



International periodic scientific journal

—*ONLINE*

www.sworldjournal.com

SWORLD Journal

ISSN 2227-6920

Medicine, veterinary medicine and
pharmaceuticals

Issue j116 (10)
Volume 06
May 2016

Published by:

Scientific world, Ltd.

With the support of:

Moscow State University of Railway Engineering (MIIT)

Odessa National Maritime University

Ukrainian National Academy of Railway Transport

State Research and Development Institute of the Merchant Marine of Ukraine (UkrNIIMF)

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Author(s), "Title of Paper," in SWorld Journal, Issue j116 (10), Vol.06 (Scientific world, Ivanovo, 2016) – URL: <http://www.sworldjournal.com/e-journal/J11606.pdf> (date:...) - page - Article CID Number.

Published by:

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J11606-001

N.O. Abramova, N.V. Pashkovska
PECULIARITIES OF LIPID METABOLISM IN PATIENTS WITH
METABOLIC SYNDROME DEPENDING ON PRO197LEU
POLYMORPHISM OF THE GPX1 GENE

HSEI «Bukovinian State Medical University» (Chernivtsi)

Summary. Pro197Leu polymorphism of the gene GPX1 in 102 patients with arterial hypertension and concomitant abdominal obesity and 97 healthy individuals have been studied. Disorders of distribution of genotype frequencies comparing with the control group at the expense of the reduction of Pro/Pro genotype frequency have been found in the main group. Analyzing the data, the growth of risk of disorder in the GPX 1 activity in patients with Pro/Leu and Leu/Leu variants of polymorphism comparing with homozygous for the "wild" allele at 4,7 and 6,9 times respectively had been revealed. Analyzing changes of lipid metabolism depending on the Pro197Leu polymorphism of the gene GPX1, it was established that in patients with Leu/Leu genotype the elevation of low-density lipoproteins and atherogenic coefficient. Thus, Pro-allele possesses protective properties as to the reduction in the activity of glutathione peroxidase. Insulin and leptin resistance develop in the carriers of Leu-allele, which causes disturbances in lipid metabolism.

Key words: Pro197Leu polymorphism of the gene GPX1, lipid metabolism, insulin resistance, abdominal obesity, metabolic syndrome.

Introduction. Cytoplasmic glutathione peroxidase (GPX 1) is one of the selenoenzymes important for the organism functioning, present in all tissues of the human body, which takes part in detoxication of hydrogen peroxide and products of lipid peroxidation, as catalyzes the interaction of reduced glutathione with these substances [3, 8, 5, 12]. It is known that numerous pathologic processes in the organism develop in consequence of disorders in the mechanisms of antioxidant protection. Specially, in patients with insulin resistance accompanied by hyperglycemia and increased production of cytokines there arises oxidative stress. The accumulation of free radicals activates factors of transcription such as NFkB, which initiate the process of proinflammatory cytokines release [6]. The growth of free radicals results in lipid peroxidation of cellular membranes, causes atherosclerosis and endothelial dysfunction [13].

We studied single nucleotide polymorphism of the gene GPX 1 for going into the question of the dependence of these processes upon the disorders of redox homeostasis. The human gene GPX 1 is localized in 3p21 chromosome and consists of two exons. Several single nucleotide polymorphism variants of this gene have been known, but the Pro197Leu polymorphism has been under our study, at which in the position 593 the amino acid cysteine (C) is replaced with thymine (T) (C593T), resulting in substitution of the amino acid proline for leucine in the 197 codon. This mutation refers to missens - functional polymorphisms [1]. Pro-allele is «wild», while Leu- is a «mutant» allele. The presence of Leu-allele causes depression of GPX 1 sensibility to stimulating factors [9].



Thus, Bastaki et al. discovered that GPX 1 activity 6 times slows down in homozygous patients for the Leu-allele [3]. Zelkova T.V. et al. found out that the homozygous for mutant allele more often suffered from coronary artery disease and myocardial infarction at the age of until 50 years old [14].

The aim of the study. To investigate the dependence of lipid metabolism in patients with metabolic syndrome depending on Pro197Leu polymorphism of the GPX1 gene.

