

# European Journal of Clinical and Experimental Medicine

ISSN 2544-1361  
ISSN 2544-2406

Formerly: Medical Review

**Quarterly**

**Vol. 16, No. 4**

**Publication date: December 2018**



**Rzeszów, Poland 2018**

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ICV 2016 = 83.64  
MNIŚW: 7.0

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e-ISSN 2544-1361  
ISSN 2544-2406

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PUBLISHER: PUBLISHING OFFICE OF THE UNIVERSITY OF RZESZÓW  
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## ORIGINAL PAPER

Marek Biesiadecki  (ACDEFG), Sabina Galiniak  (BDFG), Dorota Bartusik-Aebisher  (DFG),  
David Aebisher  (DFG)

# Receiver operating characteristic analysis of the FeNO biomarker in the diagnosis of asthma

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## Abstract

**Introduction.** The fraction of exhaled nitric oxide (FeNO) is used as a non-invasive biomarker that reflects inflammation in the airways. It is so versatile that it is used to control asthma severity as well as to monitor response to treatment. However, the exact cut-off point of the nitric oxide level which allows one to make a precise diagnosis of asthma is unclear.

**Aim.** To examine the possibility of using advanced statistical methods such as receiver operating characteristic for the analysis of FeNO concentrations for improving the diagnosis of asthma.

**Materials and methods.** Receiver operating characteristic (ROC) was used for analyzing results to determine levels of nitric oxide which may be a prognostic indicator of asthma. The studied group consisted of 111 children including 69 asthmatic patients, and 42 age- and sex-matched healthy subjects. Measurement of exhaled nitric oxide was conducted in all subjects included in this study.

**Results.** FeNO level was higher in asthmatic patients. The analysis of results showed that the cut-off point for the FeNO concentration is 11.5 ppb. Sensitivity and specificity with the FeNO level allowed us to determine a value of the diagnostic variable of FeNO concentration of 14.0 ppb. A comparison of FeNO level and sex of the subjects showed there is no correlation between these parameters of patients.

**Conclusions.** Currently, the FeNO measurement provides complementary data in the care of a patient suffering from asthma, however analysis of more studies on a larger group of patients is needed.

**Keywords.** asthma, nitric oxide, ROC curve

## Introduction

The problem of classifying data relevant to the diagnosis of diseases are often found in medicine. Establishing a correct diagnosis requires extensive medical knowledge

and experience. Currently, it is helpful to use forecasting models based on advanced statistical analysis methods. Properly defined models show complex relationships and explain observed trends. Using advanced statistical

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 3.10.2018 | Accepted: 10.11.2018

Publication date: December 2018

Biesiadecki M, Galiniak S, Bartusik-Aebisher D, Aebisher D. *Receiver operating characteristic analysis of the FeNO biomarker in the diagnosis of asthma.* *Eur J Clin Exp Med.* 2018;16(4):253–258. doi: 10.15584/ejcem.2018.4.1

analysis may be a basis for the diagnosis of many diseases including asthma based on non-invasive as well as invasive procedures. A series of tests are used to interpret the data and created models, adjusting their selection to the problems posed.<sup>1</sup> In human physiology, nitric oxide (fraction of exhaled nitric oxide, FeNO) was initially described as an endothelial diastolic agent which is able to modulate coronary artery tension.<sup>2</sup> In 1991, Gustafsson et al. discovered nitric oxide in exhaled air in humans, which aroused interest in its role in respiratory diseases.<sup>3</sup> Subsequently, it was confirmed that in persons suffering from asthma, the concentration of nitric oxide in exhaled air is higher than in control groups.<sup>4</sup> The results of the studies had also given the basis for the description of the effect of glucocorticosteroids on the reduction of FeNO, which confirmed the endogenous origin of nitric oxide and suggested its role in the underlying asthma and airway inflammation.<sup>5,6</sup> Currently, FeNO is used as a non-invasive biomarker for detection of inflammation in the airways. It is so versatile that it can be used successfully to evaluate asthma severity and assess response to treatment. The precise level of FeNO in the asthma management algorithm has not yet been established. However there is indisputable data on the usefulness of FeNO measurements in the diagnosis of asthma, in the assessment of its control and severity, and in the selection of inhaled glucocorticoid doses and the detection of the presence of inflammation in the airways.

The aim of the article is to examine the possibility of using advanced statistical methods for the analysis of FeNO concentrations which may be helpful in the diagnosis of asthma. In particular, the cut-off point was determined and the specificity and significance were calculated. In addition, we evaluate the influence of patient sex on the level of FeNO. The obtained results were compared with previous literature data.

### Method of FeNO measurement and interpretation, factors affecting the concentration of FeNO

FeNO measurements were carried out using direct techniques using a real-time analyzer. This method is based on observations from 1997 where it was noted that the FeNO level is inversely proportional to the value of expiratory flow. This phenomenon is described as the dependence of concentration on flow. A high flow correlates with low FeNO levels and the low flow again is associated with a higher FeNO value. The dependence on flow is explained by the fact that nitric oxide appears in exhaled air as a result of diffusion occurring in the airways.<sup>7,8</sup>

Based on concentration-flow dependence and using standardized measurement techniques, the FeNO value can be used as a diagnostic tool. The position of the American Thoracic Society and the European Respiratory Society (ATS/ERS) standardizes FeNO measure-

ments for a flow of 50 ml/s.<sup>9</sup> In addition to the flow rate, FeNO may be influenced by other factors, such as age height and gender.<sup>10,11</sup>

It should be mentioned that a low concentration of FeNO cannot exclude asthma in children.<sup>9</sup>

The American Society for Thoracic Diseases recommends, among others:

- use of the measurement of exhaled nitric oxide in the diagnosis of eosinophilic bronchitis
- use of FeNO in determining the likelihood of responding to glucocorticoid treatment in patients with chronic inflammatory symptoms of the respiratory tract
- use of FeNO in monitoring of airway inflammation in patients with asthma
- interpretation of FeNO concentration < 20 ppb in children as unlikely eosinophilic inflammation and poor response to glucocorticoid treatment
- interpretation of FeNO > 35 ppb in children as indicative of eosinophilic inflammation and a good response to treatment with glucocorticosteroids in symptomatic patients
- interpretation of FeNO concentrations between 20–35 ppb in children based on the clinical situation.<sup>9,12</sup>

### Receiver characteristic operating curve

A receiver operating characteristic curve, (ROC curve), is a graphical illustration and fundamental tool used for the evolution and comparison of diagnostic systems that enable comparisons of sensitivity and specificity.

The true-positive rate is also known as sensitivity, recall or probability of detection in machine learning. The false-positive rate is also known as the fall-out or probability of false alarm and can be calculated as (1 – specificity).<sup>13</sup> The ROC methodology was first used in medicine in the late 1960s after its development in 1950s. Currently ROC is widely used in medicine and psychology, radiology, biometrics, meteorology, and other scientific areas for many years.<sup>14–17</sup> The ROC is also known as a relative operating characteristic curve, because it is a comparison of two operating characteristics as the criterion changes.

### Materials and methods

The research group consisted of children aged 6 to 14 years living in the Podkarpackie Province, which are covered by medical care in Hospital No. 2 in Rzeszów. The study group consisted of 111 children, 42 of including healthy subjects and 69 asthmatic patients, who were diagnosed according to standards. Generally 44 girls and 67 boys were examined, and their characteristics are presented in the Table 1. The level of nitric oxide was measured in all subjects included in this study by using Hyp'Air FeNO (MediSoft, Belgium) according to guidelines of ATS/ERS in September 2018.<sup>9</sup>

Table 1. Characteristics of the studied group (mean ± SD)

	n	Sex (F/M)	Age (years)	Height (cm)	Weight (kg)	BMI
healthy control	42	19/23	9.26 ± 3.18	139.32± 16.45	36.88 ± 11.57	18.72 ± 3.93
asthma	69	25/44	10.28 ± 3.74	144.34± 20.51	41.19 ± 17.08	18.91 ± 3.85

The study was approved by local Bioethical Commission.

In the statistical analysis, multivariate logistic regression analysis was performed to identify clinical features associated with asthma. In addition to the assessment of diagnostic accuracy, the sensitivity, specificity and predictive values were calculated, and the area under the curve (AUC) was calculated for the FeNO values. The statistical analysis of the data was performed using PQStat (version 1.6.6, PQStat Software, Poznań, Poland <https://pqstat.pl/>).

Results

The analysis showed that there is a significant correlation between the level of FeNO in the exhaled air and the diagnosed disease entity (p-value <0.001). The AUC is 0.879. Detailed data is given in Table 2.

Table 2. ROC Curve Analysis

ROC Curve Analysis	
Analysed variables	FeNO [bbp];disease entity
Number of unspecified	0
Number of missing data	0
Significance level	0.05
Size	111
Size STATE + (1)	69
Size STATE - (0)	42
Direction of diagnostic variable	stimulant
Prevalence	0.621622
-95% CI	0.524625
+95% CI	0.711957
DeLong's method	
AUC	0.879572
SE(AUC)	0.032277
-95% CI	0.816311
+95% CI	0.942833
Z statistic	6.688444
p-value	<0.000001
For cut-off	
Cost FN - wrong diagnosis	1
Cost FP - wrong diagnosis	1

The analysis allowed to determine the cut-off point for the concentration of 11.5 ppb FeNO yielding sensitivity and relevance, respectively, at the level of 0.928/0.643 as presented in Figure 1. Sensitivity and specificity in correlation with the FeNO concentration

was used to determine a value of the diagnostic variable of 14.0 ppb FeNO concentration as shown in Figure 2.

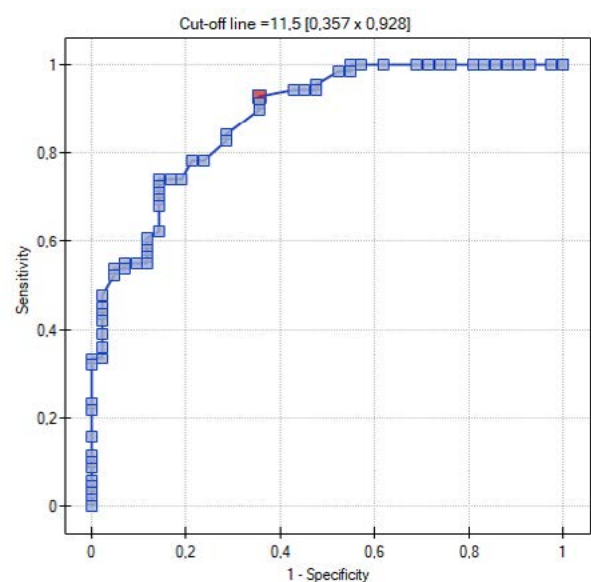


Fig. 1. ROC curve – determination of cut-off point

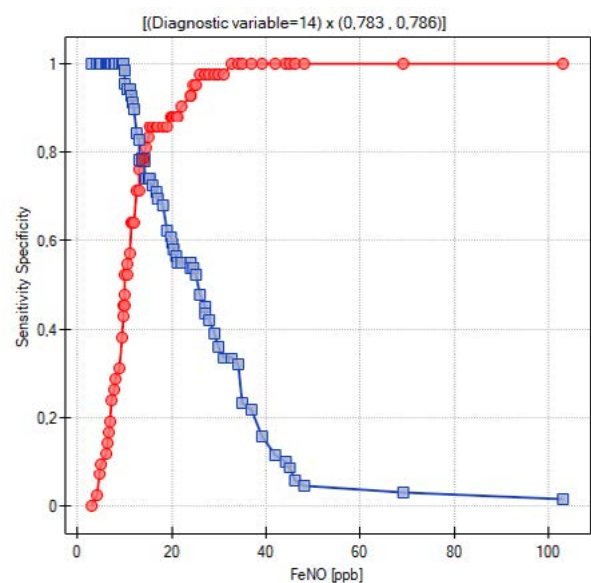
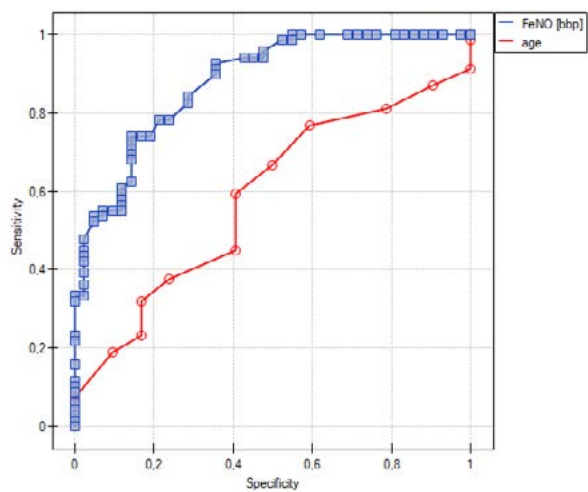


Fig. 2. ROC curve – determination of diagnostic variable

A comparison of the age of the subjects with disease showed that occurrence of asthma does not correlate with age of patients. The distribution curve presents typically a random character. Detailed data is presented in Table 3 and Figure 3.

**Table 3.** Dependent ROC curves – comparison of age and occurrence of the asthma

Dependent ROC curves - comparison	
Analyzed variables	FeNO [bbp];age;disease entity
Number of unspecified	0
Number of missing data	0
Significance level	0.05
Grouping variable	disease entity
Size	111
Size STATE + (1)	69
Size STATE - (0)	42
Variable age	
Direction of diagnostic variable	stimulant
AUC	0.584886
SE(AUC)	0.055132
-95% CI	0.476829
+95% CI	0.692943



**Fig. 3.** Dependent ROC curves – comparison of age and occurrence of the asthma

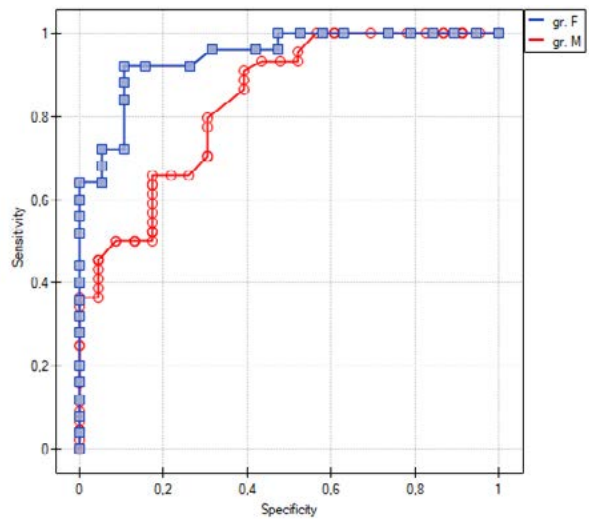
The gender of patients does not have a significant impact on the measurement results. The analysis showed that there is no significant correlation between FeNO concentration in exhaled air and gender (p-value 0.076). It is worth noting that the results of the boy's measurements were lower by an average of 11%. Detailed data is provided in Table 4 and Figure 4.

The FeNO cut-off value is 11.5 ppb (AUC 0.879,  $p < 0.001$ ) and this showed the best combination of sensitivity and specificity for the positive reaction for the whole group. The FeNO cut-off value of 32.6 ppb showed a specificity of 100%. The negative prognostic level with high sensitivity and negative predictive value was not determined. With the use of logistic regression, no significant correlation between the results obtained by boys and girls was confirmed. Currently, the FeNO

measurement provides complementary data in the care of a patient suffering from asthma.

**Table 4.** Independent ROC curves – comparison of patients' sex and FeNO level

Independent ROC curves - comparison	
Analyzed variables	FeNO [bbp];disease entity
Number of unspecified	0
Number of missing data	0
Significance level	0.05
Grouping variable	sex
Direction of diagnostic variable	stimulant
Method	DeLong
Group name	F
Size	44
Size STATE + (1)	25
Size STATE - (0)	19
AUC	0.944211
SE(AUC)	0.031646
-95% CI	0.882185
+95% CI	1
Group name	M
Size	67
Size STATE + (1)	44
Size STATE - (0)	23
AUC	0.837451
SE(AUC)	0.051184
-95% CI	0.737132
+95% CI	0.937769
AUC1-AUC2	0.10676
SE(AUC1-AUC2)	0.060177
Z statistic	1.774102
p-value	0.076046



**Fig. 4.** Independent ROC curves – comparison of patients' sex and FeNO level



## Discussion

Measurements of nitric oxide in exhaled air is considered as a parameter which provides complementary data in the care of patients suffering from asthma.

Currently, there is no significant value of FeNO which is a precise indicator of asthma. The analysis of the usefulness of nitric oxide concentration in patients with asthma as a marker of inflammation that helps in making clinical decisions has been studied and discussed in many studies. The conclusions are ambiguous; some studies have shown a close correlation between FeNO and the degree of bronchial hyperresponsiveness and others have presented only a partial correlation with no statistical significance. On the other hand, some researches have questioned the usefulness of this method in making clinical decisions. Paraskakis et al. determined FeNO levels at different expiratory flow rates in 132 children. Based on the assessment of follicular nitric oxide using a two-compartment model, they confirmed the presence of inflammatory process in small airways.<sup>18</sup>

In the present study, the relationship between FeNO level in children with asthma and results in healthy children was demonstrated. We have found that FeNO level was significantly higher in asthmatic patients as compared to healthy subjects.

Similar results were revealed by Silvestri et al. In their study, although the FeNO concentration in the group of children with asthma (mean 30 ppb) was higher than in the control group (mean 4.1 ppb), FeNO did not correlate with spirometric parameters.<sup>19</sup> Moreover, Olin et al. determined the average value of FeNO in healthy people as well as asthmatic patients. The average level of FeNO was 15.8 ppb (range between 11.4 – 22.4) in control group, while in patients with asthma FeNO level was 22.5 (range between 16 – 31.2).<sup>20</sup> Afterwards, Buchvald et al. studied healthy children aged 4-17. The geometric mean for FeNO from measurements made in 405 children was 9.7 ppb.<sup>21</sup>

Moreover, a meta-analysis of 4,691 patients with asthma conducted by Li et al. demonstrated that measurement of FeNO showed a diagnostic sensitivity of 0.78.<sup>22</sup> Wang et al. demonstrated that the optimal cut-off value of FeNO was 19.5 ppb for the diagnosis of typical bronchial asthma, while our results have indicated that the cut-off point is 11.5 ppb.<sup>23</sup> A higher cut-off point of 35.5 ppb was determined by Gao & Wu in 75 adult uncontrolled asthmatic patients and was considered as a predictor of sputum eosinophilia.<sup>24</sup>

Buchvald et al. also showed that the FeNO level was higher with age of tested subjects.<sup>21</sup> Literature data indicate that in adults there is no consistent relationship between FeNO and age, but there are reports that in children the FeNO concentration increases with age.<sup>25,26</sup> Negative correlation between FeNO and age as well as BMI in patients with asthma was also found by Rawy

& Mansour.<sup>27</sup> Our research has not confirmed a correlation between the FeNO level and sex of the examined children. Obtained results and their analysis have showed random distribution of results. It seems that the FeNO values should be higher in boys than girls, but there are conflicting results on this subject.<sup>28</sup> Nevertheless, some researchers notice that measurements of nitric oxide cannot be routinely recommended for all children with asthma.<sup>29</sup>

In summary, studies indicate that measurements of nitric oxide in the lower respiratory tract may be helpful in the diagnosis of respiratory diseases, including asthma. However, more studies of large group of patients are required to set precise points of FeNO which will be indicator of various respiratory diseases. Currently, measurements of nitric oxide may be only useful in combination with clinical outcomes and traditional respiratory tests.

## References

1. Bellazzi R, Zupan B. Predictive data mining in clinical medicine: Current issues and guidelines. *Int J Med Informatics*. 2008;77:81-97.
2. Palmer RM, Ferrige AG, Moncada S. Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor. *Nature*. 1987; 327:524-526.
3. Gustafsson LE, Leone AM, Persson MG, et al. Endogenous nitric oxide is present in the exhaled air of rabbits, guinea pigs and humans. *Biochem Biophys Res Commun*. 1991; 181:852-857.
4. Yates DH, Kharitonov SA, Robbins RA, et al. Effect of a nitric oxide synthase inhibitor and a glucocorticosteroid on exhaled nitric oxide. *Am J Respir Crit Care Med*. 1995; 152:892-896.
5. Kharitonov SA, Yates DH, Barnes PJ. Inhaled glucocorticoids decrease nitric oxide in exhaled air of asthmatic patients. *Am J Respir Crit Care Med*. 1996; 153:454-457.
6. Cordeiro D, Rudolphus A, Snoey E, Braunstahl GJ. Utility of nitric oxide for the diagnosis of asthma in an allergy clinic population. *Allergy Asthma Proc*. 2011; 32(2):119-126.
7. Silkoff PE, Mc Clean PA, Slutsky AS, et al. Marked flow-dependence of exhaled nitric oxide using a new technique to exclude nasal nitric oxide. *Am J Respir Crit Care Med*. 1997; 155:260-267.
8. Manna A, Montella S, Maniscalco M, Maglione M, Santamaria F. Clinical application of nasal nitric oxide measurement in pediatric airway diseases. *Pediatr Pulmonol*. 2015; 50(1):85-99.
9. Dweik RA, Boggs PB, Erzurum SC, et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. *Am J Respir Crit Care Med*. 2011; 184:602-615.
10. Brody DJ, Zhang X, Kit BK, Dillon CF. Reference values and factors associated with exhaled nitric oxide: U.S. youth and adults. *Respir Med*. 2013; 107(11):1682-1691.

