A. MD, PhD – Specialist and Master of Biochemistry
Zlatna Pcela – Skopje

Introduction: *Helicobacter pylori* (HP) is a part of the normal gastric flora and is the cause for more than 80% of gastric and 90% of duodenal ulcers and gastric cancer (1-2 %).

Methods: For 5 years we examined 1200 patients with dyspeptic disorders. We used the test for the presence of antibodies in serum (IgA and IgG).

Results: 690 patients were positive for HP (68 pregnant and 33 nursing women). Depending on the levels of titer of the antibodies and the confirmed diagnosis, the treatment were different. The patients with acute infection were taking the ProHerbis drops as an introductory therapy, 10-15 minutes prior to the triple therapy and after completing it, the patients go on taking ProHerbis three times a day during two months. In case the titer of the antibodies was not decreased after the first check up (45 days), the patients continued taking the drops in the next six months, 2-3 times a day 20-30 drops. 20-30% of patients after the second check up (90 days) had no decrease of the titer of antibodies and they had the initial suffering because of the resistance to the antibiotics. We administered to these patients the quadruple therapy and they go on taking ProHerbis drops in the next six months (20-30 drops), 2-3 times a day. The nursing and pregnant women with positive HP antibodies instead of triple therapy were taking 20-30 drops of ProHerbis in period of 2-3 months.

Conclusion: According to the researches performed in Belgrade at the Department of Microbiology of “Dragisa Misovic” Hospital, as well as at the Institute of virusology and immunology “Torlak”, the solution ProHerbis beside increasing the non-specific immunity shows particular bacteriostatical and bactericidal effect upon HP. We confirmed that after 45 days and especially after 90 days of the treatment.

SENSORY SUPPLY OF SKELETAL MUSCLES. MUSCLE FASCIA

Corr.-member, Prof. Dr. Wladimir Ovtcharoff, MD, PhD, DSc
Department of Anatomy, Histology and Embryology, Medical Faculty, Medical
University of Sofia,
Bulgaria

The skeletal muscles are supplied by motor nerves, but probably about 50% of the fibres are sensory. These fibres are proprioceptive and exteroceptive as well as. These sensory or afferent fibres are several types: myelinated A α fibres (proprioception

from muscle spindles and Golgi tendon organs), A β fibres (mechanoreception from Pacinian corpuscle, Ruffini corpuscles and Meissner's corpuscles), A δ fibres (pain and temperature from free nerve endings) and unmyelinated C fibres (pain and temperatures from free nerve endings). It was established that about 40% from the A δ and C fibres have a function as nociceptors. It was calculated that number of fibres conveying temperature and pain is four times bigger than that of fibres responsible for mechanoreception and proprioception. These fibres are located in the epimysium, perimysium and endomysium. In these connective tissue parts of skeletal muscles there are also postganglionic sympathetic fibres, probably connected more or lesser with vasomotor activity. Theoretically pain sensation could be transmitted via afferent part of the sympathetic reflex arch. The are data that the pain information could be conveyed by means of proprioceptive fibres from muscle spindle. According all these data it must be accepted that the skeletal muscles, that represent from 35 till 45% from the body mass send to the CNS mighty sensory input (proprioception and exteroception).

ПРОБЛЕМЪТ ЗА ГНОЙНО-НЕКРОТИЧНИТЕ РАНИ НА ДОЛНИТЕ КРАЙНИЦИ В СТАРЧЕСКА ВЪЗРАСТ

Вл.Костов,д.м.В.Василев,проф.д.м.н. Ал.Атанасов,А.Кехайов д.м.

ДМЦ "Св.Пантелеймон"София, МБАЛ Бургас, МБАЛ "Св.Ив **Рилски** 2003"

Дупница, МБАЛ "Д-Р Бр.Шукеров" Смолян

За периода 1999 - 2011 в. са наблюдавани и лекувани 791 болни , 436 мъже = 55.1 % и 145 жени = 44.8% на възраст от 64 до 88 г.,средна възраст - 69 г. 7 мес.Раните са наблюдавани при групи болни:

- при диабетно ходило - 412 болни = 52.08 %

-при атеросклероза на крайниците - 97 = 12.2 %

-при супурирани механични рани / вкл.изгаряния / - 74 = 9.3 %

-други / следоперативни - 34.1 %

Микробиологичното изследване показва полимикробна бактериална флора/стафилококи,бета,хемолитични стрептококи,при малки групи болни - пептострептококи и бацилус фражили /. При болните с диабетно ходило е прилаган единен диагностичен алгоритъм, приложен и при болшинството болни с некротично язвени провеси на **базата** на атеросклероза: анамнеза,статус,**микробиологично** изследване ,Доплер-сонография - при диабетно ходило и атеросклероза, **флебография** при болшинството от тези болни рентгенография на ходилата и подбедриците.Прилаган е и стандартен лечебен подход : локална **оксигенотерапия** - **при всички** болни с много добър резултат,хирургич **на обработка** на раните ,антибиотикотерапия по данни от антибиограмата, **редовни превръзки**, локални бани с антисептични разтвори / калиев хиперманганат,риванол,браунол /.Наблюденията показват,че при болни с хронични рани **в** старческа възраст, много добро влияние оказва локалната оксигенотерапия и регионалните бани с антисептични разтвори.Сепсис не е наблюдаван.Летални изходи не са наблюдавани.