Material and methods. Pro197Leu polymorphism of the gene GPX1 have been studied in 102 patients and 97 healthy individuals by isolation of genomic DNA from peripheral blood leukocytes, after that amplification of the polymorphic area in the state of polymerase chain reaction (PCR) was performed on the programmed PCR thermal cyclers «Amplify-4L» («Biocom», Moscow) at individual temperature response. Reagents "ДНК-сорб-В" option 100 (ФГУН ЦНИИЭ, Росія) were used for DNA isolation from lymphocytes according to instructions. PCR samples were prepared by means of the set «АмплиСенс-200-1» (ФГУН ЦНИИЭ, Росія). Products of PCR were separated using electrophoresis in 3% agarose gel in the presence of tetraborate buffer, concentrated with ethidium bromide. Fragments were visualized by transilluminator in the presence of a marker of molecular mass 100-1000 bp (Fermentas^R, USA).

Pearson's χ^2 criterion was used to estimate the correspondence of the genotype frequencies under study to theoretically expected distribution at Hardy-Weinberg's equation. Odds ratio (OR) with determination of 95% confidence interval (CI) was calculated with the aim to establish the association of polymorphic variant of the gene with a pathological phenotype.

To evaluate the dependence of lipid metabolism depending on Pro/Leu polymorphism of the gene GPX1 we divided the patients into groups in the following way: 18 patients with Pro/Pro, 59 with Pro/Leu and 25 with Leu/Leu genotypes, the control group consisted of 20 healthy individuals.

Total cholesterol (TCH), triacylglycerols (TG) (were measured using diagnostic standard sets of firm "Simko Ltd" (Ukraine)), low-density lipoprotein cholesterol (LDL cholesterol) (by turbidimetric method by Burstein) and high density lipoproteins cholesterol (HDL cholesterol) (using standard diagnostic kits of firm "Vector-Best" "HDL-Cholesterol-Novo" (Russia)) were determined photometrically on a spectrophotometer "SF-46" (Russia).

To calculate the atherogenic coefficient (AC) A.N. Klimov formula was used:

$$C = \frac{A \quad TCH - HDL}{LDL} \quad (\text{В.С. Камышников, 2000}).$$

Normally this coefficient is 2 – 3 (В.С. Камышников, 2000).

Statistical analysis of the data was carried out using the Student's t-test and Pearson's rank correlation coefficient using the software package Statistica 6.0 for Windows. The difference was considered reliable at $p < 0,05$.

Results and discussion. When assessing the distribution of genotype frequencies of the gene GPX1, it has been found that in the group of patients with



abdominal obesity against the background of arterial hypertension there takes place a significant reduction of the frequency of Pro/Pro genotype as compared with the control group ($X^2 = 7,0$, $p < 0,05$), while there hasn't been found out a reliable difference between the frequencies of Pro/Leu and Leu/Leu genotypes in the main and control groups ($X^2 = 1,9$, $p > 0,05$ and $X^2 = 2,6$, $p > 0,05$).

It has been revealed that Pro/Leu and Leu/Leu variants of polymorphism are associated with increased risk of violation of redox system in patients with metabolic syndrome compared with a group of healthy subjects (table 1). Thus, it has been found out that in patients with Pro/Leu polymorphism the risk of disturbance of GPX1 activity increases 5,2 times ($p < 0,05$, OR = 1,65, CI = 0,95% 0,94-2,90; table 1), and in patients with Leu/Leu genotype the risk of such pathology is 6,0 times higher than in persons with Pro/Pro genotype ($P < 0,05$, OR = 1,92, CI 0,95% = 0,93-3,97; table 1).

Table 1

The distribution of genotype frequencies depending on GPX Pro197Leu polymorphism gene 1 in patients with metabolic syndrome and the control group

Note: X^2 - Pearson criterion, OR - odds ratio, CI - confidence interval.

So, the risk of reduction of GPX 1 activity in a dose- dependent way is associated with the presence of «mutant» Leu-allele, while homozygous for the «wild» Pro-allele had significantly lower risk of this disturbance development. Pro-allele has protective qualities concerning the development of redox system violation.