11. Wang Y, Li L, Han R, et al. Diagnostic value and influencing factors of fractional exhaled nitric oxide in suspected asthma patients. *Int J Clin Exp Pathol.* 2015; 8(5):5570-5576.
12. Kłak A, Krzych-Falta E, Samoliński B. Rola tlenku azotu w stanie zapalnym dróg oddechowych. *Alerg Astma Immun.* 2013; 18: 91-96.
13. "Detector Performance Analysis Using ROC Curves - MATLAB & Simulink Example". [www.mathworks.com](http://www.mathworks.com). Access 11 October 2018.
14. Hajian-Tilaki K. Receiver Operating Characteristic (ROC) Curve Analysis for Medical Diagnostic Test Evaluation. *Caspian J Intern Med.* 2013; 4(2):627-635.
15. Williams BB, Flood AB, Demidenko E, Swartz HM. ROC Analysis for Evaluation of Radiation Biodosimetry Technologies. *Radiat Prot Dosimetry.* 2016; 172(1-3):145-151.
16. Peres DJ, Iuppa C, Cavallaro L, Cancelliere A, Foti E. Significant wave height record extension by neural networks and reanalysis wind data. *Ocean Modelling.* 2015; 94:128-140.
17. Youngstrom EA. A primer on receiver operating characteristic analysis and diagnostic efficiency statistics for pediatric psychology: we are ready to ROC. *J Pediatr Psychol.* 2014; 39(2):204-221.
18. Paraskakis E, Brindicci C, Fleming L, et al. Measurement of bronchial and alveolar nitric oxide production in normal children and children with asthma. *Am J Respir Crit Care Med.* 2006; 174:260-267.
19. Silvestri M, Spallarossa D, Battistini E, et al. Dissociation between exhaled nitric oxide and hyperresponsiveness in children with mild intermittent asthma. *Thorax.* 2000; 55:484-488.
20. Olin AC, Alving K, Toren K. Exhaled nitric oxide: relation to sensitization and respiratory symptoms. *Clin Exp Allergy.* 2004;34:221-226.
21. Buchvald F, Baraldi E, Carraro S, et al. Measurements of exhaled nitric oxide in healthy subjects age 4 to 17 years. *J Allergy Clin Immunol.* 2005;115:1130-1136.
22. Li Z, Qin W, Li L, Wu Q, Wang Y. Diagnostic accuracy of exhaled nitric oxide in asthma: a meta-analysis of 4,691 participants. *Int J Clin Exp Med.* 2015; 8(6):8516-8524.
23. Wang TY, Shang YX, Zhang H. Diagnostic values of fractional exhaled nitric oxide for typical bronchial asthma and cough variant asthma in children. *Zhongguo Dang Dai Er Ke Za Zhi.* 2015; 17(8):800-805.
24. Gao J, Wu F. Association between fractional exhaled nitric oxide, sputum induction and peripheral blood eosinophil in uncontrolled asthma. *Allergy Asthma Clin Immunol.* 2018; 14:21. doi: 10.1186/s13223-018-0248-7.
25. Franklin PJ, Taplin R, Stick SM. A community study of exhaled nitric oxide in healthy children. *Am J Respir Crit Care Med.* 1999;159:69-73.
26. Kissoon N, Duckworth LJ, Blake KV, et al. Exhaled nitric oxide concentrations: online versus offline values in health children. *Pediatr Pulmonol.* 2002; 33:283-292.
27. Rawy AM, Mansour AI. Fraction of exhaled nitric oxide measurement as a biomarker in asthma and COPD compared with local and systemic inflammatory markers. *Egypt J Chest Dis Tuberc.* 2015; 64(1):13-20.
28. Tsang KW, Ip SK, Leung R, et al. Exhaled nitric oxide: the effects of age, gender and body size. *Lung.* 2001;179:83-91.
29. Ferraro V, Carraro S, Bozzetto S, Zanonato S, Baraldi E. Exhaled biomarkers in childhood asthma: old and new approaches. *Asthma Res Pract.* 2018; 4:9. doi: 10.1186/s40733-018-0045-6.



## ORIGINAL PAPER

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# Symptoms of menopause and health of women during perimenopause

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## Abstract

**Introduction.** Perimenopausal age is the time in a woman's life, when her reproductive capacity declines. Characteristic symptoms in the majority of systems accompany this process.

**Aim.** The aim of the study was to determine the symptoms of menopause and investigate the most common health problems in perimenopausal women.

**Materials and methods.** The study involved 180 women in perimenopausal age (45-55 years). The subjects were mainly residents of rural areas (65%) and married (84%). Most of them declared secondary education (57%). A questionnaire developed by the authors was used in the study.

**Results.** Most women observed typical menopausal symptoms mostly between 45 and 49 years of age. Most often, these were hot flushes, the second place was night sweats, and the third place was insomnia. Almost 40% of women are treated for chronic diseases, most of them for hypertension, thyroid disease and diabetes.

**Conclusions.** The changes associated with perimenopausal age in the majority of respondents include genitourinary system, respiratory system, skeletal system and metabolic changes. Level of education influences the level of knowledge among women on the menopause. Women from rural areas used non-pharmacological methods to mitigate the symptoms of menopause to a greater extent.

**Keywords.** menopause, perimenopausal age, women, health

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 11.09.2018 | Accepted: 31.10.2018

Publication date: December 2018

Nagórska M, Sowa A, Wardak K, Lesińska-Sawicka M. *Symptoms of menopause and health of women during perimenopause.* Eur J Clin Exp Med. 2018;16(4):259–266. doi: 10.15584/ejcem.2018.4.2

Introduction

Menopause or climacterium is a natural process resulting from declining ovarian function. During this period, numerous disorders appear, which are both of psychogenic and somatogenic character, and they are mainly the result of changes occurring due to the reduction of estrogen secretion, by the aging ovaries. Before menopause occurs, there are changes in the female body that are progressing. They usually last for 5-6 years and occur mostly at the age of 42-47. In Poland, this period is on average between 47 and 51 years of age.<sup>1,2</sup>

The term menopause is used to describe the last menstrual period in a woman's life. According to the *North American Menopause Society* (NAMS), menopause is a physiological stage, defined as the last menstrual period in a woman's life and suppression of ovarian function. Natural menopause is diagnosed after 12 months without menstruation. It occurs on average in women aged 52, but may occur between 40 and 58 years.<sup>3</sup> It is accompanied by characteristic ailments from most systems. These symptoms, known as fallout or climacteric syndrome, include: hot flushes, night sweats, palpitations, insomnia, mood swings, irritability and can be very annoying.<sup>4,5</sup>

Menopause is divided into several periods. Premenopause is the time between the period of full fertility and menopause, occurring usually around 40 years of age. During this time, no hormonal disturbances are experienced. Only in laboratory tests an elevated level of FSH is found. Perimenopause is a period that begins shortly before menopause and lasts up to 12 months after its occurrence. Characteristic symptoms, the so-called fallout may occur then. In about 40% these cycles are anovulatory. The level of estrogen and progesterone decreases and the level of FSH and LH increases. The number of Graaffian follicles drops relatively quickly in the ovaries. In about 40% these cycles are anovulatory. Menopause means the last bleeding. The occurrence of the last menstrual period depends on the number of Graaffian follicles. Their greatest amount occurs in the fetal period and decreases as the years go by. Female fertility begins to gradually decline at the age of 35. It was also proved that in women who had menarche late, the climacteric period will appear relatively early. Lifestyle,

general health, genetic factors also affect the appearance of menopause. It is accelerated by: stress, poor diet, smoking, diabetes, drugs that lower estrogen levels, chemotherapy, immune system diseases, ovarian removal, radiation therapy. Postmenopausal period is the time when no monthly bleeding appear. In the woman's body significant hormonal changes occur - decreased progesterone and estrogen levels as well as high levels of FSH and LH.<sup>6,7</sup>

In addition to physiological symptoms, somatic disorders including the circulatory system, skeletal system, skin, urogenital and mental systems from irritability and mood changes to depression often appear in this period.<sup>4</sup> The aim of the study was to determine menopausal symptoms and health issues in women during this period.

Material and methods

The study covered 180 women in the perimenopausal period (45-55 years), residents of the Subcarpathian Voivodeship. The inclusion criterion was the age of women in the range of 45-55 years. Research carried out in the period from January to March 2015. The majority of women had secondary education (57.2%), 27.2% had higher education, and 15.6% had primary education. The city, as a place of residence, was indicated by 34.4% of women, and the countryside - 65.6% of the respondents. The majority of the respondents were married (84.4%), and 15.6% of the respondents were single (Table 1).

The diagnostic survey method, the survey research technique were used and the research tool was the questionnaire developed by the authors. The differences between variables were verified using the Pearson chi square test. The level of significance was adopted at  $p < 0.05$ . Statistica 2.0 was used for calculations.

Results

In 24.4% of women, menarche occurred between 11 and 12 years of age. The first menstrual period most often occurred in women between 13 and 14 years (52.8%), and at the age of 15 and over in 22.8% of women.

A group of 8.9% of women have never been pregnant. 22.2% of women had one pregnancy and 36.7%

Table 1. Socio-demographic data of the surveyed women

Age	45-47		48-50		51-55	
	56	31.1%	50	27.8%	74	41.1%
Education	primary		secondary		higher	
	28	15.6%	103	57.2%	49	27.2%
Place of residence	city		countryside			
	62	34.4%	118	65.6%		
Marital status	married		single			
	152	84.4%	28	15.6%		

Table 2. Obstetric and gynecological history

Age at menarche	11-12		13-14		15 and more			
	44	24.4%	95	52.8%	22	22.8%		
Parity	0		1		2		3 and more	
	16	8.9%	40	22.2%	66	36.7%	58	32.2%
Age at the first birth	<18		18-25		26-35		>35	
	18	10.0%	106	58.9	40	22.2%	2	1.1
History of gynecological conditions	yes		no					
	70	61.1%	110	38.9%				
Gynecological syrgeries	yes		no					
	70	61.1%	110	38.9%				
Age at the first symptoms	35-44		45-49		50-54			
	44	24.4%	112	62.2%	24	13.3%		
Typical menopause symptoms	yes		no					
	178	98.9%	1	1.1%				
Ob.-gyn consultation	yes		no		I am planning			
	42.2%		42.2%		15.6%			
HRT using	yes		no		I am planning			
	12.2%		80.0%		14	7.8%		
Constant gynecological care	yes		no					
	146	81.1%	34	18.9%				
Comorbidities	yes		no					
	71	39.4%	109	60.6%				

were pregnant twice. A group of 32.2% of women were pregnant at least 3 times. 10.0% of women gave birth to their first child before the age of 18. The women surveyed most often gave birth to the first child when they were between 18 and 25. The group of 22.2% of women gave birth to the first child between 26 and 35 years old. The group of 7.8% of respondents never gave birth.

Most women (98.9%) observed typical menopausal symptoms. Almost a quarter (24.4%) of women had the first symptoms of menopause between 35 and 44 years of age. Most frequently the surveyed women observed such symptoms between 45 and 49 years of age (62.2%). A group of 13.3% women - between 50 and 54 years of age. More than half of women (61.1%) were diagnosed with gynecological disease (most often endometriosis and uterine fibroids) and the same percentage of women underwent gynecological procedures. Under the constant care of the gynecologist there were 81.1% of women. 39.4% of women are treated for chronic diseases, most of them for hypertension, thyroid disease and diabetes (Table 2).

All respondents observed the occurrence of typical menopausal symptoms. Most often, these were hot flushes (82.2%), the second place was night sweats (61.1%), and the third place was insomnia (45.0%). 41.1% of women reported heart palpitations and 38.3%

of subjects reported lower energy. To a lesser extent, women observed bone and joint pains, decreased concentration and memory problems. Fig. 1.

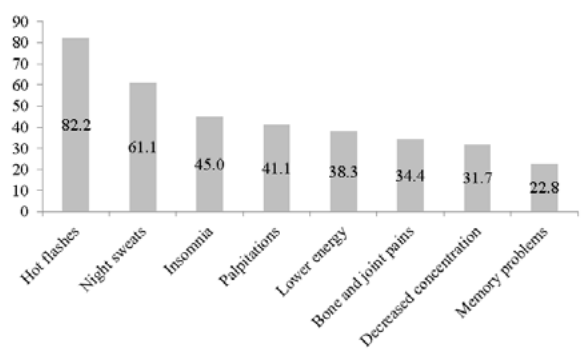


Fig. 1. Symptoms of menopause in the surveyed women

When analyzing the results of the study, it was not found that the incidence of somatic problems typical of the perimenopausal period depended on the place of residence of women. Statistically significant differences related to the occurrence of psychiatric symptoms in the study, which were more frequent in women living in the city (90.3%) than those living in the countryside (78.0%) and the use of means to mitigate the symptoms of menopause - 81.4% of rural women and 54.8% of urban residents (Table 3).

**Table 3.** The incidence of menopausal symptoms and the place of residence.

The menopausal symptoms and the place of residence		The place of residence				p
		City		Countryside		
		N	%	N	%	
The incidence of typical menopausal symptoms	Yes	62	100	116	98.3	0.3026
	No	-	-	2	1.7	
Problems within the reproductive system	Yes	32	51.6	54	45.8	0.4553
	No	30	48.4	64	54.2	
Problems within the urinary system	Yes	51	82.3	84	71.2	0.1031
	No	11	17.7	34	28.8	
Problems within the respiratory system	Yes	45	72.6	88	74.6	0.7721
	No	17	27.4	30	25.4	
Changes in the skeletal system	Yes	53	85.5	98	83.1	0.6731
	No	9	14.5	20	16.9	
Metabolic changes	Yes	54	87.1	102	86.4	0.9021
	No	8	12.9	16	13.6	
Problems within the cardio-vascular system	Yes	22	35.5	36	30.5	0.4973
	No	40	64.5	82	69.5	
Sexual dysfunctions	Yes	32	51.6	70	59.3	0.3213
	No	30	48.4	48	40.7	
Weight gain from the onset of menopause	No	23	37.1%	36	30.5%	0.3709
	Yes	39	62.9%	82	69.5%	
Psychiatric symptoms	Yes	56	90.3%	92	78.0%	<b>0.0394</b>
	No	6	9.7%	26	22.0%	
The use of means to mitigate the symptoms of menopause	Yes	34	54.8%	96	81.4%	<b>0.0002</b>
	No	28	45.2%	22	18.6%	

**Table 4.** Self-assessment of knowledge about menopause and education of the respondents

Self-assessment of knowledge about menopause	Education						p
	Primary		Secondary		Higher		
	N	%	N	%	N	%	
Very good	2	7.1	14	13.6	9	18.4	0.2044
Good	14	50.0	56	54.4	32	65.3	
Satisfactory	10	35.7	29	28.2	8	16.3	
Unsatisfactory	2	7.1	4	3.9	0	0.0	

13.9% of women assessed their state of knowledge about menopause as very good. A good level of knowledge in this field was declared by 56.7% of the respondents, satisfactory knowledge by 26.1% of people, and poor by 3.3% of the women. The analysis of the research showed that a higher level of knowledge about menopause and related problems was declared more often by women with higher education (18.4%). A good level of knowledge in this area was declared more often by women with higher education (65.3%). Satisfactory level of knowledge was most often indicated by people with primary education (35.7%), but these differences were not statistically significant (Table 4).

The respondents asked about the methods of alleviating the symptoms of fallout usually indicated a change in diet to easily digestible, which was declared by 13.9%. Most women, however, did not change their

diet (86.1%). 42.2% of the women declared active lifestyle. Among the used forms of physical activity, Nordic walking was the most frequently mentioned (36.1%). Running was on the second place (21.1%). To a lesser extent, women chose fitness (13.9%), Zumba (12.8%), swimming (12.2%) or gym (11.1%). Few women chose team sports (3.3%). However, almost every fourth respondent (23.3%) did not do any sport. Fig. 2.

The use of pharmacological or non-pharmacological agents to eliminate the symptoms of the fallout was indicated by 72.2% of the women. Among non-pharmacological agents, the respondents most often used soya preparations. The group of 27.8% of the respondents did not use any methods. Hormone replacement therapy (HRT) was used by 12.2% of women, and a group of 7.8% of the respondents declared using HRT in the future.

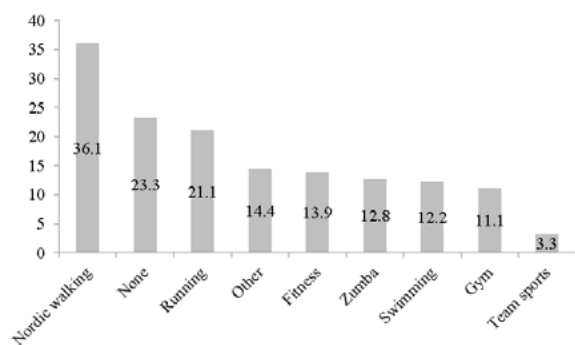


Fig. 2. Forms of physical activity

One of the aims of the paper was to identify health problems during menopause and many women confirmed in the study that apart from physiological symptoms, health problems also appear in this period.

Respiratory symptoms occurred in the group of 73.9% of women. The most common symptom indicated by the respondents was panting (66.9%). To a lesser extent, shortness of breath (22.6%), dyspnea (27.0%), chest pain (15.0%) were indicated.

Cardiovascular symptoms occurred in the group of 32.2% women.

Among cardiovascular ones, the most frequently mentioned were coronary heart disease or heart failure (31.0%). Some respondents also had a heart attack (6.9%).

The skeletal problems were indicated by 83.9% of women. The subjects most frequently mentioned back pains (66.9%). In the second place were sacral pain (47.0%), and the third place was pain between the shoulder blades (26.5%). To a lesser extent, the women experienced pain of the thoracic spine, decreased body

height, hump, susceptibility to fractures or changes in the spine.

The occurrence of metabolic changes was indicated by 86.7% of women. The respondents most often observed an increase in body weight from 2 kg to 20 kg (68.6%), followed by a slower metabolism (51.9%) and constipation (44.2%). To a lesser extent, women observed an increase in LDL cholesterol, an elevated level of fasting glycaemia or a decrease in LDL cholesterol.

Skin lesions appeared in most women (89.4%). In this group, skin dryness most frequently occurred (77.0%). To a lesser extent, discoloration (28.0%) or flaking (12.4%) appeared.

The incidence of genital problems was indicated by 47.8% of women. Most women (75.0%) stated that they had urinary symptoms. Nearly 40% of women had bladder infections and urinary incontinence. The group of 34.1% women indicated frequent urination, and a quarter of them urination at night (nocturia).

The occurrence of sexual dysfunction associated with menopause has been observed by over half of the respondents (56.7%). Most often it was a libido disorder (58.8%). To a lesser extent, dyspareunia (29.4%), lack of orgasm (23.5%) appeared. The group of 13.7% of the respondents did not notice such problems.

Psychiatric symptoms as a result of menopause were indicated by 82.2% of women. Most often, these symptoms were related to mood swings (71.6%), in every fourth woman appeared melancholy and fear of aging (25.7%). In addition, the respondents indicated the emergence of depressive moods, fear of losing femininity or loss of respect for oneself (Table 5).

Table 5. The most frequent conditions in women in individual systems

	N	%	N	%	N	%	N	%
Respiratory system	panting		shortness of breath		dyspnea		chest pain	
	120	66.9%	79	22.6%	66	27%	27	15%
Cardio-vascular system	coronary heart disease		heart failure		palpitations		heart attack	
	68	37.8%	48	37.0%	61	34.1%	45	25.2%
Skeletal system	pain in the spine		Sacral pain		back ache		thoracic pain	
	28	15.6%	103	57.2%	49	27.2%	31	17.2%
Digestive system and metabolism	increase in body weight		slower metabolism		constipation		elevated level of glycaemia	
	62	34.4%	118	65.6%	79	44.2%	35	19.9%
Changes on the skin	dryness		discolouration		flaking			
	138	77%	50	28.0%	22	12.4%		
Urinary system	bladder infections		urinary incontinence		frequent urination		nocturia	
	68	37.8%	66	37.0%	61	34.1%	45	25.2%
Reproductive system	libido disorder		dyspareunia		lack of orgasm		no change	
	105	58.8%	52	29.4%	42	23.5%	24	13.7%
Psychological realm	mood swings		lower mood		fear of aging		depression	
	128	71.6%	47	26.4%	46	25.7%	36	20.3%

## Discussion

The perimenopausal period is a difficult stage in life for most women, because then numerous health problems occur associated with hormonal changes taking place in the body as a result of the decrease in the hormonal function of the ovaries. Almost all respondents observed typical symptoms of menopause, most often they appeared between 45 and 49 years, i.e. in the range indicated in Pertyński's study.<sup>8</sup>

In the study group, the most common symptoms associated with menopause were: mood swings, irritability, concentration disorders, sweating, skeletal changes (osteoporosis), weight gain, skin changes, bladder symptoms and problems in the vulva and vagina. In similar papers, the same symptoms appeared, for example in Stachoń study the most common symptoms were: irritation, hot flushes, sleep disorders, sudden mood changes.<sup>7</sup> In turn in Makara-Studzińska's study low mood, problems in the joints and muscles, physical and mental fatigue and irritation were found.<sup>9</sup>

The most serious health problems of menopausal women are vasomotor symptoms, metabolic changes, insomnia and mood swings. The women observed hot flashes, night sweats, insomnia, palpitations and a drop in energy. To a lesser extent - bone and joint pain, decreased concentration or memory problems were observed. The most frequent symptoms of the menopausal period in the studies of Mroczek et al. were headache, excessive nervousness, while in the studies of Skrzypulec et al. - hot flushes and sweating.<sup>10, 11</sup>

It is also worth citing the results of studies investigating the relationship between menopause and sleep disorders. Tao et al. in the study conducted in China, showed that sleep disorders are not related to menopause, in contrast to Polish studies in which Słopeń et al. demonstrated such dependence.<sup>12, 13</sup>

Analyzing in detail the disorders caused by menopause, almost the entire group of the respondents indicated the occurrence of metabolic changes. Most often it was an increase in body weight (68.6%), slow metabolism (51.9%), and constipation (44.2%). This could have been the cause of increased weight in some subjects, which since the appearance of menopause has been noticed by one-third of respondents, indicating that the weight gain ranged from 2 kg to 20 kg.

During this period, the probability of onset of somatic diseases increases significantly in women. Grzechocińska et al. indicates that many women are beginning to develop systemic diseases, for example obesity, hypertension, diabetes, ischemic heart disease, and in Pawlak's research respondents most often suffered from arterial hypertension, osteoporosis, arthritis, asthma and diabetes.<sup>4, 2</sup> Our research has also shown that 40% of women were treated for chronic diseases, most often it was arterial hypertension, thyroid disease and diabetes.