THE ROLE OF TUMOR NECROSIS FACTOR-ALPHA MEMBRANE-ASSOCIATED RECEPTORS IN DIFFERENT MODELS OF LUNG INJURY

Krynytska I.Ya. (associate professor, PhD), Marushchak M.I. Ya (associate professor, PhD), Horbachevsky ternopil state medical university, Ukraine

TNF- α is produced by many different cell types. The main sources in vivo are stimulated monocytes, fibroblasts, and endothelial cells. Macrophages, T-cells, B-lymphocytes, granulocytes, smooth muscle cells, eosinophils, chondrocytes, osteoblasts, mast cells, glial cells, and keratinocytes also produce TNF α after stimulation. TNF exerts pleiotropic effects by linking two high affinity membrane-associated receptors (TNF-Rs) of 55 and 75 kDa on a variety of cells. Soluble forms of the human 55 kDa TNF-R (sTNFRI) and the 75 kDa receptor (sTNF-RII) appear to be released from the cell surface by proteolytic cleavage of the extracellular domains of these membrane associated receptors.

Nonlinear male rats (weight range 200-230 g) were used in all experiments. For modeling of acid aspiration-induced acute lung injury anesthetized rats underwent tracheostomy and insertion of a fine-bore cannula into the anterior segment of the left lung. This was followed by the instillation of either 1.0 mL/kg HCl, pH 1.2 (n = 12) or 1.0 mL/kg saline in control rats (n = 12). All animals were studied at 2- 24 hours after acid aspiration. For modeling of hepatopulmonary syndrome (HPS) anesthetized rats underwent common bile duct ligation (CBDL) (n = 12). Sham rats underwent mobilization of the common bile duct without ligation (n = 12). All animals were studied at 31-day after CBDL or sham operation. Blood serum was analyzed for the percentage of neutrophils and monocytes which present TNF-alpha membrane-associated receptor TNF-RI and TNF-RII by the help of JC-1 using Beckman Coulter flow cytometer.

The percentage of neutrophils which present TNF-alpha membrane-associated receptor TNF-RI, by 2 h after acid aspiration, was significantly increased compared with control group (in the blood serum: $34,32 \pm 0,32$ vs $7,17 \pm 1,63$, ($p < 0,001$)). Such high percentage of neutrophils was observed during all experiment (24 hours).

The percentage of monocytes which present TNF-alpha membrane-associated receptors TNF-RI and TNF-RII, at 31-day after CBDL, were significantly decreased compared with control group (in the blood serum: $5,1 \pm 0,5$ vs $3,9 \pm 0,2$, ($p < 0,05$), $13,2 \pm 2,3$ vs $7,5 \pm 0,8$, ($p < 0,05$)).

The increased amount of neutrophils, which present TNF-alpha membrane-associated receptor TNF-RI, in blood indicates about increased the readiness of these cells to realize the main pathological effects of TNF- α , including programmed cell death in case of acid aspiration-induced acute lung injury.

The decreased amount of monocytes, which present TNF-alpha membrane-associated receptor TNF-RI and TNF-RII, in blood indicates about increased synthesis of soluble forms of TNF- α receptors in case of HPS.

So, in HCl-induced acute lung injury disorders of tumor necrosis factor alpha system occurs. The increase of TNF and TNF-RI in bronchoalveolar lavage are more intensive than in blood with the progression of the disease was determined. In case of HPS also disorders of tumor necrosis factor alpha system occurs, but more intensively are synthesized soluble form of TNF-RII.

MIDDLE MASS MOLECULES AS A MARKER OF ENDOGENOUS INTOXICATION IN CASE OF COMBINED EFFECT OF TOXICANTS IN RATS

Kulitska M.I. Ya (assistant professor, PhD)
Horbachevsky ternopil state medical university, Ukraine

In the pathogenesis of many diseases, known to modern medicine, landmark is given to syndrome of intoxication. The endogenous intoxication or endotoxiosis is defined as accumulation of excess of products of normal or pathological metabolism and cellular responses in tissues and biological fluids of the body. Pretty accurate criterion of the presence and severity of endogenous intoxication syndrome in the body is the content of middle-mass molecules (MMM). They consist of peptides, glycopeptides, products of fibrinogen degradation, albumin, thrombin, fragments of collagen and other substances of protein nature, as well as derivatives of lipids, phospholipids, etc. MMM are used as a marker of intoxication of various origins and their content allows to determine the severity of the pathological process.

The aim of our study was to study the dynamics of middle-mass molecules content in case of combined injury of rats by chemical factors.

Nonlinear male rats weighing 180-190 g were used in all experiments. Animals were divided into 2 groups: Group 1 - control animals, Group 2 - animals with acute injury, which was modeling by a single intragastric administration of sodium nitrite at a dose of 70 mg / kg body weight, and after 24 h additionally was injected lead chloride at a dose of 6.5 mg / kg and cadmium chloride at a dose of 6 mg / kg.

The degree of severity of endotoxemia was evaluated by contents of middle-mass molecules in blood serum of experimental animals with the calculation of the coefficient of middle-mass molecules (K) as the ratio of MMM_1 to MMM_2 where MMM_1 - is MMM content determined at a wave length of 254 nm, and MMM_2 - MMM content, determined at a wave length of 280 nm.

All animals were studied at 31, 4, 7, 14 day from the beginning of experiment.

Experimental results allow to assess the dynamics of MMM contents in the blood serum of white laboratory rats, which were modeling an acute toxic injury by chemical factors. This observed increase in MMM fraction with higher molecular weight, which are products of degradation of proteins, enzymes, nucleotides and structural proteins. At 1 day of the experiment reported K increase - by 35.5 % compared with a group of control rats, which indicates a marked increase in both chain and aromatic amino acids in the peptide components of MMM. Effects of toxicants led to a significant increase in serum K rats' blood serum at 4 day of experiment also - by 42.9 %. The maximum K was observed at 7 day of experiment - by 51.4 % compared with a group of control animals. Research has shown, that in case of acute injury in rats caused by the action of chlorides of cadmium and lead and sodium nitrite, at 14 day of experiment K was slightly reduced - by 14.1 % compared with the 7 day, but still significantly higher than control. The increasing of MMM contents was considerable for pool of MMM_{280} , indicating marked increase in aromatic amino acids in the middle-mass molecules.