When studying the dependence of indices of lipid metabolism on Pro197Leu polymorphism of GPX1 gene, a significantly 28,2%, 46,9% and 36,8% higher level of LDL in patients with Pro/Pro, Pro/Leu and Leu/Leu genotypes respectively in relation to the group of healthy individuals was found ($p < 0,05$). In homozygous group for mutant allele LDL level was 27,8% higher than in homozygous group for

| Genotypes | <i>Cases</i> | <i>Controls</i> | X^2 | p | OR | 0,95% CI |
|----------------------------|--------------|-----------------|-------|-------|------|-------------|
| | 102 | 97 | | | | |
| Genotype frequency Pro/Pro | 0,176 | 0,402 | 12,91 | 0,002 | 0,32 | 0,17-0,61 |
| Genotype frequency Pro/Leu | 0,578 | 0,454 | | | 1,65 | 0,94-2,90 |
| Genotype frequency Leu/Leu | 0,245 | 0,144 | | | 1,92 | 0,93-3,97 |

wild allele ($p < 0,05$) (table 2).

1,9, 2,3 and 2,7 times higher level of HDL in patients with Pro/Pro, Pro/Leu and Leu/Leu genotypes respectively in relation to the group of healthy individuals was found. There was no significant difference between groups according to PRO197Leu polymorphism ($p < 0,05$).



Statistically significant elevation of TCH in all groups was revealed in relation of healthy individuals, with Pro/Pro - genotype 40.3%, with Pro/Leu - by 45.4%, and Leu/Leu - 61 1% respectively without probable intergroup differences. Also significant increase in the content of TG in patients with Pro/Pro, Pro/Leu and Leu/Leu genotype was 2,4, 2,6 and 3,2 times higher compared with a group of healthy individuals ($p < 0,05$).

Patients with Leu/Leu genotype had 73,9% higher AC than in group with Pro/Pro – genotype ($p < 0,05$). CA was respectively 3,8, 4,9, 6,6 times higher in patients with Pro/Pro, Pro/Leu and Leu/Leu genotypes than in control group ($p < 0,05$).

These results coincide with the data by Hironori Kobayashi and co-authors, who revealed GPX1 in adipocytes and described the reduction in activity of this enzyme in hypertrophied adipocytes of patients with type 2 diabetes. The authors believe that inhibition of phosphorylation of insulin receptors with subsequent development of insulin resistance develops against the background of free radical activation in adipocytes in patients with diabetes mellitus type 2 and reduced GPX1 production [11].

Table 2

Peculiarities of indicators of lipid metabolism and anthropometric features in hypertensive patients with metabolic syndrome according to Pro197Leu polymorphism of the gene GPX 1

| Index | Genotypes GPX 1 , n=102 | | | Control group, n=20 |
|----------------------------|---|---|-----------------------------|---------------------|
| | Pro/ Pro | Pro/ Leu | Leu/ Leu | |
| LDL, conventional units | 50,72±2,683 $p_1 < 0,05$ $p_2 > 0,05$ $p_3 < 0,05$ | 58,14±2,967 $p_1 < 0,05$ $p_2 > 0,05$ | 64,80±3,234 $p_1 < 0,05$ | 39,56±2,118 |
| HDL, mmol/l | 1,00±0,048 $p_1 < 0,05$ $p_2 > 0,05$ $p_3 > 0,05$ | 0,85±0,056 $p_1 < 0,05$ $p_3 > 0,05$ | 0,73±0,039 $p_1 < 0,05$ | 1,95±0,027 |
| Total cholesterol, ммоль/л | 6,12±0,159 $p_1 < 0,05$ $p_2 > 0,05$ $p_3 > 0,05$ | 6,34±0,063 $p_1 < 0,05$ $p_3 > 0,05$ | 7,03±0,042 $p_1 < 0,05$ | 4,36±0,029 |
| Triacylglycerols, mmol / L | 2,28±0,217 $p_1 < 0,05$ $p_2 > 0,05$ $p_3 > 0,05$ | 2,47±0,183 $p_1 < 0,05$ $p_3 > 0,05$ | 3,06±0,128 $p_1 < 0,05$ | 0,95±0,144 |
| Atherogenic coefficient | 5,09±0,163 $p_1 < 0,05$ $p_2 > 0,05$ $p_3 < 0,05$ | 6,51±0,218 $p_1 < 0,05$ $p_3 > 0,05$ | 8,87±0,349 $p_1 < 0,05$ | 1,34±0,112 |

**Notes:**

1. n - number of observations;
2. * - the probability of changes in relation to control;
3. ** - the probability of changes in relation to the group with Pro / Leu-genotype;
4. *** - chance changes in relation to group with Leu / Leu genotype

Accumulation of cholesterol and respectively, associated with this process elevation of AC is caused by inhibition of lipoprotein lipase against the background of insulin resistance, that is provoked by activation of lipid peroxidation. According the literature data, activation of lipid peroxidation in carriers of Leu allele is an important mechanism in atherosclerotic damage of vascular wall, that greatly increases risk of cardio-vascular complications development in these patients [7, 8].