Regarding the incidence of changes in the skeletal system, as much as 83.9% of women indicated them. Most often, these were spinal pains and sacral pain. The loss of bone mass is very rapid in women in the first years after menopause, due to estrogen deficiency. Hormonal therapy, regular physical activity and proper nutrition may delay bone changes.<sup>14</sup>

On the other hand, respiratory symptoms were most often caused by panting (66.9%). Symptoms of the cardiovascular system occurred in the group of 32.2% women. Among cardiovascular symptoms, the respondents most often mentioned coronary heart disease or heart failure. Only one third of the respondents did not have symptoms from this system. Skin changes (dry skin, discoloration) appeared in 89.4% of women. Three quarters of the studied women suffered from urinary problems. The most common symptoms were bladder infections (37.8%), urinary incontinence (37.0%) and frequent urination (34.1%). Noszczyk suggests that estrogen supplementation may reduce skin hardening to a certain degree, but it may have a lower impact on wrinkles that do not respond to estrogen therapy.<sup>15</sup>

The occurrence of sexual dysfunctions induced by menopause was observed by over half of the surveyed women (56.7%), the most frequently mentioned were libido disorders (58.8%) and dyspareunia (29.4%). The lack of orgasm during sexual intercourse was experienced by almost one quarter of the respondents. According to a study conducted by Johnson in England, 78.4% of the subjects between 45 and 59 years of age were sexually active.<sup>16</sup> According to Lew-Starowicz, 64.2% of women between 50 and 54 years of age are sexually active in Poland.<sup>17</sup> However, it should be emphasized that many women in this period of life are lonely due to breakup in relationship or widowhood.

Most of the respondents had psychiatric symptoms. Most often they were mood swings (71.6%). To a lesser extent, there were states of melancholy, fear of aging, depression of varying degrees or to a different degree fear of losing femininity. In the studies of Sakson-Obada et al., women also pointed to the occurrence of similar symptoms: mood swings, anxiety, psychological tension or attention deficit.<sup>18</sup> M. Synowiec-Piłat's research showed that care of mental health in the menopausal age became evident in educated women who had regular physical activity. 81% of the respondents practicing physical exercises once a week, admitted stress reduction and better psychological well-being.<sup>19</sup>

Statistical analysis of the collected material showed that women with higher education assessed their knowledge about menopause and health related problems better. A good level of knowledge in this area was declared by over half of the respondents, and satisfactory knowledge was provided by over a quarter of the respondents.



It was found that women living in cities had more knowledge about HRT than women from the countryside. Among the respondents 81.1% were under constant supervision of the gynecologist. Women who were not under the care of a gynecologist were inhabitants of the countryside. Research of Kózka et al. shows that during menopause, women hardly ever control their health or do not follow the doctor's instructions. Only 42% of the studied population admitted that they regularly perform control tests, including breast self-examination.<sup>20</sup>

At this stage of life, women are particularly vulnerable to cervical and ovarian cancer, which is why they need regular gynecological and cytological tests.<sup>16</sup> The obtained results indicate that only 42.2% of women consulted the gynecologist with problems related to menopause. HRT was used by 12.2% of women - city inhabitants. The group of 7.8% of the respondents consider the use of HRT in the future, and 80% of the respondents have not used it so far, because they decided that they do not need it (32.9%), they were afraid of the harmful effects of hormonal agents (30.4%) and possible side effects (24.1%). In the studies of Pawlak et al., majority of the respondents did not use HRT (88.3%).<sup>2</sup>

In order to relieve menopausal symptoms, women use both pharmacological and non-pharmacological means, as indicated by 72.2% of women surveyed. Inhabitants of the countryside have a greater knowledge of non-pharmacological methods of dealing with the problems of menopause. On the other hand, conducting an active lifestyle as a way to minimize perimenopausal symptoms was declared by 42.2% of women. Among the used forms of physical activity, the inhabitants of the countryside preferred Nordic walking, and urban residents preferred running. Physical activity is one of the most important determinants of health condition in perimenopausal women.<sup>21</sup> In the study by Pawlak et al., women chose the most frequently physical exercises and swimming and in the study Mędręła-Kuder, respondents to ease the relief of menopausal symptoms, they most often used HRT (90%), relaxation and avoidance of stress (76%), herbs (57%) and physical activity (33%).<sup>2,22</sup>

The studies carried out indicate that among the women surveyed occurred typical menopausal symptoms and health problems. It would be necessary to undertake educational activities aimed at modifying the health behavior of women in the perimenopausal age.

## Acknowledgments

The authors thank all women who took part in the study.

## Conclusions

1. Hot flushes, sweating, insomnia and palpitations are the symptoms of menopause that most often occur in the studied group of women.

2. The respondents most frequently complained of the genitourinary, respiratory and skeletal symptoms as well as metabolic changes.
3. Women from the countryside more rarely declared psychiatric problems and more often used non-pharmacological methods to relieve menopausal symptoms.
4. The perimenopausal period is conducive to the occurrence of certain diseases such as diabetes, hypertension, cardiovascular diseases and obesity.

## References

1. Gołąb B, Traczyk W. *Anatomia i fizjologia człowieka*. Łódź: Wyd. Ośrodek Doradztwa i Szkolenia Jaktorów; 1997: 284-295.
2. Pawlak IE, Wolińska I, Mroczek B. Impact of climacteric and depressive symptoms on the quality of life of postmenopausal women. *Fam Med Prim Care Rev*. 2016;18,3:325-331. doi.org/10.5114/fmpcr/62338
3. North American Menopause Society. Publications, Clinical Care Recommendations, Chapter 1, Menopause <https://www.menopause.org/publications/clinical-care-recommendations/chapter-1-menopause> (accessed 12.08.2018).
4. Grzechocińska B. Problemy okresu menopauzy. Możliwości terapii. *Medycyna Rodzinna*. 2004; 2:55-60.
5. Słopeń R, Warenik-Szymankiewicz A. Przekwitanie. In: Bręborowicz G.H. ed., *Położnictwo i Ginekologia*. Warszawa: PZWL; 2013: 716-725.
6. Łepecka-Klusek C. *Pielęgniarstwo we współczesnym położnictwie i ginekologii*. Warszawa: PZWL; 2010: 35-39.
7. Stachoń AJ. Feeling of the selected climacteric symptoms depending on the climacteric phase and type of menopause. *Menopause Review/Przegląd Menopauzalny*. 2013;12(4):315-320. doi:10.5114/pm.2013.37847.
8. Pertyński T, Stachowiak G. Menopause - facts and controversies. *Endokrynologia Polska/Polish Journal of Endocrinology*. 2006; 57 (5): 525-534.
9. Makara-Studzińska M, Kryś-Noszczyk K, Jakiel G. The influence of selected socio-demographic variables on symptoms occurring during the menopause. *Menopause Review/Przegląd Menopauzalny*. 2015;14(1):20-26. doi:10.5114/pm.2015.48637.
10. Mroczek B, Wróblewska I, Jamrocha K. Jakość życia kobiet w okresie menopauzy. *Fam Med Prim Care Rev*. 2014; 16(2): 136-137.
11. Skrzypulec V, Naworska B, Drosdzol A. The impact of climacteric symptoms on functioning and quality of life among women in perimenopausal stage. *Menopause Review/Przegląd Menopauzalny*. 2007;6(2):96-101.
12. Tao MF, Sun DM, Shao HF. Poor sleep in middle-age women is not associated with menopause per se. *Braz J Med Biol Res*. 2016; 49(1): 1-8. doi: 10.1590/1414-431X20154718.
13. Słopeń R, Wichniak A, Pawlak M, Słopeń A, Warenik-Szymankiewicz A, Sajdak S. Disturbances of sleep con-

- tinuity in women during the menopausal transition. *Psychiatr Pol.* 2015;49(3):615-23. doi.org/10.12740/PP/33442
14. Somer E. Wpływ odżywiania na zdrowie kobiety. Warszawa: Wyd. Amer. 1998: 56.
15. Noszczyk M. ed. *Kosmetologia pielęgnacyjna i lekarska.* Warszawa: PZWL; 2010: 78.
16. Johnson A. Sexual attitudes and lifestyles. *Semin Reprod Endocrinol.* 1997; 15: 91-100.
17. Lew-Starowicz Z. *Raport – życie seksualne Polaków.* Warszawa: SMG-KRC; 1992: 220.
18. Sakson-Obada O, Wycisk J. The body self and the frequency, intensity and acceptance of menopausal symptoms. *Menopause Review/Przegląd Menopauzalny.* 2015;14(2):82-89. doi:10.5114/pm.2015.52150.
19. Synowiec-Piłat M. Chosen social life quality determinants of 50-year-old female Poles in relation to their health status. *Menopause Review/Przegląd Menopauzalny.* 2010; 9(6):385-389.
20. Kózka M, Prażmowska B, Dziedzic M, Semczak M. Styl życia kobiet w okresie menopauzalnym – badania wstępne/Women's Lifestyle during Menopause Transition Years (Perimenopause) – Introductory Research. *Prz Med Uniw Rzesz Inst Leków.* 2013; 1: 61–74.
21. Dąbrowska J, Naworska B, Dąbrowska-Galas M, Skrzypulec-Plinta V. The role of physical activity in menopause. *Menopause Review/Przegląd Menopauzalny.* 2013;11(6):445-448. doi:10.5114/pm.2012.32535.
22. Mędreła-Kuder E. Poziom wiedzy na temat zagrożeń i dolegliwości okresu klimakterium wśród kobiet w wieku przedmenopauzalnym. *Rocz Panstw Zakł Hig.* 2011; 62(1):71-75.



## ORIGINAL PAPER

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# Changes in body proportions of children and adolescents from Rzeszów during a 35-year period from 1978/79–2013/14

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### Abstract

**Introduction.** Environmental conditions have been changing over the years and the body's capacity to adapt affects human development, its growth and typogenesis.

**Aim.** To confirm the secular trend in the population of children and adolescents aged 4 to 18 from Rzeszów in the last 35 years in terms of growing and differentiation body proportions.

**Materials and methods.** In 2013/2014, a total of 1,563 children from Rzeszów were examined. The length of the trunk, the upper limb, the lower limb, the width of the shoulders and the width of the hips were measured and the following indices were calculated: trunk length, upper limb length, lower limb length, inter-limb, hip-shoulder and shoulder width. The data was subjected to statistical analysis and compared to the data collected in 1978/79, 1993/1994 and 2003/2004.

**Results.** During the 35-year period, the following symptoms were observed: elongation of upper and lower limbs in both sexes, increase in shoulder width in boys from 15-18 years of age, and in girls generally in the entire examined age, tendency to decrease in hip width in both sexes in most age classes.

**Conclusions.** The secular trend in the population of children and adolescents aged 4 to 18 from Rzeszów in the last 35 years regarding growth process and differentiating body proportions was confirmed.

**Keywords.** anthropometry, growth, proportion, secular trend

### Introduction

The somatic (morphological) development of a human is often associated with an increase in the size of the body – called the process of growing.<sup>1</sup> The popular rule is that until the end of the process of growing the length of individual parts is greater: the trunk – three times, the upper limbs – four times, the lower limbs – five times.<sup>2</sup> The most popular anthropometric parameters that charac-

terize the growing process are body height, body mass, head circumference, chest circumference and waist circumference.<sup>3</sup> These data are entered into the health book at birth and after the health balance at a given age.<sup>4</sup> During the health balance, a further evaluation of the chest circumference is not recommended, evaluation of the head circumference is recommended until the third year of life, and the assessment of body height and

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 25.09.2018 | Accepted: 10.10.2018  
Publication date: December 2018

weight is carried out until adulthood and longer.<sup>2,5-11</sup> An important material aspect of human somatic development, apart from growing, is differentiation - perfecting the structure. Among other things, it includes changes in body composition (fat mass and fat free mass), the formation of typical body proportions (typogenesis) or gender-related differences (sexual dimorphism).<sup>1</sup> In anthropometry, the parameters describing the process of differentiation are proportion ratios. In the literature on the subject, Quetelet's index WQ2 (Body Mass Index, BMI) is most commonly used.<sup>2,3</sup> It is used to assess the nutritional status.<sup>12</sup> The quotient of waist circumference and body height serves to differentiate obesity types in children and adolescents starting from the pre-school age.<sup>13</sup> Research with other anthropometric parameters is rarely carried out.<sup>14</sup>

An important direction of anthropometric research is the study of the secular trend, understood as changes in somatic development occurring between generations, recognized as a non-evolutionary phenomenon, having an adaptive character, under the influence of changes in civilization development.<sup>15,16</sup> Changes in body structure reflect the condition of the natural and social environment.<sup>17</sup> In addition, subsequent generations differ in the frequency of individual genes.<sup>17</sup> The secular trend is expressed by the acceleration (acceleration of development) of some and the deceleration (slowdown of development) of other developmental parameters.<sup>2</sup> An example of the phenomenon of acceleration is the increase in mean body height in subsequent generations, the occurrence of post-puberty height increase at an earlier age, changes in body proportions - within the lower limbs with the tendency to having long limbs.<sup>2</sup> These changes are a sensitive marker of the biological condition of a given population.<sup>17</sup> Studies on the secular trend are most often carried out on the basis of the previously mentioned body weight as well as body height and BMI. The present study, however, presents the data from a different perspective.

### Aim of the study

To confirm the secular trend in the population of children and adolescents aged 4 to 18 from Rzeszów in the last 35 years in terms of: 1. growing - characterized on the basis of such anthropometric features as: trunk length (sst-s), the upper limb length (a-daIII), the lower limb length (B-sy), shoulder width (aa), hip width (c-ic) and 2. differentiation the proportions of body structure - using selected coefficients formed from the above-mentioned features: trunk length index, upper limb length index, lower limb length index, inter-limb, hip-shoulder ratio and shoulder width.

### Materials and methods

Assessments of changes in morphological development of children and adolescents from Rzeszów were made

in 1978/79, 1993/94, 2003/04 and 2013/14. During all these years, the research methodology was conducted according to the same principles.<sup>18-24</sup> Anthropometric research covered 2,378 persons in 1978/79 (1,176 boys and 1,056 girls), 1993/94 - 2586 (1,300 boys and 1,286 girls), while in the 2003/04 2,560 people (1,280 boys and 1,280 girls). A random sample of children and adolescents was taken in all three series in order to be representative. In the years 1978/79 - 2003/04, a mean of 80 boys and 80 girls were examined in each age group.<sup>19</sup> Samples for testing were randomly drawn without repetition. A written consent for the tests was obtained from the Education Office, the President of Rzeszów, the directors of individual schools and parents, whereas the oral consent was expressed individually by every child before the start of the measurements. In 2013/14, the respondents were selected in the same way as in the previous series, trying to keep similar numbers of boys and girls in particular age classes, but difficulties occurred. They concerned the consent of parents and the respondents themselves to carry out measurements, which, as is known, are not invasive, and therefore they pose no threat to health and life. Finally, over 5% of the population of children and adolescents from Rzeszów was examined, taking into account the sex from 4 to 18 years of age in each age class. Data on the number of live-born boys and girls in the examined age classes were obtained from the Central Statistical Office in Rzeszów. In total, 1,563 people were examined, including 779 boys and 784 girls. We also observed that the basic group of both boys and girls in each age class was not less than 50 people. The examined children were healthy and did not have a disability certificate. It was not possible to gather a sufficiently large group of 3-year-old boys and girls due to the lack of consent of parents and guardians. The examinations of 3-year-olds were also disproportionately prolonged in time.<sup>19,21-23</sup> For all of the above series, anthropometric measurements were made based on the technique by Martin and Saller.<sup>20</sup> In anthropometric studies, the following features were taken into account: trunk length (sst-s), length of the upper limb (a-daIII), length of the lower limb (B-sy), shoulder width (a-a) and hip width (ic-ic). Based on the collected data, the ratios of body structure were calculated: length of trunk, length of upper limb, length of lower limb, inter-limb, hip-shoulder and shoulder width.<sup>18,20</sup> As in previous studies, the collected data was statistically developed. Selected numerical characteristics of the tested parameters were determined: the arithmetic mean ( $\bar{x}$ ) - in all discussed series, median (Me), standard deviation (s) in all discussed series, 25th and 75th percentile (C25, C75). The analysis of variance (ANOVA) was used for statistical calculations.<sup>21-23</sup> To answer the question of whether the population of children and adolescents from Rzeszów continues to exhibit the phe-

nomenon of secular trend, a comparative analysis of statistical characteristics of selected anthropometric features and ratios from the series 1978/79, 1993/94, 2003/04 and 2013/14 was made.<sup>24</sup>

Results

Intergenerational variability of height and body mass of Rzeszów children and adolescents examined in the time interval 1978/79 - 2013/14 was presented in an earlier publication.<sup>22</sup> The tendency of changes and diversity in the morphological structure of the body over generations can be illustrated by comparing particular dimensions with each other (Tables 1-10). It seems, however, that the best time variation of the body shape describes the proportions between dimensions expressed in the form of ratios of proportions (Tables 13-24). At the same time, data for the 2013/14 series contained in Tables 1-10 may serve as a development standard for children and adolescents from Rzeszów aged 4 to 18 in the terms of parameters studied.

On the basis of a comparative analysis during the 35-year period of 1978/79-2013/14 and 10-year period of 2003/04-2013/14 some changes in the development of selected somatic features were observed. After 35 years, the trunk of Rzeszów boys is extending at the age of 5 up to 9, at the age of 11, from 13 to 16 years of age and at the age of 18 (Tables 1, 11). In girls examined in the same time interval, the trunk is also extending from 8 to 10 years of age. In the remaining age classes, mean trunk lengths are lower (between 4-5 and 12-15 years) or close (6, 7, 11 and 16-18) (Tables 2,12). During the 10-year period of 2003/04-2013/14, the trunks in boys are getting longer only in the age range from 14-16 years. In the remaining age classes, mean trunk lengths are lower (between 4-5, 7, 9-12 and 17 years) or close (6, 8, 13 and 18) (Tables 1-11). In girls in the same age group, the

tendency to shorten the trunk dominates, except for the ages 8, 9, 16 and 17, where the average values are similar (Tables 2,12).

In both boys and girls, the upper limb are getting longer. This process is also strongly marked in the 10-year period of 2003/04-2013/14 (Tables 3,4,11-12).

In boys after 35-year period, also the lower limb lengthening is observed. During the 10-year period of 2003/04-2013/14, this process did not take place, except for 18-year-olds, in whom the average length of the lower limb was higher by 0.8 cm (Tables 5,11). In girls during the 35-year period, the lower limbs became much longer. A comparative analysis of the mean length values of the lower limbs in the time interval 2003/04-2013/14 showed the presence of the process of elongation of the lower limbs only at the age of 17 and 18. In the remaining age classes, the absolute differences between the mean values of the discussed parameter assume lower or similar values (Tables 6, 12).

In the course of the 35-year period and the 10-year period in boys, the phenomenon of shoulder widening between 15-18 years of age has been noticed. After 10 years, the shoulders are also getting wider at the age of 9, 10 and 12-13 years (Tables 7, 11).

In turn, in girls a tendency of shoulders narrowing occurs (Table 8,12). Both in boys and girls in the compared series, the hips are getting narrower (Tables 9-12).