So, the effect of these chemical factors resulted in statistically significant increase of endogenous intoxication, that shows an increase in contents of MMM.

ПЪРВИ ОПИТ ОТ ПРИЛОЖЕНИЕ СПОСОБА НА ПРОФ У.З.ЗИГИРОВ ПРИ КОМБИНИРАНА ПЛАСТИКА НА ГОЛЕМИ СРЕДИННИ ВЕНТРАЛНИ ХЕРНИЙ.

В.Василев ед.м, доц. д-р А.Кехайов д.м, проф.А.Атанасов,д.м.н
МБМ - Бургас, МБМ "Св.И.Рилски 2003 " Дупница

По литературни данни аутопластичните методи при хирургичното лечение на хернии на **предната коремна стена**, допускат рецидиви **21.3-63,7%,което налага** търсене на **нови** способности за хирургично лечение.

Проф.У.З.Загиров и коял. /2008/ предлагат нов метод на комбинирана аутопластика + пластика на полиетиленово платно при хирург.лечение на големи и **гигантски** средини и **вентрални хернии**.Способът се **заключва в: изрязвана** на стария оперативен цикатрикс,отсоя ване **нашироко** извън **граници** на **кожата** с подкожната мастна **тъкан**, пластика на **задната стена** на корема и след отваряне на задната стена на влагалището на правите коремни мускули под него и преперитоално се пришива алопластичен материал като се дренира **надеждно**.

Ние приложихме **метода** при **17 болни** за периода 2008-2011 год.с **гигантски** следоперативни ентрални хернии по **бялата** линия и след пластика на фасцалномуоскулния слои, под едната стена на влагалището на мускули ректи абдоминис, пришивахме добре с единични конци **полиетиленово** мрежесто или цяло платно като **над** платното поставяме тръбен **полиетиленов** дрен тип "Редон" и раната се затваряше послойно. Усложнения не са наблюдавани .Болните са изписани в **добро състояние и всички** са проследени 6 месеца сле операцията **без да е наблюдаван** рецидив.

Макар и след малък брой наблюдения считаме способите на У.З.Зигиров кол за **надежден и рационален** способ при хирургичното **лечение** на гигантски срединни вентрални херния

- а.ексцизия на цикатрикса и отваряне на коремната кухина,
- б.поставян е на полиетиленова протеза под задния ръб на влагалището на правите коремни мускули,
- в.аутопластика на мускулно-фасцалнияслой на коремната стена и алопластика на полиетиленова протеза.

ЗА ПЛАСТИКА НА КОРЕМНАТА СТЕНА ПРИ СЛЕДОПЕРАТИВНИ ВЕНТРАЛНИ ХЕРНИИ С ПРОТЕЗА

В. Василев, Е.Лефтеров , доц. д-р А. Кехайов , проф, дмн. А. Атанасов, М. Савов, В. Пенчев, В. Полянов

МБАЛ Бургас, МБАЛ "Св. Ив. Рилски", МБАЛ "Д-р Бр. Шукеров ", Смолян

Оперативното възстановяване на **коремната стена** при **първични** и следоперативни хернии, **заема** трето място в **структурата** на **хирургичните операции** в коремната област.Въпросът е актуален като се има в **предвид** и **процентът** на **рецидивите** при **тези операции** - **31,3 - 63.7%** по литературни данни.**Прилагането** на **синтетични протези / платна /** е позволило **да се** прилагат и **нови методи**.За периода 2000 - 2010 г. са оперирани за хернии на **предната коремна стена / първични и рецидивни/** 3626 болни в болниците на Бургаска ,

Смолянска и Кюстендилска области, с различни методи на хирургично възстановяване като **под наше** наблюдение и оперирани са били 369 болни на възраст 19 - 82 г/ средна възраст 57 г. 2 мес./: 224 мъже=60,7 % и 145 жени а 39,2 %. Установените следоперативни хернии са били: след холецистектомия с паракостален разрез пи Кохер - 93 = 25,2 % след срединна лапаротомия по бялата линия – 174=47,2%, след херниотомия по повод ингвинални хернии- 192 болни =27.7 % .Прилаган, е пластика на коремна стена с полиетиленово платн Surgi-Mech по следната методика: изсичане на кожата следоперативен ръбец,отваряне на корема с разрез по хода на формираната херния,**щателна** хемостаза,възможно послйсно затваряне на коремната кухина с единични шевове до нейното пълно херметизиране.Прилага се методът на възстановяване без **напрезание по Лихтенщайн** модафикация **на метода при** ингвинална херниотомия (**широко прилаган и в** институтите на Руската академия **на медицинските науки** и други постсъветски **републики/**. **Фасция** абдоминис **суперфициалис** се възстановява с единични шевове като с дисталното ламбо се пххва под цроксималното ламбо **и** двата пласта се **пришиват** с единични шевове положени един под друг **също без напрежение**.Над така възстановената повърхностна, **фасция** се **пришива** полиетиленово платно от типа Surgy-Mech, също с единични **конци до пълтно** възстановяване на **първокачаният дефект**. Поставя се **аспирационен** подкожен **дренаж**; **следва пълно** възстановяване на оперативната рана.Усложнения **и рецидиви до 2 години след операцията не са наблюдават**.