Conclusions.

1. In patients with arterial hypertension against the background of abdominal obesity the risk of reduction of glutathione peroxidase 1 activity is associated in a dose-dependent manner with the presence of «mutant» Leu-allele, while homozygous for the «wild» Pro-allele had a significantly lower risk of this disorder.

2. The presence of Leu-allele in genotype of patients with metabolic syndrome is connected with the disorder of lipid metabolism in a result of insulin and leptin resistance development and characterized by low-density lipoprotein level and atherogenic coefficient elevation

Prospects further research. The survey results indicate the necessity of development of effective measures for lipid metabolism correction in patients with metabolic syndrome.

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J11606-002

Butyrsky A., Selivanov A., Fomochkin I., Sherendak S., Khilko S.,
Skoromny A.

DYNAMICS OF LIFE QUALITY AT PATIENTS AFTER DIFFERENT OPERATIONS FOR CHRONIC COMBINES HEMORRHOIDS

*S. Georgievsky Medical Academy, Vernadsky Crimean Federal University
5/7 Lenin bly, Simferopol, 295006*

Abstract. The paper discusses the problem of life quality parameters changes in patients undergone different surgical interventions for chronic combined hemorrhoids. The investigation was carried out with inquiry SF-36. 125 patients were shared into 3 groups depending on the type of surgery. The most significant and evident changes are observed in 12 months after separate closed hemorrhoidectomy that is associated with the small number of complications in early and remote post-operation period.

Key words: chronic combined hemorrhoids, surgical management, results, life quality

Introduction.

Incidence of chronic combined hemorrhoids (CCH) makes 130-145 per 1000 of adults, and its frequency in the general structure of rectum pathology makes ~ 40% [1]. Despite introduced new surgical technologies, incidence of post-operation complication and duration of hospital stay do not decrease [3].

Medical sources describe issues of CCH surgery rather widely [5, 6, 12, 14]. In spite of multiple methods of surgery and their modifications with studying their early and remote results, the last ones do not satisfy surgeons and patients [4].

Literature review.

The most frequent surgery in CCH is hemorrhoidectomy (HE). Now they use three its types: opened HE (Milligan-Morgan surgery, MMS); closed HE with restoration of anal mucosa by knot/uninterrupted suture (Ferguson surgery, FS), in USA it's considered the method of choice; submucosal HE (Parks surgery) with advantage of that is anal mucosa is not dissected together with piles but cut by arch-shaped incision, a pile is separated from submucosal layer, its crux is ligated, pile is cut, its stump remains in submucosal layer .

All these operations have disadvantages: localization and type of surgery foresees shown tenderness after surgery and within 2-4 weeks after it, anal sphincter is in state of spasm that supports pain, wound heals up to 4 weeks, and a patient needs daily wound washing, using wound-healing ointments and strips, pain-killers intaking, limiting physical activity.

Data of literature testify to recovery rate after HE ~ 85-90% of patients but at them one reveals following complications: suppurative (2%), intensive pain (34-41%), bleeding (1.5-2%), dysuria (6-18%), anal strictures (2%), anal sphincter incompetence (1%), relapsing up to 7.5% [12, 13, 14].

Life quality (LQ) in CCH patients before and after surgery was studied by certain authors [10, 24, 77, 79]. But, taking into account introduction of the new



method of surgery – separate closed hemorrhoidectomy (SCHE) [12], we carried out the original research to study remote results of suggested surgery.

Database and methods.

The search was carried out among 125 patients been admitted at the Crimean Medical University Hospital. There were 62 women (49.6%) and 63 men (50.4%) at age of 22-73 years old (mean age 46.5±1.6). The patients underwent different types of HE: I group (51 pts) – underwent MMS, II group (49) – underwent FS, III group (25) – underwent SCHE. More detailed characteristics are given in tables 1 & 2.