The intergenerational phenotypic variation described is also noted in the proportions of the body structure of children and adolescents from Rzeszów. According to Wanke's classification, the examined boys from the series 1978/79 are characterized by a medium trunk from 3-5 years of age, 1993/94 – at the age of 3–4 years, 2003/04 – between 3 and 6 years and from 2013/14 – at 5 and 6 years of age.<sup>20</sup> In the other age classes, boys have short trunk in all compared series

Table 1. Mean values of trunk length (sst-sy) in boys (cm)

Age	(sst-sy)										
	Boys										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>S</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>C</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	29.9	2.8	28.9	1.6	31.9	4.1	-	-	-	-	-
4	31.0	2.4	30.3	1.9	32.7	3.5	29.8	29.1	2.7	27.9	31.5
5	32.3	2.1	32.5	2.0	34.1	3.3	33.1	32.6	3.3	30.9	34.7
6	33.7	2.2	34.2	1.6	35.5	3.1	35.3	35.1	2.1	33.6	36.8
7	35.6	2.2	35.0	1.7	36.9	3.0	36.2	36.5	3.8	31.3	38.3
8	36.9	2.1	36.0	2.0	37.9	2.7	38.1	38.5	3.3	35.0	41.2
9	37.8	1.9	37.2	2.4	39.6	3.4	38.4	38.5	2.4	37.5	39.1
10	38.8	2.0	38.0	2.0	40.9	3.3	38.9	39.0	3.0	37.6	40.8
11	40.1	2.2	39.4	2.4	42.0	3.4	41.1	40.3	4.7	39.1	41.3
12	41.8	2.3	40.4	2.2	43.0	4.3	41.4	40.0	3.4	38.7	44.3
13	43.7	2.9	42.0	2.4	44.7	3.7	44.6	45.2	2.9	41.9	47.0
14	45.5	3.4	44.5	2.9	45.9	4.0	47.6	46.0	5.0	42.8	50.8
15	47.1	3.1	46.8	2.5	47.3	4.1	48.6	47.4	3.5	45.8	51.7
16	48.7	2.6	48.5	2.9	49.0	4.1	50.9	49.4	5.5	47.4	53.0
17	49.8	2.3	49.4	2.8	50.1	3.9	49.6	51.8	5.5	45.3	53.9
18	50.4	2.2	50.0	2.6	51.3	4.1	51.2	51.1	3.2	48.9	53.5

Table 2. Mean values of trunk length (sst-sy) in girls (cm)

Age	(sst-sy)										
	Girls										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>S</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>c</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	29.4	2.3	28.0	1.8	32.5	4.3	-	-	-	-	-
4	30.8	2.2	30.2	1.7	33.3	3.2	30.3	30.4	2.1	29.4	31.7
5	32.2	2.4	32.0	1.9	34.8	2.9	31.8	31.8	2.0	30.4	33.0
6	33.8	2.3	33.6	2.2	35.9	2.9	34.1	34.5	1.9	33.2	35.0
7	35.3	1.9	35.3	2.0	36.4	3.3	35.0	34.3	2.7	33.3	36.5
8	36.1	1.9	36.2	2.0	37.1	3.1	37.1	35.4	4.6	34.0	38.8
9	37.0	2.0	37.2	2.1	38.4	4.6	38.6	38.0	3.7	37.0	40.1
10	38.4	2.1	38.3	2.2	40.3	3.0	39.2	39.5	3.2	38.0	41.8
11	40.2	2.5	39.6	2.4	41.3	4.6	40.6	37.8	7.7	34.2	50.4
12	42.1	2.5	41.2	2.4	42.8	3.5	41.2	39.6	2.6	38.9	41.4
13	44.1	2.1	43.0	2.4	44.1	3.0	42.3	42.5	3.8	40.0	44.6
14	45.4	2.1	44.6	3.0	44.6	2.7	43.2	43.1	2.0	41.8	44.9
15	45.8	2.3	45.4	2.5	45.6	3.3	45.2	45.3	4.3	42.3	49.3
16	46.3	2.3	45.9	2.6	46.2	2.9	46.4	47.0	3.3	44.1	48.4
17	46.8	2.1	46.5	2.6	46.7	2.7	46.8	45.4	4.8	44.2	49.2
18	47.1	2.1	47.0	2.3	47.4	2.7	46.9	46.9	2.8	46.3	49.9

Table 3. Mean values of upper extremity length (a-daIII) in boys (cm)

Age	(a-da <sub>III</sub> )										
	Boys										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>S</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>c</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	41.8	2.1	40.5	2.3	41.7	3.4	-	-	-	-	-
4	44.1	2.4	43.5	2.0	44.5	2.9	44.6	44.0	2.9	42.0	45.5
5	46.4	2.7	47.4	2.2	48.8	2.9	49.0	49.0	3.0	46.6	50.1
6	49.6	2.7	50.3	2.2	51.0	2.7	53.4	53.0	4.3	51.0	58.0
7	53.3	2.7	52.6	2.5	54.6	4.9	57.1	57.0	3.0	54.8	59.0
8	56.5	2.8	55.1	3.2	57.0	3.3	59.1	59.2	2.5	58.0	61.2
9	58.9	2.9	57.5	2.8	60.2	3.8	62.4	63.0	3.6	59.5	64.0
10	60.9	3.2	59.4	3.0	61.8	3.3	64.4	64.0	3.2	62.3	67.0
11	63.0	3.2	62.2	2.9	64.5	3.0	66.0	66.0	3.3	65.0	67.0
12	65.8	3.6	65.3	3.7	67.5	5.5	70.4	70.0	4.4	67.0	73.5
13	69.2	4.2	67.8	3.5	70.1	3.9	72.4	72.5	2.1	69.7	75.3
14	71.9	4.2	72.2	3.5	73.5	4.5	79.0	79.5	4.7	75.2	83.5
15	74.2	3.9	74.9	3.5	75.6	4.8	81.0	80.0	3.0	79.6	81.0
16	76.2	3.5	75.7	3.3	78.5	4.5	82.1	81.4	2.9	80.2	83.6
17	77.1	3.2	76.3	3.8	78.9	3.9	84.0	83.0	3.4	81.6	85.8
18	78.1	3.6	76.8	3.6	79.9	3.7	84.1	84.4	2.1	82.2	85.8

Table 4. Mean values of upper extremity length (a-daIII) in girls (cm)

Age	(a-da <sub>III</sub> )										
	Girls										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>S</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>c</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	40.8	2.0	39.4	2.0	41.1	2.9	-	-	-	-	-
4	43.5	2.2	43.1	2.0	43.5	2.5	45.5	46.1	2.0	43.0	47.0
5	46.2	2.6	46.6	2.0	46.7	3.0	48.2	48.0	1.9	47.0	49.4
6	49.3	3.0	49.2	2.7	50.2	2.9	49.9	50.3	3.5	47.0	52.0
7	52.2	2.9	52.1	2.3	54.0	3.1	55.5	56.0	4.3	52.9	58.1
8	54.7	3.0	53.8	2.6	56.2	2.9	58.3	58.0	3.3	56.0	61.0
9	57.1	3.0	56.1	2.8	58.3	5.6	62.6	63.3	3.8	61.1	65.3
10	59.8	3.0	59.1	2.6	60.7	4.5	65.3	66.0	3.4	62.5	67.8
11	63.0	3.5	61.5	3.7	64.2	4.9	67.1	66.3	4.4	63.4	69.7
12	65.7	3.6	64.9	3.3	68.5	3.9	70.3	70.0	3.4	68.8	73.0
13	68.1	3.3	67.5	3.6	70.0	3.8	71.2	71.0	1.2	70.0	72.0
14	69.3	3.0	69.2	3.4	70.8	3.5	73.5	73.8	1.9	72.4	74.7
15	69.7	3.0	69.3	3.3	71.2	3.9	74.0	73.7	3.1	73.0	76.0
16	69.9	3.2	69.4	3.5	71.8	3.7	75.4	75.3	1.5	74.5	76.5
17	70.0	3.2	69.4	3.9	72.5	5.0	76.7	76.4	1.9	75.4	77.0
18	70.1	3.5	69.5	3.3	72.5	3.5	76.9	76.4	2.2	75.8	77.9

Table 5. Mean values of lower extremity length (B-sy) in boys (cm)

Age	(B-sy)										
	Boys										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>C</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	43.8	2.8	43.6	2.6	46.9	3.5	-	-	-	-	-
4	47.7	2.8	48.5	2.6	49.7	3.1	49.0	49.1	3.5	46.5	51.5
5	52.3	3.3	53.0	2.7	55.0	3.9	51.3	51.3	2.9	49.5	53.2
6	56.1	3.3	57.1	2.5	58.3	3.3	56.4	56.7	3.9	53.7	59.0
7	60.4	3.1	60.4	2.9	65.0	4.0	64.9	63.7	5.7	61.6	69.6
8	65.4	3.7	64.5	3.9	68.8	3.9	66.9	67.3	4.0	65.4	68.5
9	68.8	4.1	68.2	3.1	72.1	4.3	70.7	71.1	3.9	69.2	72.3
10	71.5	3.9	71.3	3.7	76.9	4.6	75.7	75.1	3.9	73.3	78.2
11	74.2	3.7	75.8	3.7	79.2	5.1	76.8	75.9	3.4	74.0	79.5
12	78.0	4.4	79.3	4.8	83.3	7.7	80.4	79.3	2.0	78.9	82.5
13	81.3	5.2	83.3	4.1	86.6	4.9	82.1	80.5	4.6	79.0	85.5
14	85.0	5.1	88.0	4.7	91.2	5.3	88.9	89.0	4.8	86.0	92.0
15	89.1	4.7	91.0	4.0	94.5	7.6	93.2	92.9	2.0	91.7	94.8
16	91.1	4.5	92.2	4.0	95.5	6.7	95.5	95.8	2.6	94.6	97.2
17	91.7	4.1	92.4	4.0	95.9	3.8	95.6	96.0	3.3	92.9	97.8
18	91.9	4.7	92.7	4.2	96.5	4.0	97.3	96.1	3.9	94.2	100.6

Table 6. Mean values of lower extremity length (B-sy) in girls (cm)

Age	(B-sy)										
	Girls										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>C</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	43.6	2.5	43.8	2.7	47.1	3.5	-	-	-	-	-
4	47.9	2.9	48.6	2.5	48.7	3.0	47.4	47.3	1.4	46.3	48.4
5	52.1	3.4	52.4	2.4	53.9	3.1	52.5	52.9	2.5	50.9	54.4
6	55.9	3.4	56.4	3.3	58.0	3.7	55.2	54.5	4.3	51.5	58.5
7	59.9	3.5	60.4	2.9	64.9	4.3	63.7	64.8	6.4	59.1	67.6
8	63.7	3.9	64.0	3.2	69.5	4.3	66.3	67.7	3.9	64.0	69.0
9	67.3	3.7	67.8	3.3	71.8	5.0	69.7	71.1	5.5	65.1	74.5
10	71.1	4.2	71.9	3.7	74.3	4.7	74.7	77.0	7.0	71.0	79.9
11	74.7	4.5	75.6	4.1	79.5	5.2	76.4	77.1	3.6	73.5	80.0
12	78.6	4.2	80.2	3.8	84.6	5.8	84.5	84.8	4.4	82.5	88.5
13	81.9	4.2	83.8	4.2	86.3	4.5	86.6	86.4	4.2	85.4	90.0
14	83.0	3.6	84.4	4.2	87.8	4.5	87.0	86.9	2.5	85.4	88.0
15	83.0	4.0	84.4	3.8	87.7	5.2	87.9	88.4	4.4	85.5	88.6
16	83.0	4.3	84.4	4.8	88.7	5.0	88.9	89.7	3.7	88.7	90.2
17	83.2	3.7	84.4	4.3	88.7	4.7	92.7	90.8	5.6	88.8	96.3
18	83.3	4.1	84.4	3.7	88.8	3.9	93.7	94.0	5.2	91.2	96.0

Table 7. Mean values of shoulder width (a-a) in boys (cm)

Age	(a-a)										
	Boys										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>s</i>	$\bar{x}$	<i>Me</i>	<i>s</i>	<i>C</i> <sub>25</sub>	<i>C</i> <sub>75</sub>
3	21.6	1.3	21.6	1.1	22.2	1.5	-	-	-	-	-
4	22.4	1.9	22.9	1.5	23.4	1.5	22.0	21.5	1.5	20.5	23.0
5	23.6	1.6	24.2	1.1	24.5	1.8	23.0	23.0	1.5	22.0	24.0
6	25.2	1.3	25.5	1.3	25.6	2.9	25.1	25.0	1.4	24.5	26.5
7	26.6	1.3	26.6	1.8	26.8	1.9	25.9	25.8	1.9	25.0	27.0
8	27.7	1.3	28.0	1.3	27.1	1.4	26.9	26.8	1.8	26.0	28.0
9	28.7	1.3	29.0	1.3	28.1	1.9	28.8	28.0	1.8	27.5	30.0
10	29.5	1.3	29.6	1.6	28.5	2.8	29.0	29.3	1.7	27.3	30.1
11	30.4	1.4	31.0	1.4	29.1	1.9	29.2	29.0	1.9	28.0	30.0
12	31.5	1.6	32.1	1.7	30.0	2.9	31.4	31.5	2.0	30.0	33.0
13	32.9	2.0	33.4	1.6	31.7	2.8	32.8	32.5	1.8	32.0	34.5
14	34.5	2.3	35.0	1.8	33.9	2.7	34.0	33.5	1.4	33.0	35.0
15	35.9	2.2	36.4	2.3	35.5	2.1	37.2	37.0	1.8	35.5	38.0
16	37.0	1.9	37.6	2.1	36.7	2.0	38.3	38.0	1.9	37.0	39.5
17	37.8	1.6	38.5	2.4	37.5	2.0	38.5	39.0	1.8	36.8	40.0
18	38.4	1.6	38.9	2.3	37.9	2.1	39.4	39.5	0.9	38.5	40.3

Table 8. Mean values of shoulder width (a-a) in girls (cm)

Age	(a-a)										
	Girls										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	21.6	1.2	21.3	1.0	22.2	1.5	-	-	-	-	-
4	22.6	1.3	22.9	1.4	23.4	1.7	21.5	21.3	0.9	21.0	22.0
5	23.7	1.3	24.0	1.1	24.2	1.5	22.7	22.5	0.9	22.0	23.0
6	25.3	1.2	25.1	1.8	25.7	1.2	23.6	23.3	1.6	22.0	25.0
7	26.4	1.3	26.3	1.2	26.6	1.9	25.6	25.0	1.9	25.0	27.0
8	27.2	1.3	27.4	1.3	26.9	1.5	26.7	27.0	1.7	26.0	28.5
9	28.2	1.3	28.6	1.9	27.9	1.5	27.0	27.3	1.3	26.0	28.0
10	29.1	1.5	29.9	1.7	28.7	1.6	27.6	27.5	1.3	26.5	28.5
11	30.3	1.7	31.4	1.7	29.3	2.2	27.9	28.0	1.6	26.5	29.0
12	31.7	1.8	32.4	1.3	30.3	2.2	30.8	31.0	0.8	30.1	31.2
13	33.0	1.8	33.6	1.5	32.0	2.0	31.0	31.1	0.8	30.2	31.4
14	33.7	1.6	34.0	1.6	33.0	2.3	31.0	30.0	1.5	30.0	31.8
15	34.1	1.4	34.2	1.8	33.4	1.9	31.5	31.2	1.5	31.0	32.0
16	34.4	1.5	34.8	1.7	33.5	1.8	32.1	32.0	0.6	32.0	32.5
17	34.6	1.6	35.1	2.0	34.0	2.0	33.2	33.2	1.0	32.5	34.0
18	34.7	1.6	35.1	1.6	34.0	2.2	33.6	34.0	1.1	33.0	34.5

Table 9. Mean values of hip width (ic-ic) in boys (cm)

Age	(ic-ic)										
	Boys										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	16.3	0.9	15.8	0.8	17.2	1.6	-	-	-	-	-
4	17.2	1.0	16.4	0.9	17.8	1.1	16.1	16.4	0.9	15.5	17.0
5	17.9	1.1	17.2	0.7	18.5	1.5	16.5	16.5	1.0	16.0	17.0
6	18.5	1.0	18.4	1.0	18.8	1.3	18.1	17.5	2.0	16.5	20.0
7	19.3	1.1	18.8	1.6	20.0	2.5	19.1	19.8	1.8	18.0	20.0
8	20.1	1.1	19.8	1.5	20.5	2.0	19.2	18.5	1.5	18.0	20.0
9	20.8	1.1	20.6	1.1	21.4	2.3	21.2	20.0	3.1	19.0	21.8
10	21.4	1.2	21.1	1.2	21.8	3.0	21.1	20.5	2.0	20.0	22.0
11	22.0	1.2	22.0	1.4	21.9	2.5	21.1	21.0	1.4	20.5	21.5
12	22.7	1.4	22.8	1.7	22.5	2.9	22.5	22.0	1.3	21.5	22.5
13	23.7	1.6	23.5	1.2	24.0	2.0	22.7	22.5	2.2	21.0	24.0
14	24.8	1.7	25.0	1.7	25.3	2.1	25.1	25.4	1.6	24.0	26.0
15	25.9	1.5	26.0	1.6	26.7	2.2	25.9	26.0	0.6	25.6	26.5
16	26.7	1.4	26.6	1.4	27.1	2.4	26.3	26.8	1.1	25.0	27.0
17	27.3	1.4	27.3	1.8	27.5	2.0	26.7	26.3	1.6	25.5	28.1
18	27.8	1.4	27.3	2.1	27.7	2.0	27.2	27.5	0.5	27.0	27.5

Table 10. Mean values of hip width (ic-ic) in girls (cm)

Age	(ic-ic)										
	Girls										
	1978/79		1993/94		2003/04		2013/14				
	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	s	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	16.3	0.8	15.3	0.8	16.9	1.8	-	-	-	-	-
4	17.0	0.8	16.4	1.0	17.4	1.5	15.2	15.3	0.9	14.5	16.0
5	17.8	1.0	17.2	1.1	18.0	1.5	16.4	16.5	0.9	15.5	17.0
6	18.6	1.1	17.9	1.4	18.9	1.7	17.0	17.0	1.0	16.0	17.5
7	19.2	1.2	18.7	1.4	19.2	2.0	18.9	18.0	2.2	17.0	20.0
8	19.8	1.2	19.5	1.2	19.6	1.8	19.4	19.5	1.8	18.0	20.0
9	20.5	1.2	20.4	1.3	20.5	2.1	20.0	20.0	1.1	19.0	21.0
10	21.3	1.4	21.4	1.3	20.9	1.9	20.8	20.1	1.6	20.0	21.0
11	22.5	1.7	22.3	1.6	22.0	2.0	21.1	21.8	1.6	19.8	22.3
12	23.5	1.7	23.5	1.4	23.1	2.4	22.9	23.5	1.1	22.0	24.0
13	24.3	1.5	24.8	1.8	24.5	2.5	23.0	23.0	1.0	22.5	24.0
14	25.1	1.4	25.8	1.8	26.0	2.1	23.2	23.0	1.6	21.5	25.0
15	25.6	1.4	26.0	1.9	26.5	2.1	23.5	23.5	0.7	23.0	24.0
16	26.0	1.4	26.4	1.5	26.7	2.0	24.0	23.6	1.7	23.0	24.5
17	26.3	1.5	26.4	1.5	26.7	1.8	25.6	25.4	0.6	25.0	26.0
18	26.4	1.6	26.4	1.3	26.7	1.7	26.2	26.3	1.6	25.0	27.3



**Tabela 11.** Absolute differences between mean values of trunk length, upper and lower extremity length, shoulder and hip width in boys from the series 1978/79-2013/14 and 2003/2004-2013/14

1978/79 – 2013/14					Age	2003/04 – 2013/14				
sst-sy	a-da	B-sy	a-a	ic-ic		sst-sy	a-da	B-sy	a-a	ic-ic
-1.2	0.5	1.3	-0.4	-1.1	4	-2.9	0.1	-0.7	-1.4	-1.7
0.8	2.6	-1.0	-0.6	-1.4	5	-1.0	0.2	-3.7	-1.5	-2.0
1.6	3.8	0.3	-0.1	-0.4	6	-0.2	2.4	-1.9	-0.5	-0.7
0.6	3.8	4.5	-0.7	-0.2	7	-0.7	2.5	-0.1	-0.9	-0.9
1.2	2.6	1.5	-0.8	-0.9	8	0.2	2.1	-1.9	-0.2	-1.3
0.6	3.5	1.9	0.1	0.4	9	-1.2	2.2	-1.4	0.7	-0.2
0.1	3.5	4.2	-0.5	-0.3	10	-2.0	2.6	-1.2	0.5	-0.7
1.0	3.0	2.6	-1.2	-0.9	11	-0.9	1.5	-2.4	0.1	-0.8
-0.4	4.6	2.4	-0.1	-0.2	12	-1.6	2.9	-2.9	1.4	0.0
0.9	3.2	0.8	-0.1	-1.0	13	-0.1	2.3	-4.5	1.1	-1.3
2.1	7.1	3.9	-0.5	0.3	14	1.7	5.5	-2.3	0.1	-0.2
1.5	6.8	4.1	1.3	0.0	15	1.3	5.4	-1.3	1.7	-0.8
2.2	5.9	4.4	1.3	-0.4	16	1.9	3.6	0.0	1.6	-0.8
-0.2	6.9	3.9	0.7	-0.6	17	-0.5	5.1	-0.3	1.0	-0.8
0.8	6.0	5.4	1.0	-0.6	18	-0.1	4.2	0.8	1.5	-0.5

**Table 12.** Absolute differences between mean values of trunk length, upper and lower extremity length, shoulder and hip width in girls from the series 1978/79-2013/14 and 2003/2004-2013/14

1978/79 – 2013/14					Age	2003/04 – 2013/14				
sst-sy	a-da	B-sy	a-a	ic-ic		sst-sy	a-da	B-sy	a-a	ic-ic
-0.5	2.0	-0.5	-1.1	-1.8	4	-3.0	2.0	-1.3	-1.9	-2.2
-0.4	2.0	0.4	-1.0	-1.4	5	-3.0	1.5	-1.4	-1.5	-1.6
0.3	0.6	-0.7	-1.7	-1.6	6	-1.8	-0.3	-2.8	-2.1	-1.9
-0.3	3.3	3.8	-0.8	-0.3	7	-1.4	1.5	-1.2	-1.0	-0.3
1.0	3.6	2.6	-0.5	-0.4	8	0.0	2.1	-3.2	-0.2	-0.2
1.6	5.5	2.4	-1.2	-0.5	9	0.2	4.3	-2.1	-0.9	-0.5
0.8	5.5	3.6	-1.5	-0.5	10	-1.1	4.6	0.4	-1.1	-0.1
0.4	4.1	1.7	-2.4	-1.4	11	-0.7	2.9	-3.1	-1.4	-0.9
-0.9	4.6	5.9	-0.9	-0.6	12	-1.6	1.8	-0.1	0.5	-0.2
-1.8	3.1	4.7	-2.0	-1.3	13	-1.8	1.2	0.3	-1.0	-1.5
-2.2	4.2	4.0	-2.7	-1.9	14	-1.4	2.7	-0.8	-2.0	-2.8
-0.6	4.3	4.9	-2.6	-2.1	15	-0.4	2.8	0.2	-1.9	-3.0
0.1	5.5	5.9	-2.3	-2.0	16	0.2	3.6	0.2	-1.4	-2.7
0.0	6.7	9.5	-1.4	-0.7	17	0.1	4.2	4.0	-0.8	-1.1
-0.2	6.8	10.4	-1.1	-0.2	18	-0.5	4.4	4.9	-0.4	-0.5

(Tables 13). In girls, on the basis of Kolasa’s classification, long-trunk occurs in 3-year-olds from the series of 1978/79 and 2003/04 test between the age of 3-6.<sup>20</sup> The medium trunk in the series of 1978/79 appears from 4-6 years of age, 1993/94 - at the age of 3-4 years, 2003/04 - in 7-year-olds, while in the sample of 2013/14 - in 4-6 years of age. For girls from all series, in other age categories, short trunk is characteristic in terms of physical proportions (Table 14).

The mean values of the upper limb index in boys and girls show that the subjects from the series 1978/79, 1993/94 and 2003/04 have shorter limbs in the whole studied ontogenesis section. Their peers from the 2013/14 series have short limbs only at the age of 4, and in the other age classes they have mean length limbs (Table 15–16). In turn, in girls from the 2013/14 series short limbs are observed at the age of 4–7 years of age and at the age of 13–14, and in the remaining age classes, medium length limbs – similar as in boys (Table 16).