MODERN APPROACHES TO DRUG DELIVERY FOR TREATMENT OF OPHTHALMIC DISEASES

V. Andonova¹, M. Kassarova¹, T. Naydenov²

¹Faculty of Pharmacy, Medical University Plovdiv, Bulgaria

²Bulgarian Pharmaceutical Union

Introduction: For the treatment of various diseases of the eye most commonly used formulations are applied topically - to the eyeball or in the conjunctival sac. The greatest application have the eye solutions that are the most numerous group of drugs currently used. They have several major drawbacks: low ocular bioavailability - less than 5% of the administered drug is absorbed and inconvenience for the patient because of frequent applications. Much of medicinal substances have a technological difficulties because of their low water solubility and low permeability through biological membranes. When these are combined with disadvantages of conventional forms of ocular absorption, obtaining an effective product with high therapeutic activity and reduced side effects is a major challenge at present. During the last decade the investigations on the preparation and application of more effective drug delivery systems on the basis of the nanosupports from biocompatible and biodegradable polymers increase considerably.

There are different approaches to produce microemulsions, nanosuspensions, nanoparticles, niosomes, dendrimers, microneedle, liposomes, cyclodextrins, contact

lenses, intraocular implants, hydrogel systems, iontophoresis, gene delivery and etc. Especially important aspects are the choice of polymer and method for inclusion of the drug in nanosized carrier.

The stability, uniformity of particle size, speed control of release of the active substances, the place of his release, their adaptation to industrial manufacture of sterile products are the main problems in the development of these drug release and drug delivery systems.

Method: Literature reviews of 165 articles.

Results: Drugs from different groups such as antibiotics, corticosteroids, nonsteroidal antiinflammatory drugs, β -blockers, antisense oligonucleotides are examined in their inclusion in nanosupports of biodegradable polymers: poly lactic acid, gelrite gellan gum and sodium alginate, chitosan, β -cyclodextrins, hydroxypropyl- β -cyclodextrin, Eudragit RS100® and RL100®, poloxamer analogs/carbopol etc. Exploration is being carried via various technological approaches for the inclusion of drug substances in the carriers: by an emulsion polymerization technique; the electrostatic anchorage of the coating onto the nanocapsules; the use of the previously synthesized copolymer for the formation of the nanoparticles; using an emulsification/solvent evaporation method; a coacervation process and cross-linkage; temperature, pH and ion mechanism of gellation and many other different approaches.

Conclusions: Given the research in this field, we believe that nanotechnology will play a crucial role in the future of ophthalmic products. In the future, the main emphasis on research will be placed on achieving a noninvasive implementation aimed at sustained release of drugs for diseases of both ocular segments.

EXPERIMENTAL STUDY OF ANTI-INFLAMMATORY AND ANALGESIC EFFECTS OF STANDARDIZED EXTRACTS OF DRIED PLANT DRUGS.

D. Penkov, M. Kassarova, I. Kostadinov, M. Georgieva, D. Delev, I. Kostadinova, T. Naydenov

Faculty of Pharmacy, Medical University Plovdiv, Bulgaria
Margarita Kassarova

Introduction: The object of this study is the preparation of extracts from aerial parts of *Geranium Sanguineum*, *Astragalus Glycyphyllos*, *Erodium Cicutarium*, *Vincetoxicum officinalis*, and study of a number of pharmacological and immunological effects of these extracts.

Phyto-chemical analysis of the extracts was made using HPLC system Varian, RP C18 column and UV detector with variable wavelength. To test the anti-inflammatory and analgesic effects were used two model extracts - EXT1 - dry extract of the four drugs and EXT2 – thick extract. Thick extract was obtained by the method of percolation and subsequent condensation by evaporation of the solvent on a rotary evaporator. Dry extract was obtained using spray dryer.

Method: The study of anti-inflammatory effect was conducted by the method of carageenan-induced paw edema.

Nociceptive (analgesic) tests - Test "hot plate" - the method of Woolfe & McDonald and test "Randall-Selitto" – analgesy-meter.

Results:In acutely treated animals, the group receiving indometacin as a reference substance with anti-inflammatory effect showed a significant reduction of the carrageenan induced edema, when compared with the control group treated with saline solution. Statistically reliable results were registered at 2, 3 and 4 hours ($p < 0,0001$; $p = 0,001$; $p = 0,001$). Experimental groups showed no statistically significant differences compared with the control group. In chronically treated animals, indomethacin demonstrated significant anti-inflammatory activity when compared with the controlled group. Experimental groups treated with either extract in both doses tested (1g/kg and 2g/kg), showed no statistically significant differences compared to the controlled group.

The analgesy-meter test uses the mechanical pain stimulus. As a reference substance for the analgesic effect was used Metamizole sodium at a dose 150mg/kg. In acutely treated animals, metamizole showed a significant analgesic effect of the 2-3 hr ($p = 0.049$). The extract showed no reliable analgesic effect (excluding the dose of 1g/kg EXT2, 1st hour, $p = 0.031$). In chronically treated animals, metamizole has analgesic effect on the 1st, 2nd and 3rd h, ($p = 0.014$, $p = 0.009$, $p = 0.002$). From the experimental groups, reliable analgesic effect shows only the group treated with extract 1 dose 2g/kg the 2nd and 3rd hour ($p = 0.037$, $p = 0.022$).