Table 1

Statistical characteristics of observed groups

| Group | Number of patients | Sex (M/F) | Mean age, years | Mean disease duration, years |
|-------|--------------------|-----------|-----------------|------------------------------|
| I | 51 | 33/18 | 47,6±1,4 | 10,7±1,2 |
| II | 49 | 18/31 | 46,2±1,4 | 10,4±1,1 |
| III | 25 | 10/15 | 44,3±2,1 | 11,8±2,2 |

Table 2

Clinical-and-functional characteristics of observed groups (CCH degrees) (abs./%)

| degree group | I | II | III | IV |
|--------------|-----|---------|---------|---------|
| I (n=51) | 0 | 15/29,4 | 24/47,1 | 12/23,5 |
| II (n=49) | 0 | 15/30,6 | 32/64,3 | 2/5,1 |
| III (n=25) | 2/8 | 13/52 | 7/28 | 3/12 |

Thus, all the groups are identical according to all cohort features (sex, age, duration, and clinical-and-functional characteristics) and representative.

To evaluate the LQ after the surgical treatment we used the scale of standardized inquiry SF-36 – non-specific inquiry for LQ assessment that reflects general well-being and the degree of satisfaction of human vital activity those impact patient’s health. SF-36 consists of questions combined into 8 scales. Indexes in every scale are made from 0 to 100 (more score – better health).

Statistical processing was made by methods of variation statistics with determination of evidence with the set “Microsoft Excel for Windows XP” programs. Evident difference testified to possibility of transferring obtained conclusions to common totality (permissible index for medical research – p<0,05) [7].

Results. Discussion and analysis.

Long-time morbid condition with expressed physical discomfort incl. CCH, is the powerful stress factor impacting psychological and physiological components of human health.

LQ assessment in CCH is of great importance for characteristics of the disease and determination of efficacy of therapy. In all the patients with CCH such symptoms as pain, weakness, work capacity significantly impact the physical state and perception of own condition. Total LQ adds characteristics of pathological process,



its dynamics under treatment influence that facilitates individualization of therapeutic approaches and clearance of forecast [8].

The data of patients' LQ research after different types of surgery are given in the table 3.

Table 3

Patients' LQ after surgery for CCH

| Index | Before surgery | In 12 months after surgery | | |
|---------------------------|----------------|----------------------------|------------------------|-----------------------|
| | | group I (n=51) | group II (n=49) | Group III (n=25) |
| General Health | 26.4±1.9 | 48.5±2.1 ¹² | 46.9±3.2 ¹² | 58.1±3.6 ¹ |
| Physical functioning | 22.4±1.8 | 49.7±1.7 ¹² | 51.3±2.4 ¹² | 62.4±2.9 ¹ |
| Role-Physical functioning | 27.6±1.7 | 46.9±2.8 ¹² | 50.2±3.3 ¹² | 72.5±2.8 ¹ |
| Role-Emotional | 24.8±2.6 | 48.6±3.2 ¹² | 49.5±2.7 ¹² | 61.5±3.7 ¹ |
| Social functioning | 26.1±1.7 | 54.2±1.9 ¹² | 51.5±2.5 ¹² | 68.3±3.5 ¹ |
| Bodily Pain | 28.7±2.5 | 52.1±1.9 ¹² | 54.3±1.7 ¹ | 61.4±3.4 ¹ |
| Vitality | 26.9±1.9 | 48.5±1.9 ¹² | 51.2±2.4 ¹² | 61.9±2.8 ¹ |
| Mental Health | 32.6±1.1 | 47.8±2.1 ¹² | 55.2±2.3 ¹² | 71.2±4.8 ¹ |

Notes: ¹ – difference evident (p<0,05) with pre-operation parameter, ² – difference evident (p<0,05) with group III.

The analysis demonstrates that any surgery impacts the patients favorably, improving all the sides of their life: all the parameters in 12 months after surgery in all the groups are evidently more than before treatment. Further analysis shows that between the patients from groups I and II and the patients from group III there is also evident difference in all parameters except bodily pain (groups I and III) that is quite explainable taking into account disease duration and peculiarities of patients' clinical- and-psychological status after HE [10].

Comprehensive result been obtained in analysis of inquiry SF-36 demonstrated advantages of SCHE in CCH treatment. In 12 months после finishing treatment one obtained following data: parameter «General Health» evidently increased in all groups but in group III – evidently more than in groups I и II. Analogous trends are marked in parameters «physical functioning», «role-emotional activity», «social; functioning», «vitality», and «mental health». There is no evidence between groups II and III on parameter «bodily pain» that testifies to close results I n these groups, where closed methods of HE were explored. This point of view is shared by A. Poyda [9].