Considering the mean values of the lower limb index, it was found that the boys from all discussed series are characterized by short-limbs, with the exception of subjects from the 2003/04 sample aged 13-15, who have medium length limbs (Table 17). In girls, mean values of the lower limb index in the samples 1978/79, 1993/94 and 2003/04 indicate short limbs throughout the entire examined age range. After 35 and 10 years, this feature persists up to 15 years of age. At the age of 16-18, in the 2013/14 sample, medium length limbs appear (Table 18).

The temporal changes described above in the length of lower and upper limbs with age in boys and girls from Rzeszów illustrate the mean values of the inter-limb index in terms of Wolański’s classification.<sup>20</sup> In boys, the mean values of the inter-limb index indicate the elongation of the lower limbs in the series 1978/79 from 9 years of age, 1993/94 - from the age of 8 years and 2003/04 - from 7 years of age. As a result, as illustrated in Table 19, at the age of 18, the representatives of these series are

Table 13. Mean values of trunk length index in boys

Age	$(sst-sy) / (B-v) \times 100$							
	Boys							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	31.0	30.3	31.1	-	-	-	-	-
4	30.1	29.7	31.0	29.0	28.7	2.3	27.4	30.4
5	29.7	29.5	30.4	30.7	30.4	2.3	29.0	31.9
6	29.4	29.2	30.0	29.8	30.5	2.9	28.2	31.6
7	29.4	28.9	29.2	28.6	28.1	2.0	26.9	29.5
8	28.9	28.2	28.9	29.3	29.3	2.5	26.8	31.6
9	28.4	28.0	28.8	28.0	28.3	2.0	27.0	29.5
10	28.2	27.7	28.6	27.4	27.3	1.1	26.7	28.1
11	28.2	27.4	28.7	28.1	27.5	2.1	27.0	28.5
12	28.1	27.1	28.2	27.1	26.9	1.4	26.3	28.5
13	28.1	27.1	28.4	28.9	29.3	1.4	27.5	29.5
14	28.0	27.2	27.7	28.3	27.8	2.3	26.7	29.2
15	28.1	27.6	27.7	27.0	26.5	1.6	26.2	28.3
16	28.3	28.0	27.9	28.7	28.1	2.5	27.0	29.7
17	28.5	28.3	28.3	27.5	28.5	2.6	25.6	29.5
18	28.6	28.5	28.7	28.4	28.0	1.6	27.4	29.6

Table 14. Mean values of trunk length index in girls

Age	$(sst-sy) / (B-v) \times 100$							
	Girls							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	30.8	29.7	33.1	-	-	-	-	-
4	30.2	29.6	32.6	29.9	29.6	1.4	28.9	30.6
5	29.7	29.3	31.6	29.5	29.4	1.7	28.7	30.2
6	29.5	29.1	30.8	30.1	30.0	1.6	29.1	31.5
7	29.2	29.0	29.6	28.2	28.0	2.0	27.4	29.5
8	28.7	28.6	28.7	28.7	27.8	2.6	26.9	29.6
9	28.3	28.1	28.5	28.6	27.7	2.3	27.1	29.7
10	28.2	27.7	28.8	27.8	27.5	2.1	27.0	29.5
11	28.0	27.6	28.3	28.4	28.4	1.8	27.5	29.6
12	28.0	27.2	27.7	26.7	26.3	1.4	25.6	27.7
13	28.3	27.5	27.9	25.6	25.5	2.3	24.0	27.3
14	28.5	27.9	27.5	26.3	25.9	1.4	25.2	27.3
15	28.6	28.2	28.1	27.5	27.4	1.7	26.1	29.0
16	28.8	28.4	28.1	28.9	29.0	1.7	28.1	29.6
17	29.0	28.8	28.3	27.8	27.0	3.2	25.7	28.1
18	29.2	29.0	28.8	28.0	27.8	2.0	27.2	29.3

Table 15. Mean values of index of upper extremity length in boys

Age	$(a-da_{III}) / (B-v) \times 100$							
	Boys							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	43.4	42.4	40.7	-	-	-	-	-
4	42.8	42.6	42.2	43.4	43.2	1.6	42.7	44.2
5	42.6	43.0	43.4	46.1	45.5	3.2	43.7	47.2
6	43.3	43.0	43.0	45.0	45.0	2.2	43.9	45.9
7	44.0	43.4	43.2	45.2	45.2	1.4	44.6	46.0
8	44.2	43.2	43.5	45.5	45.6	1.8	45.0	46.3
9	44.2	43.3	43.8	45.5	45.7	1.6	44.6	46.4
10	44.3	43.3	43.2	45.4	45.1	1.1	44.6	46.3
11	44.3	43.3	44.1	45.3	45.3	1.4	44.6	46.6
12	44.3	43.8	44.2	46.1	46.3	1.4	45.4	46.9
13	44.5	43.8	44.5	46.9	47.1	1.0	46.3	47.6
14	44.3	44.1	44.3	46.9	46.7	2.1	46.1	47.3
15	44.2	44.2	44.2	45.0	45.1	1.6	43.5	45.9
16	44.2	43.7	44.7	46.4	46.5	0.9	45.7	47.0
17	44.2	43.7	44.5	46.6	46.7	0.9	45.9	47.2
18	44.4	43.8	44.8	46.7	46.8	1.0	46.1	47.4

Table 16. Mean values of index of upper extremity length in girls

Age	$(a-da_{III}) / (B-v) \times 100$							
	Girls							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	42.8	41.7	41.9	-	-	-	-	-
4	42.6	42.2	42.6	44.8	44.9	0.9	44.4	45.6
5	42.7	42.6	42.4	44.4	44.6	1.2	43.8	45.2
6	43.0	42.6	43.0	44.0	44.3	1.5	42.9	44.8
7	43.2	42.8	43.9	44.6	44.6	1.6	43.5	45.5
8	43.5	42.6	43.5	45.1	45.0	1.2	44.3	45.9
9	43.6	42.4	43.3	46.3	46.4	4.3	43.6	49.5
10	44.0	42.8	43.4	46.3	46.2	2.2	44.6	47.8
11	44.0	42.8	43.9	46.9	46.8	2.2	45.2	48.4
12	43.8	42.8	44.3	45.6	45.7	1.1	44.8	46.5
13	43.7	43.2	44.3	43.1	43.4	1.5	42.0	44.0
14	43.6	43.3	43.7	44.7	44.8	0.9	44.3	45.6
15	43.6	43.0	43.8	45.0	44.7	1.2	44.0	45.6
16	43.5	42.9	43.6	46.9	46.9	2.2	45.3	48.5
17	43.4	42.9	44.0	45.5	45.5	1.1	44.3	46.6
18	43.4	42.9	44.0	46.0	45.9	2.2	44.3	47.5

Table 17. Mean values of index of lower extremity length in boys

Age	$(B-sy) / (B-v) \times 100$							
	Boys							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	45.4	45.6	45.8	-	-	-	-	-
4	46.3	47.5	47.1	47.6	47.9	2.2	46.8	49.0
5	48.1	48.1	49.0	47.9	47.9	2.7	46.5	48.7
6	49.0	48.8	49.2	47.6	47.2	1.4	46.5	49.0
7	49.9	49.8	51.4	51.3	50.7	2.3	49.6	53.5
8	51.2	50.6	52.6	51.5	51.5	2.5	49.5	53.7
9	51.7	51.3	52.5	51.5	51.1	1.4	50.7	51.9
10	52.0	52.0	53.8	53.3	52.9	1.2	52.3	54.4
11	52.1	52.8	54.1	52.7	53.0	2.1	52.3	54.3
12	52.5	53.2	54.5	52.7	52.9	1.6	51.3	54.0
13	52.2	53.8	55.0	53.2	53.1	1.3	52.0	54.4
14	52.4	53.7	55.0	52.9	52.9	1.9	51.9	54.1
15	53.1	53.6	55.3	51.8	51.4	1.4	51.1	52.2
16	52.9	53.3	54.4	54.0	54.0	1.3	53.6	54.7
17	52.6	52.9	54.1	53.1	53.0	1.3	51.9	54.3
18	52.2	52.9	54.1	54.0	54.0	1.4	53.1	54.5

Table 18. Mean values of index of lower extremity length in girls

Age	$(B-sy) / (B-v) \times 100$							
	Girls							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	45.7	46.4	48.0	-	-	-	-	-
4	47.0	47.6	47.6	46.8	47.1	1.3	45.4	48.1
5	48.1	47.9	48.9	48.4	48.8	1.7	47.2	49.7
6	48.7	48.8	49.7	48.7	49.0	1.7	47.1	50.7
7	49.6	49.6	52.8	51.1	51.4	2.3	49.1	52.6
8	50.7	50.6	53.7	51.3	52.8	2.8	49.5	53.2
9	51.4	51.2	53.4	51.6	53.5	4.6	46.5	54.9
10	52.3	52.1	53.1	52.9	54.1	2.9	53.0	54.6
11	52.1	52.6	54.4	53.4	53.4	1.6	52.5	54.1
12	52.4	52.9	54.8	54.8	55.1	1.2	53.8	55.5
13	52.6	53.6	54.6	52.4	52.8	1.9	51.1	53.5
14	52.2	52.9	54.2	53.0	53.5	2.9	53.1	54.7
15	51.9	52.4	54.0	53.4	53.4	1.6	52.5	54.1
16	51.6	52.2	53.9	55.4	55.6	2.2	53.9	56.8
17	51.6	52.2	53.8	55.0	55.3	1.2	54.0	56.0
18	51.6	52.1	53.9	55.9	56.1	2.2	54.4	57.3

Table 19. Mean values of index of proportion of upper to lower extremity length in boys

Age	(a-da <sub>III</sub> ) / (B-sy) x 100							
	Boys							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	95.4	92.9	88.9	-	-	-	-	-
4	92.4	89.7	89.5	91.4	90.1	5.2	89.2	94.6
5	88.7	89.4	88.7	96.5	95.3	8.4	91.8	99.4
6	88.4	88.1	87.5	94.7	95.9	5.9	90.8	98.3
7	88.2	87.1	84.0	88.4	88.3	4.8	84.7	91.6
8	86.4	85.4	82.8	88.3	89.4	6.1	85.1	93.6
9	85.6	84.3	83.5	88.3	90.0	4.5	87.2	91.6
10	85.2	83.3	80.4	85.1	85.3	2.0	83.5	87.0
11	84.9	82.0	81.4	86.0	85.5	4.0	83.8	88.8
12	84.3	82.3	81.0	87.5	87.2	2.7	85.3	88.2
13	85.1	81.4	80.9	88.2	89.3	6.1	85.0	93.5
14	84.6	82.0	80.6	88.9	89.0	3.9	85.5	90.3
15	83.3	82.3	80.0	86.9	86.5	2.9	84.6	89.3
16	83.6	82.1	82.2	86.0	85.5	4.0	83.8	88.8
17	84.0	82.5	82.3	87.9	87.7	2.5	85.8	89.2
18	85.0	82.8	82.8	86.4	85.9	4.0	84.2	89.2

Table 20. Mean values of index of proportion of upper to lower extremity length in girls

Age	(a-da <sub>III</sub> ) / (B-sy) x 100							
	Girls							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	93.6	89.9	87.3	-	-	-	-	-
4	90.8	88.7	89.3	96.0	94.9	3.2	94.6	97.9
5	88.7	88.9	86.6	91.9	90.8	4.1	88.9	94.5
6	88.2	87.2	86.5	90.5	91.3	3.8	89.3	93.3
7	87.1	86.4	83.2	87.4	88.9	4.9	83.3	90.8
8	85.9	84.0	80.9	88.1	87.2	4.6	85.0	89.6
9	84.8	82.7	81.2	89.8	88.9	4.5	86.7	91.3
10	84.1	82.2	81.7	87.4	88.9	4.9	83.3	90.8
11	84.3	81.3	80.7	87.8	89.3	4.9	83.7	91.2
12	83.6	80.9	81.0	83.2	83.7	2.2	81.8	84.9
13	83.1	80.5	81.1	82.2	82.7	2.4	80.7	83.6
14	83.5	82.0	80.6	84.5	84.9	4.0	82.0	88.1
15	84.0	82.1	81.2	84.2	84.6	4.0	81.7	87.8
16	84.2	82.2	80.9	84.8	85.2	4.2	83.5	86.0
17	84.1	82.2	81.7	82.7	82.0	5.7	79.7	86.5
18	84.1	82.3	81.6	82.4	81.7	5.7	79.4	86.2

Table 21. Mean values of hip-to-shoulder index in boys

Age	(ic-ic) / (a-a) x 100							
	Boys							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	75.5	73.1	77.5	-	-	-	-	-
4	76.8	71.6	76.1	73.2	73.5	6.7	67.0	75.0
5	75.8	71.1	75.5	71.7	70.0	4.8	68.0	74.1
6	73.4	72.1	73.4	72.1	71.7	4.8	68.6	75.0
7	72.5	70.7	74.6	74.1	73.2	6.7	69.7	78.5
8	72.6	70.7	75.6	71.2	71.4	5.0	67.3	73.8
9	72.5	71.0	76.2	73.6	75.0	4.9	72.2	77.2
10	72.5	71.3	76.5	72.8	73.1	6.7	66.8	74.8
11	72.4	71.0	75.3	72.3	70.6	5.3	70.0	75.0
12	72.1	71.0	75.0	71.7	70.0	4.8	68.0	74.1
13	72.0	70.3	75.7	69.2	70.1	3.4	68.4	71.3
14	71.9	71.4	74.6	73.9	74.2	4.4	70.8	75.8
15	72.1	71.4	75.2	69.6	70.2	3.5	68.8	71.7
16	72.2	70.7	73.8	68.7	69.0	3.4	68.0	71.5
17	72.2	70.9	73.3	69.3	70.1	3.4	68.4	71.3
18	72.4	70.2	73.1	68.7	69.2	3.1	67.3	71.4

Table 22. Mean values of hip-to-shoulder index in girls

Age	(ic-ic) / (a-a) x 100							
	Girls							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	75.5	71.8	76.1	-	-	-	-	-
4	75.2	71.6	74.4	71.1	71.5	2.5	69.0	73.2
5	75.1	71.7	74.4	72.1	71.7	3.7	69.7	74.6
6	73.5	71.3	73.5	72.2	71.3	3.9	70.5	72.7
7	72.7	71.1	72.2	73.9	72.3	6.8	68.6	78.4
8	72.8	71.2	72.9	72.7	71.8	3.9	71.0	72.2
9	72.7	71.3	73.5	74.1	72.6	6.8	68.6	78.0
10	73.2	71.6	72.8	75.3	74.7	4.9	71.5	78.5
11	74.2	71.0	75.1	75.6	75.6	5.2	70.1	80.9
12	74.1	72.5	76.2	74.4	76.2	4.1	71.1	77.8
13	73.6	73.8	76.6	74.2	73.8	4.4	70.5	77.8
14	74.5	75.9	78.8	74.8	74.2	5.5	70.1	78.1
15	75.1	76.0	79.3	74.6	74.6	5.0	70.2	77.7
16	75.6	75.9	79.7	74.8	75.0	5.2	70.4	77.2
17	76.0	75.2	78.5	77.1	77.7	2.6	76.1	79.3
18	76.1	75.2	78.5	78.0	78.1	4.5	75.5	82.0

Table 23. Mean values of shoulder width index in boys

Age	(a-a) / (sst-sy) x 100							
	Boys							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	72.2	74.7	69.6	-	-	-	-	-
4	72.3	75.6	71.6	73.8	73.9	5.0	70.6	76.8
5	73.1	74.5	71.8	69.8	69.9	5.3	66.6	73.1
6	74.8	74.6	72.1	71.1	71.8	7.8	63.2	76.2
7	74.7	76.0	72.6	71.5	72.2	7.8	63.6	76.6
8	75.1	77.8	71.5	71.3	72.0	7.8	63.4	76.4
9	75.9	78.0	71.0	75.0	73.8	5.1	71.6	78.5
10	76.0	77.9	69.7	74.6	75.0	4.6	72.3	78.4
11	75.8	78.7	69.3	71.1	71.8	7.8	63.4	76.4
12	75.4	79.4	69.8	76.0	76.3	4.8	72.7	79.5
13	75.3	79.5	70.9	73.5	73.5	2.4	71.6	74.5
14	75.8	78.6	73.9	72.0	71.7	6.5	69.9	76.8
15	76.2	77.8	75.0	76.5	76.8	4.8	73.2	79.5
16	76.0	77.5	74.9	75.2	75.3	4.6	72.5	78.6
17	75.9	77.9	74.8	77.6	77.9	4.0	74.3	81.1
18	76.2	77.8	73.9	77.0	77.3	4.8	73.7	80.5

Table 24. Mean values of shoulder width index in girls

Age	(a-a) / (sst-sy) x 100							
	Girls							
	1978/79	1993/94	2003/04	2013/14				
	$\bar{x}$	$\bar{x}$	$\bar{x}$	$\bar{x}$	Me	s	C <sub>25</sub>	C <sub>75</sub>
3	73.5	76.1	68.3	-	-	-	-	-
4	73.4	75.8	70.3	70.9	70.1	3.5	69.4	73.0
5	73.6	75.0	69.5	71.7	71.0	5.2	68.7	74.7
6	74.8	74.7	71.6	69.2	69.5	4.6	64.3	73.4
7	74.8	74.5	73.1	73.2	73.7	6.0	69.4	77.7
8	75.3	75.7	72.5	72.0	70.7	4.2	68.5	75.3
9	76.2	76.9	72.7	70.0	68.6	5.5	66.6	73.4
10	75.8	78.1	71.2	70.4	70.1	3.5	68.9	72.5
11	75.4	79.3	70.9	68.7	67.0	6.8	62.9	75.0
12	75.3	78.6	70.8	74.8	74.8	7.2	70.7	80.5
13	74.8	78.1	72.6	73.3	73.3	7.2	69.2	79.3
14	74.2	76.2	74.0	71.8	71.0	5.2	68.7	74.7
15	74.4	75.3	73.2	69.7	70.0	4.6	64.8	73.9
16	74.3	75.8	72.5	69.2	69.5	4.6	64.3	73.4
17	73.9	75.5	72.8	70.9	70.1	3.5	69.4	73.0
18	73.7	74.7	71.7	71.6	70.5	3.4	69.0	72.5

successively long-legged (1978/79) and very long-legged (1993/94 and 2003/04). In the 2013/14 sample, the long-arms feature persists until 9 years of age and reappears at the age of 13-14. For the other age classes, medium limbs are characteristic, which indicates a proportional shortening of the lower limbs in the sample of 2013/14. As a result of this process, 18-year-olds from the 2013/14 series have medium-length limbs (Table 19).

In girls, the long arms feature (from very long arms to long arms) is manifested in various ways: in the 1978/79 sample - up to age of 7, 1993/94 - 6 years, 2003/04 - up to 4 years old, and 2013/14 - up to 11 years of age. Girls from the 1978/79 series are long-legged in the age range of 9 up to 18 years. In girls from the 1993/94 series, long-leggedness appears at the age of 8, and from 9 to 18 years they are characterized by very long legs. Long-leggedness is characteristic from 7 to 18 years of age for subjects from the 2003/04 sample. The greatest variation in the proportions of the upper limbs and lower limbs was observed in them in 2013/14. In this case, up to 6 yrs. they are very long-armed, and then up to the age of 11 years long-armedness persists. 12-year-old and from 14-16-year-old girls are long-legged, while 13, 17- and 18-year-olds are very long-legged. As a result, 18-year-olds of 1978/79 and 2003/04 series are characterized by long legs, and from the 1993/94 and 2013/14 - very long legs (Table 20).

The proportions of body structure in boys can also be demonstrated with the hip-shoulder index, according to Wanke's classification.<sup>20</sup> For boys from the 1978/79 series, mean proportions are characteristic, except for 4-year-olds (female proportions). The subjects from the 1993/94 series aged 3-4 and 6 have mean proportions, and in the other age classes - male. Boys from the 2003/04 series are characterized by female proportions at 3, 9 and 10 years of age, and in other age categories - medium ones. In the studied group from 2013/14, the mean proportions are between 4-7, 9-12 years old and 14 years old, while male ones in 8- and 13-year-olds, as well as from 15-18 years of age (Table 21). The mean values of the hip-shoulders index according to Kolasa's interpretation, in girls from all compared series indicate male proportions. The exceptions are the examined 16-year-olds from the 2003/04 sample, which have mean proportions (Table 22).

A comparative analysis of the mean values of the shoulder width index showed for boys (according to Wanke's classification) and for girls (according to Kolasa's approach) differentiation of the proportion of body structure in the compared series.<sup>20</sup> For boys from the 1978/79 trial, medium-sized shoulders are characteristic in the entire examined segment of ontogeny. In the examined subjects from the 1993/94 series, the mean shoulders last from 3 up to 7 years, and from 8-18 years they are already wide. The boys from the 2003/04 series

are characterized by narrow shoulders at the age of 3 years and from 10-12 years of age, and in the age range 4-9 and 13-18 - medium ones. In turn, representatives of the 2013/14 series from 4-16 years of age, with the exception of 5-year-olds (narrow shoulders), are characterized by medium-sized shoulders, and 17-18 years - broad ones (Table 23). Differentiation in the proportions of body structure in relation to the discussed index is also observed in girls in individual series and age classes. Subjects from the 1978/79 sample are characterized by mean shoulders throughout the compared age range. Girls from the 1993/94 series from 3-9 yrs. and at the age of 14-18 are characterized by mean shoulders, while from 10-13 years - broad ones. In the 2003/04 trial, narrow shoulders occur from 3-6 years of age, in 8-year-olds, between 10-13 and 16 and 18 years. In the other age classes, the shoulders are medium. In turn, in the 2013/14 series, narrow shoulders are typical for the respondents from 4-6, 8-11 and 14-18 years. Mean shoulders are characteristic for 7-, 12- and 13-year-olds, so they are relatively rarely represented in the proportions of body structure in this sample (Table 24).