The hot plate test use a thermal pain stimulus. In acutely treated animals, metamizole showed a significant analgesic effect of the 1st hour ($p = 0.024$). In the experimental groups no statistically significant differences with the control. In chronically treated animals, metamizole showed reliable analgesic effect on the second and third hour ($p = 0.012$, $p = 0.007$). In the treated groups, statistically reliable analgesic effect was observed in the group treated with extract 2, dose of 1g/kg, on the first, second and third hours ($p = 0.024$, $p = 0.029$, $p = 0.021$). At a dose 2g/kg in the first 2 hours, although not statistically reliable, the effect is significantly more pronounced than that of the control. At the third hour was statistically significant ($p = 0.005$).

Conclusions:Both extracts showed analgesic effect only on chronic administration. In extract 1, the anti-nociceptive effect is against mechanical pain stimulus, and in extract 2 – against thermal irritation, which is mediated from supraspinal mechanisms.

For statistical treatment of results was used software SPSS 11.0. For comparison of performance between groups was used Independent Sample t Test in level of significance $p < 0.05$.

THE INFLUENCE OF THE PHARMACEUTICAL INDUSTRY ON THE PRESCRIBING HABITS: COMMUNICATION WITH PHYSICIANS AND ITS EVOLUTION IN THE LIGHT OF INFORMATION TECHNOLOGIES DEVELOPMENT

T. Naydenov, A. Stoimenova, G. Petrova

Department of social pharmacy and pharmacoconomics, Faculty of pharmacy,
Medical University-Sofia

Introduction: The impact of marketing activities of pharmaceutical companies on the attitude and prescribing habits of physicians has always been one of the topics

discussed in the specialized literature. Situated in an extremely complex regulatory environment, pharmaceutical companies are constantly trying to gain maximum benefit from marketing tools, which in turn leads to increased intensity and frequency of interaction between representatives of pharmaceutical companies and physicians. According to some publications, pharmaceutical companies spend about 30% of turnover on marketing, 90% of these funds are dedicated for prescribers-related activities, giving a clear indication of pharmaceutical industry priority channels for modeling of medicinal products use. The aim of this study is to review publications on the impact of pharmaceutical company representatives on physicians' prescribing habits and to outline the main tendencies in this important and intensive communication.

Materials and methods: Literature search was done through MEDLINE/PubMed, Scopus database, Web of knowledge search as well as an Internet-based search with key words "pharmaceutical company", "medical representative", "prescribing habits", "influence", "physicians" and "e-detailing". The current mini review is based on total of 37 publications (1977-2011) satisfying the search criteria.

Results: Physicians are involved in various forms of communication with the pharmaceutical industry as participation in clinical trials, training programs, conferences, symposia, informal meetings with company representatives and others. Many studies showed that the information provided by pharmaceutical companies' representatives is often used by physicians in their daily practice. The perception of doctors regarding the efficiency and quality of medicinal products or reputation of the pharmaceutical company which submits them to the market is directly related to their idea of image and reliability of the company. Several studies have shown that the likelihood of doctors to prescribe a medicinal product and to promote the inclusion of a medicinal product in the hospital list is directly dependent on their presence at an event sponsored by the pharmaceutical company.

Conclusions: The roles of physicians in the use of drugs are various as they are involved in diagnostics, prescribing of medicinal products, education of patients etc. Physicians influence the budget (hospital, health insurance companies, etc.), the health policy and the opinion of their colleagues. Therefore, the influence of pharmaceutical companies on the prescribers can affect each of these aspects, not just the prescribing of medicinal product for a particular patient. Building honest relationships between the pharmaceutical industry and physicians is essential for promotion of rational drug therapy. Executive and legislative authorities, the medical community and pharmaceutical industry should constantly update the rules to regulate the interaction between medical professionals and medical / sales representatives in order to achieve a balance between the need for specific information and rational prescribing.

SUPERDISINTEGRATS: THE POTENCIAL OF NATURAL EXCIPIENTS

Todor Naydenov¹, Margarita Kassarova², V. Andonova²

¹Bulgarian Pharmaceutical Union

²Faculty of Pharmacy, Medical University Plovdiv, Bulgaria

Background: Drug delivery through oral route is the most preferred and accepted way of application by the patients. Solid dosage forms are popular because

of ease of administration, accurate dosage, selfmedication, pain avoidance and most importantly the patient compliance. Over the last 30 years, orally disintegrating tablets are gaining considerable importance. Novel orally disintegrating tablets technologies address many patient and pharmaceutical needs from enhanced life cycle management to convenient dosing particularly for pediatric, geriatric and psychiatric patients who have difficulty in swallowing.

There are different approaches to produce orally disintegrating tablets. Freeze drying, molding, and compression; compression is the most widely used method. Some methods are focused on unique granulation methods, such as spray-drying and flash-heating, to make shear form formulations; some are focused on selecting specific excipients such as water-insoluble calcium salt, specific disintegrant combination, and specific sugar combination; and some are focused on special treatment after compression, such as sublimation, sintering, and humidity treatments. The key to orally disintegrating tablets formulations is fast disintegration, dissolution, or melting in the mouth, and this can be achieved by producing the porous structure of the tablet matrix or adding superdisintegrant and/or effervescent excipients.

Method: Literature reviews of 135 articles.

Results: There are a lot of disintegrants and super-disintegrants on the market and most of them can be considered for use in orally disintegrating tablets. Typical examples include Crospovidone (Kollidon CL, Polyplasdone XL), Croscarmellose sodium (Ac-Di-Sol®, Nymce ZSX®, Primellose®, Solutab®, Vivasol®), Sodium starch glycolate (Explotab®, Primogel®, Vivastar P) and Ion exchange resins.

Some authors investigate natural substance and compare them with synthetic or semi-synthetic super disintegrates in formulation of orally disintegrating tablets.