LQ after HE and mini-invasive methods are described in papers by F. Gyulmamedov et al. [6] and V. Mishalov [8].



The obtained results of comparative evaluation earnestly show that SCHE on efficacy, incidence of complications, and remote results is high-efficient operative intervention, and may be the real alternative to standard methods of HE.

CONCLUSIONS

1. Our research demonstrate that SCHE is the optimal in respect of post-operation complications prevention, facilitates rapid restoration of all parameters of patients' LQ. It makes possible to recommend it as the operation of choice in CCH management and real alternative for MMS, and FS.

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**UKRAINIAN MEDICAL DYNASTIES IN HALYCHYNA**

*Medical University of Warsaw,
Warsawa, ul. Zhvirki and Vigouroux 61, 02-091*

Abstract. The article analyzes the achievements of local doctors and scientists in the process of formation of Ukrainian medicine. We give a brief description of contribution of K.Voievidka, V.Yanovych, O.Malaniuk, Ye. Ozarkevych, Ya. Okunevskiy, N. Polotniuk-Prystai, R. Yarosevych and others doctors. Methodological basis of the research are leading positions of the theory of scientific knowledge, system-structural and cultural approach as a methodological way of studying of educational phenomena and pedagogical processes. The author applied anthroposophic approach that gave a reason to interpret this phenomenon through the prism of values, knowledge and norms of behavior.

Key words: medicine, Ukrainian doctors, Halychyna.

An Analysis of the vital activity of Ukrainian doctors in Galicia of the late XIX – early XX century argues that work of local doctors became a good foundation and a prerequisite for the creation of Ukrainian public health care system which was an alternative to the state one. It is selfless (unselfish, sacrificial and free) labor of Ukrainian doctors that provided medical care for Ukrainians (and members of other ethnic groups) for the period. Ukrainian doctors - patriots, citizens, so called «suspilnyky» – became true devotees of domestic medicine, they were its founders. It is they who laid a solid foundation for its further development.

Family of Okunevskiy is a classic example of a dynasty of physicians in Western Halychyna. In the family of Danylo Okunevskiy who was a priest, there were four children. Three sons devoted themselves to medicine: Ipolit Okunevskiy (1834-1902 gg.) became a priest and a doctor; Kyrylo Okunevskiy (? -?) was a doctor, one of the first Ukrainian, who was educated as a pharmacist and Athanasius Okunevskiy.

Athanasius Okunevsky was born in 1833 in Ternopil region. In 1860 he graduated from the Lviv General Greek Catholic seminary. In 1863 he was ordained to the priestly rank. He married Carolyn Luchakivska. The first place of his work was Zalishchyky town, in 1864 - the city of Berezhany, and later in 1865 – Dolzhanka village in Ternopil district. Here his daughter, Sofiia Okunevska, was born on May 12, 1865. In 1866 the family moved to Rusiv, and in 1867 Athanasius Okunevskiy became a pastor in Sadky village near Zalishchyky. Suddenly, in 1870 his wife died. After his wife's death he moved to Bukovyna. Here he was working for eight years as a parish priest in Sathora [2; 3; 8].

In 1878 A. Okunevskiy asked for Metropolia`s permission to study at the Medical Faculty of the University of Vienna. In 1881 he successfully graduated as a doctorate of medicine. Since 1881 he had been working as a district doctor in Starozhyntsi (Bukovyna), later – in Kimpulunha (territory of Romania). In 1887 Athanasius Okunevskiy became a delegate of World Congress of doctors [2].



It is not surprising that his daughter, Sofiia Okunevska (1865-1926 gg.), also wanted to become a doctor. She entered the history of domestic medicine as the first woman doctor in Halychyna. She was also the first Ukrainian in the region, who in 1885 graduated from Lviv academic gymnasium. When making the final exam an audience was crowded, there were Ivan Franko, Ivan Nechui-Levytskyi, Oleksandr Konyskyi with his daughter, Ivan Belei, etc. In 1887 Sofiia entered the University of Zurich to the Medical Faculty and successfully graduated from it in 1895 and earned a doctorate (Doctor of Medicine degree). Sofiia Okunevska became the first woman doctor in the Austro-Hungarian Empire and the first woman in Western Ukraine, which gained university education [3; 5, p. 48].