The comparative analysis shows that visible changes in body composition have occurred over the course of 35 years in the population of children and adolescents from Rzeszów. During the 35-year period, the following symptoms were observed: elongation of upper and lower limbs in both sexes, increase in shoulder width in boys from 15-18 years of age, and in girls generally in the entire examined age, tendency to decrease in hip width in both sexes in most age classes. The ongoing developmental processes have manifested in changes in the proportion of body structure. Short-trunk is characteristic for 18-year-olds of both sexes from all compared series, and in boys - short-limbs determined on the basis of the lower limb index.

## Discussion

Monitoring the growth processes and differentiation, which is indication of somatic development and the secular trend, causes many difficulties and is not systematic. For example, Argentina lacks systematic assessment of the process of growth and nutritional status in school-aged children.<sup>25</sup>

The commonly conducted anthropometric studies are not uniform methodologically. In comparison to current and previous surveys, different choice of anthropometric parameters and a different technique of their implementation, as well as with heterogeneous naming are encountered.<sup>18,20-24</sup> In anthropometric studies, the following features were taken into account: trunk length (sst-s), length of the upper limb (a-daIII), length of the lower limb (B-sy), shoulder width (a-a) and hip width (ic-ic). To compare, the researchers from Lodz used the height of the lower part of the body (B-ic), the width

of the arms (a-a), the intertrochanteric distance (tro-tro).<sup>26</sup> The same parameter (B-ic) is referred to as the height of the lower half of the body<sup>26</sup> or the height of the spikes.<sup>27</sup> The feature (B-ic) can therefore be determined by various measurement methods: in the mid axillary line, from the base to the iliac crest<sup>28</sup> or from the base to the anterior iliac spine.<sup>20,27</sup> Similarly to the study of the proportions between the upper and lower part of the body, various indicators are used: Lower Body - Upper Body Ratio (LUR), or the index of the lower limb length.<sup>17,20,27</sup> The most frequently and most uniformly collected measurements are body weight, body height (B-v) and BMI.<sup>2-13,20-25,27-38</sup>

The methods of anthropometric evaluation are used not only to identify disorders of the growth process (short stature), or disturbances of the nutritional status (malnutrition, obesity) but also to differentiate the body proportions.<sup>39-40</sup> For example, the Body Proportion Card (BPC) is published that allows the assessment of body proportions based on measurements of sitting height and length of the lower limb.<sup>14,41</sup> Chinese researchers have shown that the lower the values of the ratio of the lower limbs length to the sitting height, the higher the values of blood pressure.<sup>42</sup> This study also serves the role of the biological reference system. Anthropometric length parameters: body height, length of the upper limb, lower limb, arm and forearm are strongly correlated with one other.<sup>43</sup> In South Korea, detailed anthropometric studies containing various parameters (length, width, circumferences, ratio indices) describing the body of children and adolescents, including sex and age, are used e.g. in the clothes and shoes industry.<sup>38</sup>

In children and adolescents with health conditions, abnormal differentiation of body proportions occurs. Measurement of anthropometric features and the use of ratio coefficients allowed to determine that children with cystic fibrosis are characterized by short lower limbs and a long trunk in relation to body height, compared to healthy peers, while children operated on due to spinal cord herniation and hydrocephalus are characterized by short lower limbs and short trunk in relation to body height.<sup>28,44</sup> Other researchers have observed that girls with the Turner syndrome burdened with dwarfism have a more disturbed length of the upper and lower limbs than the length of the trunk. Growth hormone treatment in this group of girls significantly accelerates the growth rate, mainly due to the increase in trunk length, and to a lesser extent, lower limbs and does not compensate for the disturbances of body proportions characteristic for this syndrome. This phenomenon is probably connected with strongly conditioned genetic determination of body proportions.<sup>36</sup> Girls with the Turner's syndrome have shorter lower limbs and longer trunk not only in relation to healthy peers, but also to the peers with dwarfism.<sup>37</sup>

Most research on the secular trend is based on body weight, body height (B-v) and BMI. Below are some examples. It is believed that the rate of body height increase is accelerated, and the final height of the body is reached at earlier age.<sup>25,45</sup> Research conducted among 24,070 children aged 5 to 17 in Bogalusa (LA) in the United States confirms this trend in the period from 1973 to 1992. In addition, a reduced percentage of short stature was found. Basic data of Argentinian children aged 6 to 12 years were compared: body height, body mass, BMI collected in 1990 (1049 people) and in 2005-2007 (935 people). A disharmony in the secular trend was found between the body height and mass leading to increased incidence of overweight and obesity. The incidence of overweight increased by 4.4% and obesity by 5.9%, reaching respectively: 17.0% and 7.8%. There were no differences between sex, but in younger children excess body mass was higher than in the case of the body height.<sup>25</sup> Chinese researchers observing the secular trend on the basis of research conducted among 1,269,655 children, in 1985, 1995, 2000, 2005 and 2010, found that the incidence of weight gain before the age of 9 is responsible for the increasing prevalence of overweight and obesity among Chinese children and lack of acceleration of body height after the age of 12.<sup>29</sup> The acceleration of body height and weight has taken place in the last fifty years in the Seychelles, Indian Ocean. The body height curve is steeper than body weight - which confirms the tendency to overweight and obesity. At the same time, there is a significant improvement in social, economic and nutritional conditions. Researchers believe that acceleration of development is associated with the improvement of living conditions.<sup>31</sup>

The results of research on the secular trend are important for the determination of recommendations, preventive behavior and education.<sup>32,46</sup> The example may be the need to prevent the growing problems of overweight and obesity at the beginning of the 21st century among children from the city of Guangzhou in China, or to reduce the differences in body height between the rural areas of Guizhou and urban Shanghai.<sup>33</sup> It is generally believed, however, that better socio-economic conditions favor acceleration of body height and inferior acceleration of body mass.<sup>33,34</sup>

Studies on the secular trend based on different parameters than body weight, body height or BMI are less frequently performed. Thanks to the additional application of a waist circumference, researchers determined an increase in the incidence of abdominal obesity in children aged 6-13 years living in the city of Arequipa, Peru, located at the altitude of 2,320 meters above sea level. In 2001, 955 people were examined, and in 2015 - 83,547. In Lodz, research was conducted on the secular trend in a total of 1576 first-year students of the Medical Academy in 1978/1979, 1882/83, 1988/89 and 2003/2004.

Over 25 years, changes in body height (B-v), lower body height (B-ic), shoulder width (a-a), intertrochanteric distance (tro-tro) and resting chest circumference were analyzed. In both sexes, lower body height (B-ic), intertrochanteric (tro-tro) distance, and deceleration of the resting chest circumference were found. In the female sex, acceleration of shoulder width (a-a) caused blurring of sex differences of this feature. Intra-generational changes in body height (B-v) in both sexes in the last fifteen years have not been confirmed.<sup>26</sup> In our studies, acceleration of the length of the upper limbs (a-daIII) was observed in both sexes, both in 35 and 10-year period. Lower limb acceleration (B-sy) in both sexes is observed over a period of 35 years, but in the last decade it only occurs in the age groups: 17-year-old girls, 18-year-old girls and boys. In 35 and 10-year periods, shoulder width acceleration (a-a) is observed in boys and deceleration of shoulder width in girls (a-a) and hip width (ic-ic) in both sexes. Boys in younger age groups continue to have moderate-size trunk, while short trunk is found in older age groups and in girls of all age groups. On the basis of the upper limb index in both sexes, in the last 10 year period, we observe the transition to the long limb type from the short-limb type. On the basis of the index of the lower limb length, it can be determined that in all series in both sexes short-limbs are observed, except for girls aged 16-18 years from the last series (they have medium-limbs).

The studies on the secular trend among sick children and adolescents are conducted extremely rarely. The secular trend is also observed in the population of girls with the Turner's syndrome. Acceleration of birth body weight, birth body height and body height before growth hormone treatment was demonstrated.<sup>35</sup>

The effect of various processes taking place in all spheres of development (somatic and functional, mental, social, sexual) is to obtain a set of attributes assigned to adults, and thus to achieve maturity. Their order and onset of full maturity in individual spheres of development does not occur simultaneously, which leads to dissociation (fission) of maturation and the formation of internal conflicts.<sup>2</sup> A nicely built, slender and proportional body is a reason for satisfaction. In the absence of satisfying this need, adaptive disorders may be conducive to the development of negative health behaviors. Important issues of adolescence are: lowered mood, school difficulties, lack of acceptance in peer groups, depression, suicide attempts, self-mutilation, nicotineism, addiction to psychoactive substances, premature sexual initiation, harmful and risky sexual behavior, reckless driving.<sup>48-52</sup> Knowledge of the typogenesis, individualized deletion of development trajectory and rationalization of problems may also help in resolving some internal conflicts.<sup>53</sup>

## Conclusions

The secular trend was confirmed in the population of children and adolescents aged 4 to 18 from Rzeszów in the last 35 years in terms of growing and differentiation in the proportion of body structure.

Further monitoring of trends in children and adolescents from Rzeszów is required.

## References

1. Wolański N. *Rozwój biologiczny człowieka*. Warszawa: PWN; 2005:1-543.
2. Woynarowska B. *Rozwój fizyczny oraz motoryczny dzieci i młodzieży*. W: Kawalec W, Grenda R (red). *Pediatrics*. Tom I. Warszawa: Wydawnictwo Lekarskie PZWL; 2014:1-28.
3. Kułaga Z, Litwin M, Grajda A, et al. Normy rozwojowe wysokości i masy ciała, wskaźnika masy ciała, obwodu talii i ciśnienia tętniczego dzieci i młodzieży w wieku 0-18 lat. *Stand Med Pediatr*. 2015;1;12;Sp1.
4. Książeczka Zdrowia Dziecka. Ministerstwo Zdrowia. Zgodna ze wzorem Rozporządzenia Ministra Zdrowia z 9 listopada 2015 r., załącznik 6.
5. Jodkowska M, Oblacińska A. Badanie profilaktyczne dzieci w wieku niemowlęcym. *Med Prakt Pediatr*. 2014;4:92-102.
6. Jodkowska M, Oblacińska A. Profilaktyczne badanie lekarskie w wieku poniemowlęcym i przedszkolnym. Bilans zdrowia dzieci w wieku 2 i 4 lat. *Med Prakt Pediatr*. 2014;5:90-102.
7. Jodkowska M, Oblacińska A. Standardy w profilaktycznej opiece zdrowotnej nad dziećmi i młodzieżą w wieku szkolnym. *Med Prakt Pediatr*. 2015;1:97-103-109.
8. Oblacińska A, Jodkowska M. Bilans zdrowia ucznia III klasy szkoły podstawowej. *Med Prakt Pediatr*. 2015;2:103-118.
9. Oblacińska A, Jodkowska M. Bilans zdrowia dzieci w wieku 5 lat oraz dzieci objętych rocznym obowiązkowym przygotowaniem przedszkolnym. *Med Prakt Pediatr*. 2014;6:90-99.
10. Jodkowska M, Oblacińska A. Bilans zdrowia ucznia I klasy gimnazjum i I klasy szkoły ponadgimnazjalnej. *Med Prakt Pediatr*. 2015;4:102-108.
11. Oblacińska A, Jodkowska M, Woynarowska B. Bilans zdrowia ucznia kończącego szkołę ponadgimnazjalną. *Med Prakt Pediatr*. 2015;4:95-99.
12. Kułaga Z, Róźdzynska-Świątkowska A, Grajda A, et al. Percentile charts for growth and nutritional status assessment in Polish children and adolescents from birth to 18 year of age. *Stand Med Pediatr*. 2015;12:119-135.
13. Rerksupphol S, Rerksupphol L. Waist Circumference, Waist-to-Height Ratio and Body Mass Index of Thai Children: Secular Changes and Updated Reference Standards. *JCDR*. 2014;8:5-9.
14. Hattori K, Hirohara T, Satake T. Body proportion chart for evaluating changes in stature, sitting height and leg length in children and adolescents. *Ann Hum Biol*. 2011;38:556-560.



15. Weisensee KE, Jantz RL. An Examination of the Differential Effects of the Modern Epidemiological Transition on Cranial Morphology in the United States and Portugal. *HB*. 2016;1:30–37.
16. Sanna E, Palmas L. Changes in body and head dimensions in urban Sardinian children (3–5 years) from 1986 to 2001. *Ann Hum Biol*. 2003;3:295–303.
17. Wolański N. Zmiany budowy ciała ludności Polski, ich przyczyny oraz możliwości wykorzystania jako miary rozwoju gospodarczego i warunków bytowych. W: Kopyczyński M, Siniarska A (red). Budowa fizyczna człowieka na ziemiach polskich wczoraj i dziś. Muzeum Historii Polski: Warszawa; 2017:15–37.
18. Radochońska A, Perenc L. Trendy w rozwoju fizycznym u dzieci i młodzieży z Rzeszowa w dwudziestopięciolecie 1978–2004. *Prz Med Uniw Rzesz*. 2009;3:239–250.
19. Wolański N. Metody kontroli i normy rozwoju dzieci i młodzieży. Warszawa: PZWL; 1975:341–342.
20. Malinowski A, Bożiłow W. Podstawy antropometrii. Metody, techniki, normy. Warszawa, Łódź: PWN; 1997.
21. Perenc L, Radochońska A, Błajda J. Rozwój otyłości ciała u dzieci i młodzieży z Rzeszowa oraz jego zmienność na przestrzeni 35 lat. *Med Rev*. 2016;14:27–47.
22. Perenc L, Radochońska A, Błajda J. Somatic growth in children and adolescents from Rzeszów, aged 4–18, and its variability over the thirty-five year period from 1978/79 to 2013/14. *Med Rev*. 2016; 14 (3): 244–265. doi: 10.15584/medrev.2016.3.1.
23. Perenc L, Radochońska A, Błajda J. Changeableness of selected characteristics of the head in the Rzeszów children and adolescents aged 4 to 18 in during a 35-year period. *Eur J Clin Exp Med*. 2017;15(3):217–232. doi: 10.15584/ejcem.2017.3.5.
24. Radochońska A, Perenc L. Zmiany proporcji budowy ciała dzieci i młodzieży rzeszowskiej w wieku od 3–18 lat w dwudziestopięciolecie 1978–2004. *Przegl Med Uniw Rzesz*. 2010;1:30–48.
25. Orden AB, Bucci PJ, Petrone S. Trends in weight, height, BMI and obesity in school children from Santa Rosa (Argentina), 1990–2005/07. *Ann Hum Biol*. 2013;4:348–354. DOI: 10.3109/03014460.2013.778329
26. Sitek A, Szkudlarek A, Antoszewski B. Secular changes in the physical development of students of the Medical University of Łódź. *Folia Morphol*. 2007;1: 62–68.
27. Perenc L. Ocena rozwoju somatycznego dzieci operowanych z powodu przepukliny oponowo-rdzeniowej na podstawie analizy częstości występowania pomiarów antropometrycznych w przedziałach wartości przeciętnych i patologicznych. *Przegl Med Uniw Rzesz*. 2005;2:125–139.
28. Sands D, Umlawska W, Zielińska A. A cross-sectional study of growth, nutritional status and body proportions in children and adolescents at a medical center specializing in the treatment of cystic fibrosis in Poland. *Arch Med Sci*. 2015;1:155–163. DOI: 10.5114/aoms.2015.49207
29. Fu LG, Sun LL, Wu SW, et al. The Influence of Secular Trends in Body Height and Weight on the Prevalence of Overweight and Obesity among Chinese Children and Adolescents. *BES*. 2016;12:849–857. DOI: 10.3967/bes2016.114.
30. Zong Y, Xie R, Deng N, et al. Secular trends in overweight and obesity among urban children and adolescents, 2003–2012: A serial cross-sectional study in Guangzhou, China. *Sci Rep*. 2017; 7:12042. DOI:10.1038/s41598-017-12094-z.
31. Marques-Vidal P, Madeleine G, Romain S, Gabrie A, Bovet P. Secular trends in height and weight among children and adolescents of the Seychelles, 1956–2006. *BMC Public Health*. 2008;8:1–9. DOI:10.1186/1471-2458-8-166.
32. Freedman DS, Kettel Khan L, Serdula MK, Srinivasan SR, Berenson GS. Secular trends in height among children during 2 decades. *Arch Pediatr Adolesc Med*. 2000;154:155–161.
33. Xu Y, Hang L. Height inequalities and their change trends in China during 1985–2010: results from 6 cross-sectional surveys on children and adolescents aged 7–18 years. *BMC Public Health*. 2017;17:1–11. DOI: 10.1186/s12889-017-4402-9.
34. Stănescu M, Stoicescu M, Bejan LB. Secular trend of students' somatic development from different Romanian geographical regions. *EpSBS*. 2018. <http://dx.doi.org/10.15405/epsbs.2018.03.1>.
35. Woelfle J, Linberg A, Aydin F, Ong KK, Camacho-Hubner C and Gohlke B. Secular Trends on Birth Parameters, Growth, and Pubertal Timing in Girls with Turner Syndrome. *Front Endocrinol*. 2018;9:1–8. DOI: 10.3389/fendo.2018.00054.
36. Łysoń-Wojciechowska G, Romer TE, Wiśniewski A, Majcher A. Budowa i proporcje ciała dziewczynek z zespołem Turnera do 10 roku życia po 12 miesiącach leczenia hormonem wzrostu. *Ped Pol*. 1993;12:23–29.
37. Milde K, Tomaszewski P, Majcher A, Parżak B, Stupnicki R. Body proportions of healthy and short stature adolescent girls. *Pediatr Endocrinol Diabetes Metab*. 2011;14:195–200.
38. Lee Y. Estimation of body size and growth patterns in Korean boys. *JPA*. 2015;34:1–12.
39. Thompson, JK, Smolak L. Body Image, Eating Disorders, and Obesity in Youth: Assessment, Prevention, and Treatment. United Book Press, Baltimore; 2008.
40. Hermanussen M, Lieberman LS, Schönfeld Janewa V, et al. Diversity in auxology: Between theory and practice. *Anthrop Anz*. 2012; 2:159–174. DOI: 10.1127/0003-5548/2012/0133
41. Zhang YQ, Li H. Reference charts of sitting height, leg length and body proportions for Chinese children aged 0–18 years. *Ann Hum Biol*. 2015;3:223–30. DOI: 10.3109/03014460.2014.934283
42. Dong B, Wang Z, Ma J. Leg-to-trunk ratio and the risk of hypertension in children and adolescents: a population-based study. *J Public Health (Oxf)*. 2016;4:688–695. DOI:10.1093/pubmed/fdv203

43. Zhu M, Jiao YH, Xiong F, Xie F, Guo SJ, Cun YS. Analysis of limb segments length and body proportion of southern Chinese children and adolescents. *J Paediatr Child Health*. 2015;51(12):1164-71. DOI: 10.1111/jpc.12978.
44. Perenc L. Analiza częstości występowania wskaźników proporcji w przedziałach wartości przeciętnych i patologicznych. *Przegl Med Uniw Rzesz*. 2005;4: 226-351.
45. Orden AB, Vericat A, Apeztegui MC. Age at menarche in urban Argentinian girls: association with biological and socioeconomic factors. *Anthrop Anz*. 2011;68: 309–322.
46. Pochobradská K, Suchomel A. Secular trends in physical development and motor performance of preschool children (theoretical background). *ACC*. 2012;2: 174-178.
47. Cossio-Bolanos M, de Arruda M, Andruske CL, Luarte-Rocha C, Gomez-Campos R. Secular trends of physical growth and abdominal adiposity of school children and adolescents living at a moderate altitude in Peru. *Am J Phys Anthropol*. 2016; 1–8. DOI 10.1002/ajpa.23121
48. Lelek A. Pacjent nastoletni w opiece ogólnolekarskiej. *Med Prakt Pediatr*. 2016;5:95-101.
49. Janas-Kozik M, Cichoń L, Jelonek I. Szkodliwe zachowania wśród dzieci i młodych osób (do 25 roku życia). *Pediatr Dypl*. 2017;6:19-24.
50. Lenkiewicz K. Samookaleczenia w obrazie klinicznym pourazowego zaburzenia stresowego. *Pediatr Dypl*. 2015;1:27-30.
51. Kucińska A. Konsekwencje używania i nadużywania marihuany. *Pediatr Dypl*. 2015;1:31-35.
52. Özdemir A, Utkualp N, Palloş A. Physical and Psychosocial Effects of the Changes in Adolescence Period. *IJCS*. 2016;2:717-723.
53. Mummert A, Schoen M, Lampl M. Growth and Life Course Health Development. In: Halfon N, Forrest C, Lerner R, Faustman E. Handbook of Life Course Health Development. Cham: Springer; 2018:405-429. DOI 10.1007/978-3-319-47143-3\_17.



## ORIGINAL PAPER

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# BMI as a factor influencing the number of steps among physical education students

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## Abstract

**Introduction.** Organized physical activity (PA) is among factors that significantly influence the amount of realized PA.

**Aim.** The aim of this study was to collect and analyze the influence of BMI on the number of steps among women while undergoing obligatory sport camp as part of physical education studies and during study time at university.

**Materials and methods.** The studies included women (n=60) ranging from 19 to 25 years of age. Their weekly physical activity was monitored using an accelerometer ActiGraph. The significance of the differences between the results for two consecutive measurements are pointed out among the same people, but under different conditions there was assessed at-student test for the variables. Compliance of measurement was described using testing and Bland-Altman chart. For the level of statistical significance  $p < 0.05$  was adopted.

**Results.** The requirements of the WHO on the minimum physical activity were met by almost all students. There is a lack of presence of a statistically significant relationship between BMI and the number of student steps, both in the case of measurement during study time ( $R = -0.03$ ;  $p = 0.815$ ) and at camp ( $R = -0.02$ ;  $p = 0.865$ ).

**Conclusions.** Women are characterized by high activity (number of steps). BMI does not affect the number of steps for studies. Students meet the requirements of WHO (10000 steps).