It was found that Gellan gum, Xanthan gum, Modified treated agar (cogrinded agar) Modified treated guar (cogrinded guar), Husk of Plantago ovata and Mucilage obtained from leaves of Hibuscus rosasinensis, seeds of Lepidium sativum, seeds of Cydonia vulgaris and seeds of Plantago ovata have properties of superdisintegrants

Conclusions: Although there are many superdisintegrants, which show superior disintegration, the search for newer disintegrants is ongoing and researchers are experimenting with natural and modified natural products. These natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. They can also be modified in different ways to obtain tailor-made materials for drug delivery systems and thus can compete with the available synthetic excipients.

CORRECTION OF ENDOCRINE DISORDERS CAUSED BY STRESS-INDUCED HYPERPROLACTINEMIA

Petrenko Nataliia, MD, PhD

Ukraine, Ternopil state medical university by I.Ya.Horbachevskyy

Stress leads to the development of hemodynamic and metabolic changes in the human body in response to the impact of any disturbing factor. When stress is the activation of the sympathetic nervous system and hypothalamic-pituitary-adrenal glands, leading to the selection of ACTH, serotonin, and the allocation of dopamine

inhibited, which in turn leads to increased secretion of prolactin (PRL). Clinical manifestations of hyperprolactinemia are ovarian dysfunction, menstrual disorders, anovulatory syndrome, abnormal proliferative processes in target organs, galactorrhea, mastodiniya, breast.

The aim of research was to study the effectiveness of herbal drug with dopaminergic action Mastodinon regarding elimination of stress-induced hyperprolactinemia.

Materials and methods. We have examined 47 patients over time were subjected to the influence of stress (20-35 points by Taylor) and 18 healthy non-pregnant women who formed the control group (1-5 points by Taylor).

The level of stress was evaluated on a scale manifestation of anxiety Taylor (1953). The functional activity of the reproductive system was evaluated by the nature of menstrual function, levels of LH, FSH, total PRL, E2, Pg. The level of biologically active fraction (BFA) of PRL was determined in supernatant fluid after sedimentation of the macromolecule polyethylene glycol prolactin. In normal PRL content BFA took 40-60% relative to the total hormone.

Results and discussion. Result of our research show: total PRL level was slightly elevated $20,4 \pm 1,2$ IU/l, BFA PRL level was $18,6 \pm 1,1$ IU/l and 3 times higher, as compared to the control group, the content of BFA in the main group was $79,7 \pm 6,8$ % and was 1.4 times higher than in the control group, lower levels of pituitary and ovarian hormones LH ($6,2 \pm 0,6$ IU/l) and FSH ($5,8 \pm 0,5$ IU/l), E2 ($85,2 \pm 0,9$ ng/ml) and Pg ($8,0 \pm 0,5$ mg/l). In patients who have been under the influence of stress, which manifests a high or medium levels of anxiety, there is hyperprolactinemia, which is caused by increases in BFA of PRL at slightly elevated levels of total PRL, suppression of the pituitary and thus ovarian function, menstrual dysfunction seen in type hypomenstrual (47.2%) and anovulatory syndromes (70%), PMS (85.1%), galactorrhea (47.2%), mastodynia (51.2%), mastopathy (38.3%).

To treat our patients we surveyed had used the drug Mastodinon. This herbal drug with the main active substance *ahnus kastus* with proven clinical efficacy for the treatment of manifestations of hyperprolactinemia and estrogen-progestin removal of imbalances.

Under the influence of the proposed therapy, 3 months, patients noticed decrease of Algodysmenorrhea, mastodynia, PMS. Similarly, there has been a decrease in anxiety to indicators that matched the average level of the trend to low (8-18 points) due to normalization of secretion of neurotransmitters and related neuroendocrine processes. In the analysis menohramy marked reduction intensyvnoti hypomenstrual syndrome, eliminating galactorrhea.

Analysis of hormonal after treatment showed that the level of PRL decreased $15,5 \pm 1,0$ IU/l, his BFA – to $8,5 \pm 0,7$ IU/l, and its contents – to the $54,7 \pm 4.5$ %, and meet the standards and parameters of the control group. The same was likely to increase the concentration of pituitary and ovarian hormones (LH to $9,3 \pm 0,6$ IU/l, FSH – to $7,7 \pm 0,7$ IU/l, E2 ($179,2 \pm 9,9$ ng/L, Pg $20,5 \pm 1,8$ mg/l).

Conducted our study found high effectiveness Mastodinon for the reduction of stress-induced PRL, resulting in restored cyclic secretion of pituitary gonadotrophins and yachnykamy. Clinically it is manifested by normalization of menstrual and ovulatory function, reducing the intensity of clinical manifestations of

hyperprolactinemia (galactorrhea, mastodynia, Algodysmenorrhea). This enables us to recommend the use Mastodinon to treat stress-induced hyperprolactinemia.

Conclusions: 1. In patients who have been exposed to stress, there is hyperprolactinemia, which is caused by elevated levels of the active fraction bioloihchno prolaktynu.

2. Application Mastodinon showed high clinical efficacy for reducing prolactin and, accordingly, its clinical manifestations.

CONVERSATION ON SEXUAL LIFE AND HEALTH – RESEARCH AMONG THE ROMA POPULATION IN THE R.MACEDONIA

¹V. Velich Stefanovska – Prof.; ²M.Stefanovska Petkovska - Ass.Prof; ¹R. Isjanovska – Prof.; ¹B.Zafirova Ivanovska – Prof.