Sofiia Okunevska worked in Lviv «Narodna Lichnytsia» that was led by her relative, known scientist and public figure, Yevhen Ozarkevych. Here, in Lviv, Sofiia Okunevska created a school of obstetricians and gynecologists and for the first time in Western Ukraine organized courses for nurses and midwives. For her great kindness, responsive heart and a friendly attitude to the patients they called her «St. Sofiia» [2]. Sofiia Okunevska worked on scientific problems, helped Ye. Ozarkevych to conclude the Dictionary of Ukrainian medical terminology participated in the publication of the medical journal «Zdorovlie», printed scientific works [5, p. 48].

She was an activist of Ukrainian women's movement, a member of the Ukrainian association of women with higher education, established in Lviv. She was extremely talented as an author of fiction and very erudite personality; she was admired by Ivan Franko, Vasyl Stefanyk, Olha Kobylanska [4]). During the first national liberation struggle Sofiia worked as a doctor in Hminda and Svatobozhitsy (until 1919) and actually become a medical volunteer. She worked in camps for Ukrainian interned, sacrificed her career of scientist and doctor [2; 3], initiated the treatment of cervical cancer by the method of Marie Skłodowska Curie. She paid much attention to the folk medicine, studied the medicinal properties of plants. In this area she was impressed by work of famous botanist Ivan Lypa [3; 8]. Sofia Okunevska died February 24, 1926 from suppurative appendicitis. She was buried at Lychakiv cemetery in the city of Lviv [4].

One of the most famous Ukrainian doctors in Halychyna was Yaroslav Okunevskyi. He made brilliant career in the military medicine. In 1877 he entered the University of Vienna, the Faculty of Medicine. In 1884 Ya. Okunevskyi began to serve as ship's doctor of the Austria-Hungary's navy, which was based in Croatia in city of Pula. He visited not only Europe and Asia, but also Africa, America and Oceania. His medical practice was highly awarded numerous awards by many sea states. [3]

He was the author of the world's first Charter of Medical Service in Naval Forces (1900). Later, in 1914, he was promoted to Major General of Maritime Medical Service. Under his guardianship were thousands of sailors. At the beginning of World War II with the rank of rear admiral he was the head of Medical Service of the Admiralty of Habsburg fleet where he had worked with his colleagues and subordinated Ukrainian doctors – Captain V. Verbenets, Colonel O. Zarytskyi and Colonel M. Rozhankovskyi etc [1, p. 105-107]. Ya. Okunevskyi was Chief Doctor and Chief of the Main Medical Department of the Staff of naval forces of the Austro-



Hungarian Empire. For great merits (30 years of service) he became the first Ukrainian who was promoted to the Chevalier of Knight's Cross of Franz Joseph, the Knight of the Order of the Spanish queen, the French Legion of Honor, the Chinese Imperial Order of the Dragon, the highest title of Mandarin and many more awards. Ya. Okunevskyi perfectly possessed of military and medical knowledge, versed in the navigation and geography, fluently spoke English, French, Italian and German [2; 3].

At the time of national liberation struggle Rear Admiral Ya. Okunevskyi organized Ukrainian sanitary service and headed it. He supplied the drugs for the Legion of Ukrainian Sich Riflemen, helped their sanitary service, donated funds and more. After proclamation of the West Ukrainian People's Republic he headed the State Medical Mission in Vienna. He provided medical supplies for Halychyna. He sent four sanitary trains for Ukrainian Galician Army. Ya. Okunevskyi contributed to the creation of the First Hutsul Regiment of the Marine Corps, which consisted mostly of the former Austro-Hungarian sailors [3]. Yaroslav Okunevskyi visited almost all countries of the Mediterranean basin. This gave an impetus to write essays about the countries in which he traveled, called «Letters from a foreign land» – a kind of vivid picture of Europe, Asia and northeast Africa of the late nineteenth century [7].

Due to the events of the Second World War, many Ukrainian doctors of Western Ukraine were forced to emigrate to Europe or the Americas. Therefore, their case had been continued by their kids in emigration. Among such was Kseniia Lidiia Yanovych, a doctor in the US, daughter of Volodymyr Yanovych (1868-1931 gg.) who was the first Ukrainian doctor in Stanislaviv [6, p.604]. He was very popular among people, «he went to patients even in remote villages nearby». He often treated free of charge. He was a real «doctor-citizen». He was an important public figure in Halychyna of the early twentieth century. He was head of the branch of «Prosvita» association in Stanislaviv, one of the leaders of Ukrainian National Democratic Alliance (UNDO).