**Keywords.** physical activity, WGT3X-BT, accelerometer

## Introduction

Physical activity (PA) is endorsed as health enhancing, and is known to prevent and reduce both musculoskeletal disorders and mortality.<sup>1-3</sup> Recent advancements in pedometers create the opportunity for use in providing more detailed information on physical activity patterns,

rather than simply recording a tally of steps/day, even though it is limited to ambulatory physical activity. Currently, empirical studies examining steps/day translation of the daily recommendation of 60 min MVPA in adolescents are divergent, ranging from 7,500 to 14,000 steps/day.<sup>4-6</sup> Developments in technology to improve the objec-

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 11.09.2018 | Accepted: 2.11.2018

Publication date: December 2018

Herbert J, Matłosz P, Grzywacz R, Jaskierska P, Sołek A. BMI as a factor influencing the number of steps among physical education students. *Eur J Clin Exp Med*. 2018;16(4):283–288. doi: 10.15584/ejcem.2018.4.4

tive PA measurement in humans through the use of objective measures such as pedometers and accelerometers have promise.<sup>7</sup> Pedometers capture most of the variance in PA measured by accelerometers in adult populations.<sup>8</sup> The pedometer has been and continues to be a popular instrument for physical activity assessment. Recently it has been suggested that 10,000 steps should be a daily step count cut-point used to assess optimal physical activity levels.<sup>4</sup>

Various governmental and professional organizations around the world have used the 10,000 daily step recommendation as an index of high physical activity level. This daily step-based recommendation has been endorsed by the World Health Organization, National Heart Association of Australia, US Centers for Disease Control and Prevention, and American Heart Association to improve overall health.<sup>9</sup> The use of step data (usually as steps/day) is a simple means of reflecting habitual physical activity pattern, and this approach has become acceptable to many researchers and practitioners.<sup>10</sup> Moreover, walking activity has been reported as a prevalent form of leisure-time physical activity and a functional task in the daily lives.<sup>2</sup>

Body mass index (BMI) is the metric currently in use for defining anthropometric height/weight characteristics in adults and for classifying (categorizing) them into groups. The common interpretation is that it represents an index of an individual's weight status. It also is widely used as a risk factor for the development of, or the prevalence of several health issues. In addition, it is widely used in determining public health policy.<sup>11</sup>

### Aim of the study

The aim of the study was to analyze the relationship between BMI and the number of steps taken by students of physical education during obligatory sport camp as part of their studies in the Faculty of Physical Education during a standard week of education in the course of winter semester.

The hypothesis is as follows: BMI affects the number of steps, the number of steps depends on the type of activities, and students meet the requirements of the WHO (min 10000 steps).

### Material and methods

The study involved 60 female students in the Faculty of Physical Education, University of Rzeszów (Poland) who participated in sport camp and regularly attended obligatory courses during the semester. The criterion for inclusion in the project was: participation in all courses in one week with no medical contraindications. The study included healthy students who were enrolled, randomly selected at the University of Rzeszów, Poland during the 2017/ 2018 school year. The invitation to participate in the study was sent to 75 students. All participants were fully informed in writing and verbally

about the nature of the study. The consent of 75 students was obtained for participation in this study. Of those respondents, 15 were excluded from the study for the following reasons: removal of the accelerometer at any time of the study period, the device suffered mechanical error or operator error (incorrect epoch length, anthropometrics, and/or participant identification) ( $n = 10$ ), and refusal to participate in study ( $n = 5$ ). Ultimately, the study group consisted of 60 students.

Ethical clearance: Possible procedures were explained to students before signing the consent for participation in the study. Test procedures and protocols have been carried out in accordance with the Declaration of Helsinki.

The accelerometer ActiGraph WGT3X-BT (Pensacola, USA) was used in the testing. This is a three-axis accelerometer and one of the most commonly used devices to assess physical activity.<sup>12</sup> The accelerometer was placed on the waist using an elastic belt securely above the right hip bone for measuring the amount and frequency of participant movement. After a completed recording, a sensor connected to the computer via the mini USB transferred data. During the initialization, there was required information including the name of the entity, gender, height, weight, and race. Participants were instructed to have the accelerometer for seven consecutive days, 24 hours a day.

Data was collected in 60s epochs. Non-wear time was defined as 60 min of consecutive zeros allowing for 2 min of non-zero interruptions.<sup>29</sup> A wear time of  $\geq 500$  min/day was used as the criterion for a valid day, and  $\geq 4$  days were used as the criteria for a valid 7-day period of accumulated data.

ActiGraph data were analyzed using the software Actilife 6.0. Human characteristics (sex, age, were reported individually), moreover, weight and height of the body was measured. Body height was measured to the nearest 0.1 cm using a portable stadiometer Seca 213. The measurement was performed under standard conditions in an upright position, barefoot. Body mass was assessed to an accuracy of 0.1 kg using a body composition analyzer (BC-420, Tanita). Body mass index (BMI) was calculated as  $\text{kg/m}^2$ . All measurements were performed in the early morning before setting up the accelerometer according to the guidelines of the manufacturer. BMI ( $\text{kg/m}^2$ ) categories are as follows: underweight ( $18.5 <$ ), normal weight ( $18.5\text{--}22.9$ ), overweight ( $23\text{--}24.9$ ), and obese ( $25\text{--}29.9$ ) and class II obese ( $\geq 30.0$ ).<sup>9</sup>

Activity log-in during the day during the sports camp (7 days) including camp program (7.20–8.00), gymnastics and runs (9.30–13.30), open water swimming/kayak/hiking (15.30–17.30), biking/boating/different sports in the sports hall (20.00–21.00), evening animation/runs/strengthening exercises. All physical activities were held an average of 8 hours per day in the month of July. Activity log-in during the day during the semester (7 days)

included activities at the University (7.00-20.45), theoretical and practical courses (volleyball, gymnastics, karate, dancing). Classes were held an average of 6-8 hours a day divided into 50% of theoretical and 50% of practical. The classes were held in October. The studies took place in July and October; the impact of the season should not affect the divergence of test results.

A statistical analysis of the collected data was conducted using the Statistica 13.1 program, StatSoft company. It used both parametric and nonparametric tests. The choice of parameterized test subject was the fulfillment of the basic assumptions such as compliance test schedule variables with normal schedule, were verified by the W Shapiro-Wilk test. For all the variables, descriptive statistics were calculated (mean, median, minimum, maximum, the first the third quartile and the standard deviation). The significance of the differences between the results for the two consecutive measurements in the same people, but under different conditions, was assessed with Student's t- test for dependent variables or alternatively no parametric test of order pairs Wilcoxon. To verify compliance of the measurement results obtained in measuring during studies with the results obtained in measuring during camp analysis Bland-Altman was performed.

Bland-Altman charts present lines of 95% compatibility ranges for the average difference between the measurements obtained during studies and camp and points with coordinates equal to results concerning differences of measurements obtained in two conditions. Good repeatability of the results is when 95% of the measurements are located between lines of conformity (acceptable percentage of outliers is 5%).

The correlation of two variables with distribution which does not satisfy the criterion for normality of the distribution is made by using the Spearman correlation. Compliance of the measurements taken during the study and during the camp was tested and was shown using test and Bland-Altman chart. For the level of statistical significance it was adopted  $p < 0.05$ .

Results

The average age of the students in measurement I (during studies) was  $20.61 \pm 1.45$  years, and in measure-

ment II (camp)  $20.46 \pm 1.59$  years. The difference between the I and II measurement was an average of 0.15 year. The students were situated in the range from 19 to 25 years. The age of the students in two consecutive measurements did not differ significantly.

The average height of the body of tested students in the measurement I and II was  $170.42 \pm 7.86$  cm and contained in a range of values from 154 cm to 194 cm. Average body weight of the tested group in the measurement I (studies) was  $62.53 \pm 9.66$  kg, and the measurement II (camp)  $59.61 \pm 6.04$  kg. The difference between I and II measurement was an average of 2.92 kg. This difference was statistically significant ( $p = 0.038$ ). Body weight of female students during camp was lower than during studies.

The average BMI of tested group in I measurement (studies) was  $21.45 \pm 2.32$  kg/m<sup>2</sup>, and in measurement II (camp)  $20.62 \pm 2.57$  kg/m<sup>2</sup>. The difference between I and II measurement was an average of 0.84 kg/m<sup>2</sup>. This difference was statistically insignificant ( $p=0.051$ ). BMI of students during camp was lower than during studies. The range for BMI in I measurement was from 16.47 to 27.47 kg/m<sup>2</sup>, and in measurement II from 14.36 to 26.35 kg/m<sup>2</sup> (Table 1).

The average number of steps taken by the tested students during the day in measurement I (studies) was  $11,444.66 \pm 4,246.03$ , and in measurement II (camp)  $16,377.76 \pm 5,562.55$ . The difference between I and II measurement was an average of 4933.1. This difference was statistically significant ( $p<0.001$ ). The number of taken steps a day by students during camp was higher than those taken during studies. The range for the number of steps in both I and II measurement was from 548.57 to 29,123.57 (Table 2).

Only one person in the course of the semester and 2 others tested during the camp did not meet the assumptions of WHO concerning the minimum number of steps to be performed daily for health maintenance. This difference was statistically insignificant ( $p=0.592$ ).

A lack of the presence of a statistically significant correlation between BMI of tested students and the number of steps were shown, both in the case of measurement during studies ( $R=-0.03$ ;  $p=0.815$ ) and camp ( $R=-0.02$ ;  $p=0.865$ ). Statistical insignificance was found

Table 1. BMI of participants

BMI [kg/m²]	Descriptive statistics								
	n	$\bar{x}$	Me	Min.	Max.	Q1	Q3	SD	d
studies (I)	60	21.45	21.45	16.47	27.47	19.71	22.47	2.32	0.84
camp (II)	60	20.62	20.94	14.36	26.35	18.61	22.27	2.57	
P	t=1.98 p=0.051								

n – number of observations;  $\bar{x}$  – arithmetic average; Me – mediana; Min – minimum; Max – maximum; Q1 – lower quartile; Q3 – upper quartile; SD – standard deviation; t – the Student's t-test result for dependent variables; p – level of significance of differences

Source: own study

**Table 2.** Number of steps /day

Number of steps	Descriptive statistics								
	[n]	n	$\bar{x}$	Me	Min.	Max.	Q1	Q3	SD
studies (I)		60	11444.66	10546.14	528.57	21877.57	9085.43	13084.14	4246.03
camp (II)		60	16377.76	16478.00	548.57	29123.57	13684.43	19205.29	5562.55
P						Z=4.79	p<0.001		

n – number of observations;  $\bar{x}$  – arithmetic average; Me – mediana; Min – minimum; Max - maximum; Q1 – lower quartile; Q3 – upper quartile; SD – standard deviation; Z – the test result of the order of par Wilcoxon; p – level of significance of differences  
Source: own study

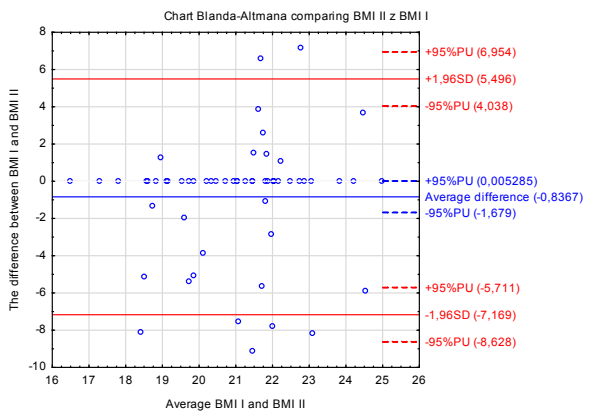
**Table 3.** The relationship between BMI and the number of steps at the time of the study and at camp

Variables	R	P
BMI and the number of steps at studies	-0.03	0.815
BMI and the number of steps at camp	-0.02	0.865
The difference between BMI and the difference in the number of steps	-0.03	0.817

R – the value of Spearman’s rank correlation; p – level of significance of differences  
Source: own study

also in the relationship between the difference in the value of BMI and the difference in the number of steps obtained between the I and II measurement (R=-0.03; p=0.817).

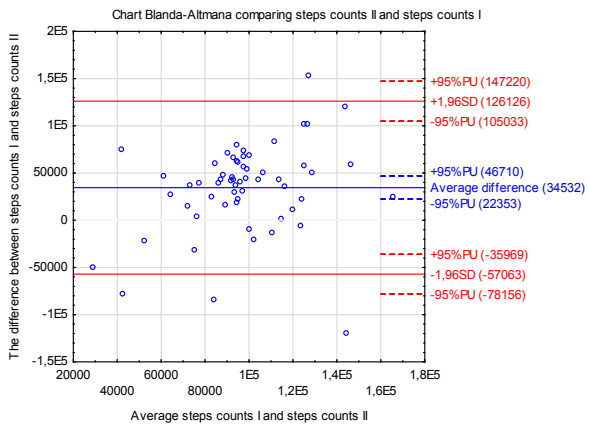
Bland-Altman chart for collected data on BMI indicates that the measurement at camp (II) gives lower results than the measurement during studies - an average of 0.84 kg/m<sup>2</sup> (line for the average difference is 0.8367 lower than absolute compliance illustrated by the line of 0). The range of span compliance was 12.665 kg/m<sup>2</sup>. In this range, there was about an 88.0% difference between pairs of measurements. Out of this range were 7 differences. This means that the coefficient of Bland and Altman was approximately 12.0%. Repeatability of measurement assessed by Bland and Altman method for BMI has not reached the criterion of the British Institute of Standardization; 95% of the differences between the results of measurement pairs was in the range of compliance for medium (Fig. 1).



**Fig. 1.** Bland-Altman Diagram for BMI  
Source: This study

Bland-Altman chart for collected data on the number of steps indicates that the measurement made at camp (II) gives higher scores than measurement during studies - an average of 4933 steps (line for the average difference is 4933 higher than absolute compliance illustrated by the line of 0). In this range, there was about a 93% difference between pairs of measurements. Out of this range were 4 differences. This means that the coefficient of Bland and Altman was approximately 7%.

Repeatability of measurement assessed by Bland and Altman method for number of steps has not reached the criterion of the British Institute of Standardization; 95% of the differences between the results of measurement pairs was in the range of compliance for medium (Fig. 2).



**Fig. 2.** Bland-Altman diagram for the number of steps  
Source: This study

**Discussion**

The aim of this study was to collect and analysis of the influence of BMI on the number of steps among women during obligatory sport camp as part of physical educa-

tion studies and during study time at university. This is one of the few studies performed that compare the same group under different conditions (sports camp and a week of study).

There is lack of studies analyzing patterns of physical activity (number of steps) for students, particularly in Poland. Special periods in the life of a young person are undoubtedly studies. New surroundings and conditions of residence often involve taking more responsibility for creating their own lifestyle. This is connected with the new conditions of social life, the lifestyle and change of work rhythm. Research shows that the amount of number of steps made by Polish students meet WHO recommendations.<sup>13</sup> It should be pointed out the fact that there are few studies on physical activity levels that depend on the Body Mass Index (BMI).<sup>14</sup>

Physical activity is estimated by subjective tools (questionnaires, surveys, interview) and objective (ActiGraph, a pedometer). In this study, an objective tool was used which allowed not only for determining the time spent, but also to measure and verify with the recommendations of the WHO's number of steps per day. Although self-reported data can provide useful insights into physical activity levels of populations or subgroups, these data have the tendency to over or underestimate true physical activity, energy expenditure, and rates of inactivity.<sup>15,16</sup>

Few studies have attempted to measure the level of agreement between self-reported measures and steps/day data as a direct/objective measure of ambulatory physical activity.<sup>17,18</sup> A popular public health message relating to pedometry is the 10,000 steps/day concept, which shows positive health outcomes in those achieving this target compared with those not achieving 10,000 steps/day. The values obtained here between an average of  $11,444 \pm 4246.03$ , and  $16,377.76 \pm 5,562.55$  steps/day has generally been classified as very active.<sup>5,6,19</sup> Research students ( $n = 25$ ) from James Cook University in Cairns, Australia performed an average of  $10,896.0 \pm 4,364.9$  steps, in turn, in similar studies, students ( $n = 73$ ) performed an average of  $9,096.7 \pm 3,955.3$  steps.<sup>20,21</sup> Research from 23 countries found that among students from Central and Eastern Europe, only 32% of men and 18% of women meet the recommended frequency of leisure time in PA.<sup>22</sup> Better results were found for students of universities from Australia, where 47% of men and 51% of women ( $n = 103$ ) have reached 10,000 steps.<sup>23</sup> In turn, in Czech students, women performed  $10,612 \pm 2,750$  steps a day.<sup>24</sup> With the above information, the hypothesis that students meet the requirements of WHO (10000 steps) has been confirmed in the case of both groups, and in addition, it has been greatly exceeded.

Moreover, the results of our research indicate that BMI does not affect the number of steps for studies ( $R = -0.03$ ;  $p = 0.815$ ) and camp ( $R = -0.02$ ;  $p = 0.865$ ), and by far

the number of steps depends on the type and characteristics of the activities. These findings suggest that the more movement activities in the field, the greater the physical activity test, as in the studies, the number of female students from various fields of study was ( $n = 323$ ) and only 2.5% did not make 10,000 steps a day.<sup>25</sup>

By analyzing the results on the level of physical activity of students depending on body mass index (BMI), it was found that women are characterized by high activity (number of steps). Similarly, the student from South Africa on a valid body mass index (BMI) was shown to be more active than their peers underweight and overweight.<sup>26</sup> As physical activity is an important factor in weight control, a larger and more consistent body of evidence of significant negative associations between habitual physical activity and adiposity has been reported in cross-sectional studies using pedometry.<sup>27,28</sup> Activities that were carried out on the training camp give the opportunity to participate in physical activity and should sustain the belief that physical movement and fresh air are factors in health promotion. Therefore, further research should outline the relationship between the physical active lifestyle and transition students into adulthood.

In conclusion, the physical environment can promote the regular involvement of students in physical activity and to assist them in adopting and maintaining an active lifestyle. Educators and health promoters must take into account a variety of factors (including natural surroundings) because they design effective interventions to promote physical activity among young people and encourage them to adopt and maintain physically active lifestyle.

## Conclusion

Women are characterized by high activity (number of steps). BMI does not affect the number of steps in our studies. Students meet the requirements of WHO (10,000 steps). The results of this study provided us with a more accurate understanding of how important activity type is in predicting the physical activity of students. The results also indicated the direct contribution of specific variables (environmental) where all classes were held outdoors.

## References





1. Steeves JA, Tudor-Locke C, Murphy RA, King GA, Fitzhugh EC, Harris TB. Classification of occupational activity categories using accelerometry: NHANES2003–2004. *Int J Behav Nutr Phys Act.* 2015;12(1):1–20.
2. Holtermann A, Hansen JV, Burr H, Sogaard K, Sjogaard G. The health paradox of occupational and leisure-time physical activity. *British Journal of Sports Medicine.* 2012;46(4):291–295.

3. Holtermann A, Marott JL, Gyntelberg F, et al. Does the benefit on survival from leisure time physical activity depend on physical activity at work? A prospective cohort study. *PLoS ONE*. 2013;8(1).
4. Colley R, Janssen I, & Tremblay M. Daily step target to measure adherence to physical activity guidelines in children. *Med Sci Sports Exerc*. 2012;44(5):977–982.
5. Adams M, Johnson W, Tudor-Locke C. A steps/day translation of the moderate-to-vigorous physical activity guideline for children and adolescents. *Int J Behav Nutr Phys Act*. 2013;10(49).
6. Fontana F, Da Silva M, Marston R, Finn K, Gallagher J. Step-count guidelines referenced on 60-minutes of moderate/ vigorous physical activity. *Motriz*. 2015; 21(1):92–99.
7. Helmerhorst HJ, Brage S, Warren J, Besson H, Ekelund U. A systematic review of reliability and objective criterion-related validity of physical activity questionnaires. *Int J Behav Nutr Phys Act*. 2012;9:103.
8. Tudor-Locke C, Ainsworth B, Thompson R, Matthews C. Comparison of pedometer and accelerometer measures of free-living physical activity. *Med Sci Sports Exerc*. 2002;34:2045–2051.
9. World Health Organization. WHO STEPS Surveillance Manual: The WHO STEP wise approach to chronic disease risk factor surveillance. Geneva, World Health Organization. 2005.
10. Bravata DM Smith-Spangler C, Sundaram V. Using pedometers to increase physical activity and improve health: a systematic review. *JAMA*. 2007;298(19):2296–304.
11. Nuttall FG. Body Mass Index: Obesity, BMI, and Health: A Critical Review. *Nutrition Today*. 2015;50(3):117–128.
12. Crouter SE, Dellavalle DM, Haas JD, Frongillo EA, Bassett DR. Validity of ActiGraph 2-regression model, Matthews cut-points, and NHANES cut-points for assessing free-living physical activity. *J Phys Act Health*. 2013;10(4):504–514.
13. Arias-Palencia NM, Solera-Martínez M, Gracia-Marco L, et al. Levels and Patterns of Objectively Assessed Physical Activity and Compliance with Different Public Health Guidelines in University Students. *PLoS One*. 2015;10.
14. Rauner A, Mess F, Woll A. The Relationship between physical activity, physical fitness and overweight in adolescents: a systematic review of studies published in or after 2000. *BMC Pediatrics*. 2013;13:19.
15. Prince SA, Adamo KB, Hamel ME, Hardt J, Gorber SC, Tremblay MS. A comparison of direct versus self-report measures for assessing physical activity in adults: A systematic review. *Int J Behav Nutr Phys Act*. 2008;5(1):56.
16. Biernat E, Piątkowska M. Overestimation of physical activity by long IPAQ in a Polish nationwide study. *Hygeia Public Health*. 2016; 51(1):87–95.
17. Miller R, Brown W. Meeting physical activity guidelines and average daily steps in a working population. *J Phys Act Health*. 2004;1(3):218–226.
18. Matton L, Wijndaele K, Duvigneaud N, Duquet W, Philippaerts R, Thomis M. Reliability and validity of the Flemish Physical Activity Computerized Questionnaire in adults. *Res Q Exerc Sport*. 2007;78(4):293–306.
19. Tudor-Locke C, Craig C, Beets M, et al. How many steps/day are enough? for children and adolescents. *Int J Behav Nutr Phys Act*. 2011;8:78.
20. Sushames A, Edwards A, Thompson F, Mcdermott R, Gebel K. Validity and Reliability of Fitbit Flex for Step Count, Moderate to Vigorous Physical Activity and Activity Energy Expenditure. *PLoS ONE*. 2016;11(9).
21. Clemente FM, Nikolaidis PT, Martins FML, Mendes RS. Physical Activity Patterns in University Students: Do They Follow the Public Health Guidelines? *PLoS ONE*. 2016;11(3).
22. Haase A, Steptoe A, Sallis JE, Wardle J. Leisure-time physical activity in university students from 23 countries: Associations with health beliefs, risk awareness, and national economic development. *Prev Med*. 2004;39(1):182–190.
23. Villanueva K, Giles-Corti B, McCormack G. Achieving 10,000 steps: A comparison of public transport users and drivers in a university setting. *Prev Med*. 2008;47(3):338–341.
24. Sigmundova D, Zaccal J, Sigmund E. The level of influence of organised physical activity on meeting the healthy criterion of 10,000 steps daily: Application of regression and formal concept analysis. *Acta Universitatis Palackianae Olomu-censis Gymnica*. 2010;40(4):15–24.
25. Sigmundová D, Chmelík F, Sigmund E, Feltlová D, Frömel K. Physical activity in the lifestyle of Czech university students: Meeting health recommendations. *Eur J Sport Sci*. 2015;13(6).
26. Cilliers J, Seneka LM, Kunneke E. The association between the body mass index of first-year female university students and their weight-related perceptions and practices, psychological health, physical activity and other physical health indicators. *Pub Health Nutr*. 2006;9(2):234–243.
27. Welk G, Blair S. Physical activity protects against the health risk of obesity. Washington, DC. Presidents' Council on Physical Fitness and Sport Research Digest. 2000;3:12.
28. Jimenez-Pavon D, Kelly J, Reilly J. Associations between objectively measure habitual physical activity and adiposity in children and adolescents: Systematic review. *Int J Pediatr Obesity*. 2009;1:1.
29. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Medicine & Science in Sports & Exercise*. 2008;40:181–188.