¹Institute of epidemiology and biostatistics with medical informatics, Medical faculty, University "St.Kiril and Metodij"- Skopje, R.Macedonia; ²School of business economics and management, University American College Skopje, R.Macedonia; Prof. Vesna Velik Stefanovska, MD MSc PhD, specialist in epidemiology

Introduction: According to the 2002 census there are approximately 53.879 (2.66%) Roma people living in the Republic of Macedonia, which represents 0.46% increase compared to the census in 1994. The natality rate among the Roma population is two times higher compared to the country average, while approximately 23% of the Roma women give birth in their homes. The lack of health insurance and inappropriate living conditions result in a significantly lower life span of around 40 years of age. **Aim:** The aim of this paper is to investigate the practice of open conversation on sexual life and health between parents and children in the Roma families in order to improve the reproductive health of this population group.

Methodology: This paper represents an analytical behavioral cross-sectional study implemented during a period of 8 months in 2011 in eleven cities in the state. A qualitative-quantitative research according to the methodology of the World Health Organization was used in the study. The questionnaire that was used explored issues on the sexual life and health regarding safe sexual behavior, sources of information as well as conversation on this issue with the family and partner. The quantitative part of the study included 900 participants in age group 14-49 years. The qualitative part consists of 16 focus group discussions and 13 in depth interviews on a total of 150 participants from the quantitative part selected in line with the pre-determined criteria.

Results: Approximately 80% of the Roma youth get their information on sexual life from the television and their peers. Only 4.2% of the young Roma openly talk with their parents on their sexual life. About 42.2% consider that their parents, especially their mothers, want to know about the sexual life of their children. According to 33.8% of the participant, both male and female equally insist on safe sexual behavior.

Discussion: The results of the research indicate that parents and children in Roma families realize the importance of open conversation on sexual life and health, especially for the benefit of the younger generations who are often victims of disinformation. Along with the need for open conversation and a closer relationship with their children, parents face insecurity in terms of how to meet this need.

Conclusion: A focused intervention is needed for a professional support of Roma families in terms of establishing and practicing of multi-generational conversation on sexual life and health which will generally result in improved reproductive health of this population.

Key words: Roma, sexual life, sexual health, open conversation, family

EPIDEMIOLOGY OF DISTAL RADIUS FRACTURE

B.Panova¹, H. Milanova¹, T. Troev¹, G.Panova² A. Apostolov²,

1 – Clinic “Physical and Rehabilitation Medicine”, MMA, Sofia, Bulgaria

2 Faculty of Medical Sciences-Stip, Macedonia

Distal Radius Fractures (DRF) are among the most common in people. The high frequency and socio-economic aspects of this traumatic disease make its epidemiological research and development of preventive strategies to reduce fracture risk particularly relevant. The social significance of the problem is based on common complications after imprecise surgical treatment and rehabilitation, as well as on the high rates of unsatisfactory functional results.

Epidemiological evidence for distal radius fractures among the population can be used for planning and organizing prevention and structuring of adequate medical care for these injuries.

Ensuring timely preventive strategy for people at high risk of fractures is a challenge for health systems worldwide. An important link between patients at risk and their proper treatment is done through the identification and risk assessment in these patients based on sound epidemiological study.

Keywords: epidemiology, distal radius fracture (DRF), frequency, osteoporosis

EPIDEMIOLOGICAL ASPECTS OF BRUCELLOSIS IN THE VELES REPUBLIC OF MACEDONIA

Shumanov Gj.¹, Jankulovska Zdravkovska M.¹, Tanevska J.²

¹ Faculty for medicine science of University "Goce Delcev" Stip, Republic of Macedonia, ²Department for Infektious Diseases, Hospital Veles, Republic of Macedonia

Aim: To analyze and present epidemiological patterns of human brucellosis cases and the main factors for the appearance and spread of brucellosis infection among animals and humans in Veles and R. Macedonia in the period from 2007 to 2011.

Material and methods: Retrospective study based on the epidemiological reports and official data on brucellosis cases from the Institute for Public Health in Skopje and other institutions from the health in R. Macedonia .

Results: From 2007 until 2011 a total of 69 brucellosis cases were reported in Veles, with a mean annual incidence rate of 27,6/100,000 (in R. Macedonia 18.9/100,000). The highest morbidity rate during this period was recorded in 2008 (29 cases and an incidence rate of 58,0/100,000), and the lowest one in 2011 (4 cases and an incidence rate of 8,0/100,000). From the total number of cases reported, 80% were

males and 20% were females. Only 5% of patients were under the age of 10, and the most of the patients were from the age group 20–39 (35.5%). Seasonal characteristics of the disease were expressed with the highest occurrence in May (18.9%), June (17.3%) . Within the total number of 69 brucellosis cases in the period 2007–2011, 46 (67%) were from rural settlements and 23 (33%) from urban areas.

Conclusion: Brucellosis was, currently is and will be a significant disease problem and concern in R. Macedonia which should be approached in a more comprehensive and organized way in the coming years.

Keywords: Brucellosis, zoonoses, epidemiology, prevention/control programme, Veles, Republic of Macedonia.

JOURNAL-BASED CME AND INTERNET POINT-OF-CARE LEARNING (POC) IN UZBEKISTAN

Zokhid Abdurakhimov, PhD, MD
(Medical Association of Uzbekistan)

Medical Association of Uzbekistan of c of 2010 prosecutes subjects of continuous medical education in Uzbekistan. Requirements for development of programs by continuous education were approved and more than 10 programs of distance learning in the form of reviews are prepared by leading experts of the Tashkent institute of improvement of doctors (TIID). In 2010-2011 9 programs on the following subjects are published already: State of health of the population of Uzbekistan; tension Stenocardia; Actual problems of oncology; Valueology, as subject of formation of a healthy lifestyle; Distsirkulyatorny venous encephalopathy: diagnostics and treatment problems; Dysphagia; Changes in an organism of the woman and discomfort able feelings during pregnancy; Modern aspects of a food of children of the first year of life; Main directions of improvement of the out-patient and polyclinic help to the population of the Republic of Uzbekistan. Continuous programs are based on principles to demonstrative medicine, developed taking into account the last achievements of medicine and intended for various specialties.