Dmytro Yarosevych, who was the son of Roman Yarosevych (1861-1934 gg.), worked in the United States as psychiatrists. He was born in Bedrykivtsi (near Zalishchyky) in the family of priest. He studied in Kolomyia gymnasium where under the influence of I. Franko, and M. Drahomanov started to «feel himself like Ukrainian». His way to medicine is from theology to philosophy, philology, and then - medicine. After finishing the Faculty of Philology in Lviv he worked in Kolomyia gymnasium, taught classical philology and Ukrainian language and literature. His student was Vasyl Stefanyk, with whom they made friends [6, p.604]. Further R. Yarosevych studied at Krakow University, Faculty of Medicine. V. Stefanyk also studied medicine there. After graduation R. Yarosevych started his medical practice in Borshchiv, where he was actively involved in social and political life of the region. He was member of the Ukrainian Social Democratic Party (USDP), of which in 1897 was chosen as a deputy to the Austrian Parliament. In Vienna he was «as an ambassador», beside political activity he also improved his medical knowledge, did «specialization in dentistry» at the Vienna clinic [6, p.604]. In 1905 he opened his dental clinic in Stanislaviv [p.605]. Simultaneously he worked as a doctor in the



clinic for the railroad. He was elected as head of the Association of Railway Doctors of Stanislaviv Directorate of State Railways» [6, p.605].

Yelysaveta Malaniuk, a daughter of the famous military doctor Osep Malaniuk (1873-1949 gg.), worked as dentist in Austria. Osep Malaniuk was a lieutenant colonel of Ukrainian Galician Army, commandant of the first military hospital in Stanislaviv. He had been devoted to military medicine for 20 years [6, p.607]. Like many doctors in Halychyna he came from a family of priest. He was born in Chortkivshchyna region. He studied medicine in Graz. He was one of the organizers of the Society of Ukrainian Students called «Sich» in Vienna. In 1909 he was graduated from doctorate of medicine in the University of Krakow [6, p.607]. During 1920-1930s he worked in Stanislaviv as surgeon and radiologist. He was the first doctor in the city who bought an x-ray machine for his office. He died in Graz (Austria) February 6, 1949.

Kost Voyevodka (1891-1944 gg.) was a famous specialist in the field of gynecology and obstetrics. He was killed by the Gestapo in March, 1944, together with his son [6, p.607]. He was born in Prague in the family of Lev Voyevodka who worked as doctor in Kitsman in Bukovina and was the founder of the Ukrainian Medical Association in Lviv. In 1909 Kost Voyevodka entered the German University in Prague, the Medical Faculty. When First World War broke, the first units of the Ukrainian Sich Riflemen (USS) were formed. Kost Voyevodka as senior doctor voluntarily joined the USS. In 1915 he got off to finish his medical education in Prague and receive a diploma. Then he returned to the army, became the doctor at first in Rozvadiv, on the Dniester, and then in Verpolyanka. In 1916 during the battle at Koniuchy K. Voyevodka got to Russian captivity. In 1917 he along with Ivan Rychlo, the doctor, organized sanitary service for USS in Eastern Ukraine. Later, in 1918, he was sent by the Government of the Ukrainian National Republic to Berlin as chief of sanitary mission for Ukrainian prisoners – «the former soldiers of tsarist army» [6, p.608]. From 1921 to 1923 he had been specialized in the field of gynecology and obstetrics in the Berlin clinic. In 1923 he became Assistant of well-known Professor Wagner in gynecological clinic at German University in Prague. In 1925 being a highly qualified specialist he returned to Halychyna and opened private clinic in Stanislaviv. Soon he became one of the best specialists among Ukrainian and foreign doctors, since 1941 he had worked as Director of the Hospital. By the way, Kost Voyevodka was one of the few doctors in Stanislaviv, who had his own car of «Mercedes» brand and held his own driver. Despite intensive medical practice, he found time for social activities. He was founder and head of the branch of ULT, longtime chairman of the Society of military graves protection, member of numerous Ukrainian associations and institutions [6, p.608].

Thus, dynasties of Okunevskiyi, Ozarkevych, Malaniuk, Voievidka played an important role in the formation and development of Ukrainian medicine. They were not only military doctors, prominent academics, medical practitioners, but also the national conscious people, active public figures, members and organizers of many Ukrainian associations.



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