15-16 tests which are printed on dense paper are attached to each remote program. Tests are numbered and have a different form of complexity and to the 3rd right answers. Having answered tests, doctors cut out and send them to editorial office of the magazine during 1 year from the edition it. At an affirmative answer and a set of the right answers more than 60 percent doctors receive the certificate on distance learning for each training program.

If in 2010 this method 140 doctors (from 151 tests) already used, in 2011 received certificates of 243 doctors. In total during 2010-2011 it was sent to Association of doctors of Uzbekistan answers to the 397th test on distance learning, from them received certificates of the 355th doctor that makes the 89th percent from all sent answers to tests.

On the one hand introduction of distance learning presented possibility to doctors, without leaving the house to increase the knowledge, growth of interest to the magazine among the doctors which circulation this year increased in 2 times on the other hand is observed. Reading various medical scientific articles, doctors through self-

education learn also new methods of diagnostics and treatment of various diseases. Thus without putting a damage of existing straight lines to a form of post degree education at refresher courses in TIID.

Since 2012 we plan to enter online education. The site online of training is now developed and it works in a test mode (<http://test.avuz.uz>). After approbation the training program will be established on our site (www.avuz.uz)

Thus, in modern conditions it is necessary to develop economically effective methods of the post-degree training which have already proved the independence in the developed countries of the world. Being addition to direct forms of professional development, distance learning allows increasing qualification without a separation from medical institutions and patients, and also gives the chance to avoid frequent expenses connected with journey, accommodation and a food. Transition to credit system of continuous medical training with an annual set of the credits, will stimulate doctors to look for ways of indirect forms of education that will allow doctors to work over increase of the qualification. Introduction of continuous medical training will promote professional development; decrease in medical errors and respectively to be a motive power of improvement of quality of medical care.

REGIONAL MUSCLE PLASTIC SURGERY IN VAST SOFT-TISSUE DEFECTS OF ARMPIT AND SHANK AFTER SEVERE TRANSPORT ACCIDENTS

Prof. Dr. D.Boshnakov ; Dr. T. Papurov; Dr. L. Blazhevski

Varna, Bulgaria; University Hospital 'St. Anna Varna' - Clinic of Orthopedics and Traumatology

Prof. Dr. Diko Boshnakov: *Clinic of Orthopedics and Traumatology Hospital 'St. Anna Varna' - Varna*

Dr. Tihomir Papurov : *Surgery Hospital 'Papurov' - Targovishte;*

Dr. L.Blazhevski: *Clinic of Orthopedics and Traumatology Hospital 'St. Anna Varna' - Varna*

Introduction. The reconstruction of vast and profound soft-tissue defects of limbs is possible with different options – regional pedicle flaps and free microvascular flaps.

Objectives. The work's objectives are to estimate the quality of regional muscle flaps in vast defects of armpit and shank soft-tissues caused by severe transport accidents, on the basis of functional and esthetic results.

Materials and methodologies. Clinical observations are based on 14 patients aged 28 to 48 years. There were vast soft-tissue defects of shank in 10 patients and armpit defects in 4 patients. Double muscle flaps /from gastrocnemius and soleus/ are applied – in shank, and cutaneous muscle “latissimus dorsi” flaps – in armpit.

Conclusion. Clinical cases, as well as observation results are presented. The qualities and advantages of applied flaps in the mentioned localizations are considered in the discussion.

DECLARATION
of the
Second International Medical Congress
of
Southeast European Medical Forum
7 - 10 September 2011
Nesebar, Bulgaria

We, the participants in the Second International Medical congress of the Southeast European Medical Forum, namely physicians from Albania, Belarus, Bulgaria, Greece, Kazakhstan, Latvia, Macedonia, Romania, Republic of Srpska - Bosnia and Herzegovina, Serbia, Ukraine, in the presence of representatives of the World Health Organization (WHO) and the President of the World Medical Association (WMA), abiding by the basic principles and responsibilities of the WHO and WMA, as well as by the priorities and goals of the unique European Strategy 2020:

1. Shall initiate joint collaboration for promotion of health and welfare of the citizens from the whole region;
2. Shall work for providing conditions for better quality of life and higher life expectancy for the people in the region;
3. Shall work for improvement of the healthcare management by providing expertise, analyses and particular problem solutions with the ambition for real involvement in the health policy of the respective countries;
4. Shall contribute to making health a priority for the whole society, the authorities, non-governmental sector, citizens, private companies, academic community and all other stakeholders.

Governments together with health-care professionals have to reconsider correlations between economics and healthcare policies.

Medical organizations should safeguard the interests of all physicians, should be self-governing bodies and quality guarantor, and should represent and work for the benefit of the profession.

The issue of healthcare funding in the region is very grave, as was indicated by the participants in the Congress, but each country should try to find solutions according to the specific local situation. What is necessary is adequate and equitably distributed healthcare budget, strong decisions on the reforms to be carried out, prioritising on investments in human capital, improvement of its productivity and better use.

It is high time that the Health Ministries and all other ministries place health issues among the priorities of the politicians and society. A basic principle of a democratic and socially responsible state should be the responsibility for health and the access to healthcare for all citizens, irrespectively of their ability to pay for medical care.

September 2011
Nesebar, Bulgaria