## ORIGINAL PAPER

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# Diversification of results of orientating questionnaire of motoric and psycho-social development in regard to the level of educational maturity (school readiness) in prematurely born children

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## Abstract

**Introduction.** Currently, one of the most common problems in neonatology is the occurrence of distant consequences of prematurity. In infants, toddlers, and children with special problems, there can be disorders in psychomotor development and in growing, and later also intellectual and cognitive disorders. Pre-school and early-school age is particularly significant in the lives of prematurely born children. In this period, usually beside the stage of somatic growth, there is intensive physical and mental development and intellectual disorders may appear.

**Aim.** Assessment of preterm training in motor skills and psychosocial development

**Materials and methods.** The research group consisted of 61 prematurely born children aged 5-8. Perinatal interviews were collected and basic anthropometric measurements were performed.

**Results.** There is no statistical significance between questionnaire results in particular areas of development, summary, age, gender, subsequent pregnancies, number of fetuses, delivery term and the type of delivery.

**Conclusions.** The Apgar disinfectant scale differentiates the results of the indicative questionnaire on motor development research. The results of the study confirm the prognostic importance of the Apgar scale in terms of development.

**Keywords.** development of premature babies, orientation study, school readiness

## Introduction

Prematurity is defined as delivery before 37th week of gestation. Premature birth creates medical, social and family problems. A premature newborn requires intensive medical care and nursing. The effects of premature

delivery as well as all the circumstances surrounding such situations are felt for many years to come. Thirty percent of children born before the 29th week of pregnancy who survive present neurological disorders, learning difficulties as well as hearing and sight impairment.<sup>1</sup>

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 13.07.2018 | Accepted: 15.09.2018

Publication date: December 2018

The prevalence of prematurity in highly developed countries has been established at the rate between 5-10%. According to the most recent data, the rate of prematurity in Poland amounts to 6.3% while the number of premature children born with very low birth weight ranges from 3,500 to 4,000 annually. In the USA, the rate of prematurity is higher and amounts to about 11.5%.<sup>2</sup> Therefore for some time epidemiological prematurity trends observed in Poland seem to be similar to those in the USA and some European countries. The percentage of death rate of infants has been slightly decreasing while the newborns still constitute the largest group among them.<sup>3</sup>

In the available Polish and foreign literature, the prognostic value of Apgar scale values for motor and social development of premature babies is widely described.<sup>4</sup> The research results show that intensity of distant after-effects of prematurity such as: increased incidence, developmental disorders that are inversely proportional to gestational age and immaturity degree at birth. Premature children frequently require long lasting treatment. Therefore, Children's Coordinated Care Program has been recently introduced in our country and it covers the following: integrated neonatal care, multispecialized pediatric care according to individual needs and rehabilitation programs for children up to 3 years of age. Children diagnosed with severe retardation or incurable life-threatening disease acquired during perinatal period or at delivery qualifies for this program.<sup>5</sup>

## Aim

Determination of the following parameters: age, gender, occipito-frontal circumference, and elements of perinatal interview differentiate the results of orientating questionnaire of motoric and psycho-social development in regard to the level of educational maturity (school readiness) in prematurely born children.

## Material and method

The research group consisted of 61 prematurely born children aged 5-8. The group was functionally homogeneous – all children underwent one year long pre-school program. The large age gap happened due to earlier enrollment of some of children to the first grade as well as one year long postponed enrollment to compulsory education. ( $\bar{x}$ =6.38 years old,  $Me$ =6 lat,  $s$ =0.73). The group consisted of 29 (48%) boys and 32 (52%) girls.

The research was approved by Bioethics Committee of Medical Faculty of The University of Rzeszów (the first resolution 7/12/2012, the last one 6/2/2017). The research was conducted between 2015-2016 at the Physiotherapy Institute of The University of Rzeszów and the Laboratory of Innovative Anthropometric Methods in the Innovative Center of Medical and Natural Sciences of the University of Rzeszów..

The research was consistent with health balance sheets and conducted in accordance with generally accepted rules and standard proceedings included in health balance of children undergoing a one year long pre-school program. Perinatal interviews were collected and basic anthropometric measurements were performed. The technique of anthropometric measurements was based on international methods applied in anthropology. The following anthropometric features were measured: weight –  $w$ , height –  $h$ , occipito-frontal circumference –  $ofc$ , with the use of medical scale (kg), anthropometer (cm), anthropometric tape (cm). Proportion coefficient was calculated: Quetelet II weight – height ratio ( $kg/m^2$  WQ2, Body Mass Index, BMI).<sup>6,7</sup>

An orientating questionnaire of motoric and psycho-social development in regard to the level of educational maturity (school readiness) in prematurely born infants was conducted. Traditionally, orientation evaluation of motoric and psycho-social development conducted during health balance sheet in this age group is obtained on the base of data from interview, analyses of questionnaire filled up by the parents, conversations and child observation. Questionnaire was elaborated by M. Jaroszyńska- Szymczuk in accordance with J. L. Black: School readiness. Pediatric Basic, 1990, 55, 2, published in "Prophylactics in pediatrics", edited by Barbara Wojnarowska WL PZWL 1998, s. 301. The questionnaire is filled in by the parent. If the number of answers YES or cumulation of YES answers in some areas is predominating, the child should be referred to Psychological-Pedagogical Out-patient Clinic (Table 1). For the purpose of this paper, the scoring system was assigned to the questionnaire (Table 1).

The dependencies between age, gender, BMI, occipito-frontal circumference, and elements of perinatal interview differentiate the results of orientating questionnaire of motoric and psycho-social development in regard to the level of educational maturity (school readiness) were statistically analyzed. Mann-Whitney non parametric test was used to evaluate the differences in an average level of measurable characteristics in two populations while Anova Kruskal-Wallis not parametric test was used to evaluate the differences in an average level of measurable characteristics in more than two populations. The correlation of two variables not complying with normal distribution criterion was elaborated with Spearman rank-based correlation coefficients. The statistical significance was assumed to be  $p < 0.05$ .

Based on the perinatal interview, it was established that the children were born from pregnancies of various order (Table 2A), with different number of fetuses (Table 2B), premature (Table 2C), by C-section or by power of nature (Table 2D). The infants were delivered healthy with different birth weight (Table 2E, 2F).

Table 1. Questionnaire, scoring

Answer	YES	NO	Sometimes YES, sometimes NO
Interpretation of an answer	Adverse	Desirable	Intermediate
Scoring	0	1	0.5

Table 2. The characteristic of group of premature children ready to enroll school based on gathered data (part I)

Perinatal Interview		
A. Order of pregnancies	N	%
The first pregnancy	31	51
The second pregnancy	15	25
The third pregnancy	5	8
The fourth pregnancy	5	8
The fifth pregnancy	2	3
The sixth pregnancy	3	5
B. Number of fetuses	N	%
Single pregnancy	39	64
Twin pregnancy	13	21
Triplet pregnancy	9	15
C. Delivery time (weeks)	N	%
24	2	3
25	0	0
26	4	7
27	6	10
28	8	13
29	1	2
30	10	16
31	5	8
32	23	38
33	0	0
34	1	2
35	1	2
D. The way of delivery	N	%
By power of nature	10	16
C-section	51	84
E. Apgar scale evaluation [points]	N	%
0–3	9	15
4–7	39	64
8–10	13	21
F. Birth weight [g]	N	%
Under 750	3	5
750–1000	10	16
1000–1500	21	34
1500–2500	26	43
Over 2500	1	2

In the perinatal period, the researched, premature children were burdened by numerous and unfavorable perinatal events (Table 3A) and hearing impairment risk factors (Table 3B). The number of unfavorable perinatal events (Table 3A) and hearing impairment risk factors (Table 3B) were calculated. Statistical scores describing BMI (Table 3C), ocf (Table 3D) and results of motoric and psycho-social development with the use of

questionnaire (Table 3E) were calculated. On the basis of the six-year balance and the interview with parents of children born prematurely in the examined group, prevalence of chronic diseases in the population was found (recurrent respiratory infections, bronchial asthma, Mpdz, refractive error), congenital malformations in 26 people (inguinal hernia, survived arterial duct, lesion labia).

**Table 3.** The characteristic of group of premature children ready to enroll school based on gathered data (part II) and anthropometric parameters

Perinatal Interview					
<b>A. Combined number of unfavorable perinatal events (one event scores 1 point): respiratory failure, respiratory distress syndrome:</b> bronchopulmonary displasia, congenital pneumonia, pneumonia, pneumothorax, respiratotherapy, passive oxygen therapy, hyperbilirubinaemia, anemia, thrombocytopenia, leukopenia, bleeding from respiratory, gastrointestinal, tract/cardiac tamponade, Rhesus incapability in main groups, blood or blood derivative transfusion, exchange transfusion, hypoxic ischemic encephalopathy periventricular leukomalacia, intraventricular hemorrhage of I-IV degree, epilepsy, convulsions different than in epilepsy, apnea, retinopathy of prematurity, patent ductus arteriosus, TORCH infections, intrauterine infections, sepsis, purulent menangitis, encephalitis, bacterial infection of digestive system, urinary tract infection, necrotizing enterocolitis, gastro- esophageal reflux, hypoglycemic, hypocalcemia, osteopenia of prematurity, intravenous administration of drugs, parenteral feeding, enteral feeding, procedure in general anesthesia.					
$\bar{x}$	Me	Min	Max	s	
11.93	12.00	0	26	5.75	
<b>B. Total number of fulfilled criterions of increased risk of hearing impairment (1 criterion scores 1 point):</b> hearing impairment running in the family, virus illnesses (measles, cytomegaly, toxoplasmosis, influenza) past by mothers in the first half of pregnancy, ear, neck and head abnormalities, high level of bilirubin in newborn >20mg% (with body weight 2500g) and over 15 % mg% with body weight under 2500 g., transfusion, small body weight (<1500 g.), bacterial meningitis, 0-3 Apgar points in the first 5 minutes, 0-6 Apgar points in 10 minutes, lack of spontaneous breath for 10 minutes or hypotension in the first two hours, cardio-respiratory failure (mechanical ventilation longer than 10 days), ototoxic medicine (aminoglycosides, duretics), the features of genetic syndrome that can coexist with sensorineural or conductive hearing loss.					
$\bar{x}$	Me	Min	Max	s	
2.09	2.00	0	5	1.39	
<b>A. Body Mass Index BMI [kg/m²]</b>					
$\bar{x}$	Me	Min	Max	S	
15.36	15.26	10.46	27.80	2.43	
<b>B. Occipito-frontal circumference ofc [cm]</b>					
$\bar{x}$	Me	Min	Max	sS	
51.59	51.50	42.00	58.50	2.72	
<b>C. Questionnaire result. scoring</b>					
Child functioning (Number of questions)	$\bar{x}$	Me	s	Min	Max
Big motorics (4)	3.24	3.50	0.92	0.00	4.00
Small motorics (3)	2.39	2.50	0.70	0.50	3.00
Hand – eye coordination (3)	2.77	3.00	0.56	1.00	3.00
Speech (6)	4.67	5.00	1.38	1.00	6.00
Spatial orientation. awareness of own body (1)	0.92	1.00	0.23	0.00	1.00
Memory(3)	2.19	2.00	0.78	0.00	3.00
Attention. activity (4)	1.86	2.00	1.17	0.00	4.00
Emotional – social maturity (4)	2.77	3.00	1.01	0.50	4.00
Summary (28)	20.80	20.50	4.20	9.50	28.00

There is not statistical significance between questionnaire results in particular areas of development, summary, and age (Table 4A), gender (Table 4B), subsequent pregnancies (Table 4C), number of fetuses (Table 4D), delivery term (Table 4E), the way of delivery (Table 5A), the sum of unfavorable events during perinatal period (Table 5D), the sum of fulfilled criterions of increased risk of hearing impairment (table 5E), BMI (Table 6A) and ofc (Table 6B).

There is statistical significance between postnatal Apgar scale evaluation and summary determined with the use of questionnaire (p=0.013), results in the follow-

ing areas: big motorics (p=0.009), hand-eye coordination (p=0.004), memory (p=0.014) (Table 5). There was not statistical significance between remaining areas and postnatal Apgar scale evaluation. The statistical significance was obtained only in relation between birth weight and hand-eye coordination (p=0.039) (Table 5C). The lower Apgar scale evaluation gave lower results in areas of big motorics (p=0.009) (Table 6D), memory (p=0.014) (Table 7B) and summary (p=0.013) (Table 7C). In all those cases the difference between children born with ill health (Apgar 0-3 points), medium (Apgar 4-6 points) and good health (Apgar 8-10 points) is

Table 4. Statistical analysis of results

A. Questionnaire results versus age (with Spearman rank-based correlation coefficients)	R Spearman	p
Big motorics	0.11	0.381
Small motorics	0.08	0.535
Hand-eye orientation	0.14	0.277
Speech	0.22	0.087
Spatial orientation, awareness of own body	0.08	0.517
Memory	0.18	0.173
Attention, activity	0.16	0.206
Emotional-social maturity	0.10	0.466
Summary	0.23	0.072
B. Questionnaire results versus gender (Mann-Whitney test)	Z	
Big motorics	0.09	0.928
Small motorics	0.98	0.327
Hand-eye orientation	0.53	0.59
Speech	0.43	0.664
Spatial orientation, awareness of own body	-1.39	0.164
Memory	0.11	0.911
Attention, activity	0.89	0.374
Emotional-social maturity	-0.87	0.383
Summary	0.43	0.670
C. Questionnaire results versus order of subsequent pregnancies (with Spearman rank-based correlation coefficients)	R Spearman	p
Big motorics	0.04	0.755
Small motorics	-0.21	0.111
Hand – eye coordination	-0.00	0.99
Speech	-0.06	0.672
Spatial orientation, awareness of own body	-0.02	0.896
Memory	0.18	0.157
Attention, activity	-0.01	0.912
Emotional – social maturity	-0.04	0.777
Summary	0.02	0.885
D. Questionnaire results versus number of fetuses (with Spearman rank-based correlation coefficients)	R Spearman	p
Big motorics	-0.04	0.767
Small motorics	0.15	0.243
Hand-eye coordination	-0.17	0.191
Speech	-0.15	0.257
Spatial orientation, awareness of own body	-0.10	0.457
Memory	-0.11	0.399
Attention, activity	-0.11	0.421
Emotional-social maturity	-0.11	0.406
Summary	-0.09	0.477
E. Questionnaire results versus term of delivery (with Spearman rank-based correlation coefficients)	R Spearman	p
Big motorics	-0.04	0.759
Small motorics	-0.10	0.456
Hand-eye coordination	0.00	0.990
Speech	-0.20	0.127
Spatial orientation, awareness of own body	-0.14	0.300
Memory	-0.60	0.627
Attention, activity	-0.04	0.757
Emotional-social maturity	-0.16	0.226
Summary	-0.13	0.320

Table 5. Statistical analysis of results

A. Questionnaire results versus the way of delivery (Mann-Whitney test)	U	p
Big motorics	221.5	0.520
Small motorics	199.0	0.284
Hand-eye coordination	246.5	0.870
Speech	240.0	0.781
Spatial orientation, awareness of own body	206.5	0.350
Memory	207.0	0.360
Attention, activity	222.0	0.532
Emotional – social maturity	250.0	0.931
Summary	253.5	0.977
B. Questionnaire result versus postnatal Apgar scale evaluation (Kruskal-Wallis test)	H	p
Big motorics	9.240	0.009
Small motorics	1.091	0.579
Hand-eye coordination	11.022	0.004
Speech	1.687	0.401
Spatial orientation, awareness of own body	3.913	0.141
Memory	8.474	0.014
Attention, activity	5.343	0.069
Emotional-social maturity	0.002	0.998
Summary	8.610	0.013
C. Questionnaire results versus birth weight (Kruskal-Wallis test)	H	p
Big motorics	0.494	0.920
Small motorics	2.727	0.435
Hand-eye coordination	8.358	0.039
Speech	1.641	0.650
Spatial orientation, awareness of own body	2.625	0.453
Memory	0.710	0.870
Attention, activity	3.083	0.378
Emotional-social maturity	2.338	0.505
Summary	2.512	0.473
D. Questionnaire results versus combined number of unfavorable events in perinatal period (with Spearman rank-based correlation coefficients)	R Spearman	p
Big motorics	0.03	0.795
Small motorics	-0.01	0.940
Hand-eye coordination	-0.22	0.093
Speech	0.09	0.485
Spatial orientation, awareness of own body	0.04	0.766
Memory	0.03	0.836
Attention, activity	-0.09	0.473
Emotional-social maturity	0.13	0.319
Summary	-0.00	0.978
E. Questionnaire results versus the sum of fulfilled criterions of increased risk of hearing impairment (with Spearman rank-based correlation coefficients)	R Spearman	p
Big motorics	-0.12	0.337
Small motorics	-0.17	0.191
Hand-eye coordination	-0.24	0.063
Speech	0.04	0.768
Spatial orientation, awareness of own body	-0.12	0.375
Memory	-0.09	0.500
Attention, activity	-0.18	0.176
Emotional-social maturity	-0.10	0.441
Summary	-0.19	0.147

Table 6. Statistical analysis of results

A. Questionnaire results versus BMI (with Spearman rank-based correlation coefficients)					R Spearman	p	
Big motorics					-0.19	0.133	
Small motorics					-0.04	0.771	
Hand-eye orientation					-0.02	0.873	
Speech					-0.17	0.192	
Spatial orientation, awareness of own body					-0.06	0.663	
Memory					-0.20	0.126	
Attention, activity					-0.16	0.225	
Emotional-social maturity					-0.05	0.681	
Summary					-0.20	0.121	
B. Questionnaire results versus ocf (with Spearman rank-based correlation coefficients)					R Spearman	p	
Big motorics					0.052	0.685	
Small motorics					-0.102	0.429	
Hand-eye coordination					0.146	0.261	
Speech					0.054	0.678	
Spatial orientation, awareness of own body					0.056	0.663	
Memory					0.199	0.123	
Attention, activity					0.213	0.098	
Emotional-social maturity					0.007	0.955	
Summary					0.141	0.279	
C. Hand-eye coordination versus birth weight							
Variable	Birth weight [g]	N	$\bar{x}$	Me	Min	Max	s
Hand-eye coordination [points]	...-750	3	2.00	2,00	1,00	3,00	1,15
	751-1000	10	3.00	3,00	3,00	3,00	0,00
	1001-1500	21	2.62	3,00	1,00	3,00	0,76
	1501- ...	27	2.89	3,00	2,00	3,00	0,29
Dependent variable: hand-eye coordination [points]	Value of bilateral comparison (Kruskal -Wallis test) H=8.358. p=0.039)						
	Independent variable: birth weight [g]						
	....-750	751-1000		1001-1500		1501.....	
	R: 15.333	R: 36.500		R: 28.881		R: 32,352	
.....-750	0.421		1.000		0,691		
751-1000	0.421		1.000		1,000		
1001-1500	1.000		1.000		1,000		
1501.....	0.691		1.000				
D. Big motorics versus Apgar scale postnatal evaluation							
Variable	Apgar scale postnatal evaluation	N	$\bar{x}$	Me	Min	Max	s
Big motorics [points]	0-3 points	9	2.44	2,00	1,00	3,50	0,88
	4-7 points	39	3.37	3,50	0,00	4,00	0,86
	8-10 points	13	3.38	4,00	2,00	4,00	0,89
Dependant variable: big motorics [points]	Value of bilateral comparison (Kruskal-Wallis test) H= 9.240. p= 0.009						
	Independent variable: Apgar scale postnatal evaluation [points]						
	0-3		4-7		8-10		
	R: 15.278		R: 33.256		R: 35.115		
0-3			0.019		0.030		
4-7	0.019				1.000		
8-10	0.030		1.000				

Table 7. Statistical analysis of results

A. Hand-eye coordination versus postnatal Apgar scale evaluation							
Variable	Apgar scale postnatal evaluation	N	$\bar{x}$	Me	Min	Max	s
Hand – eye coordination [points]	0–3 points	9	2.17	2,00	1,00	3,00	0,87
	4–7 points	39	2.40	3,00	1,00	3,00	0,37
	8–10 points	13	2.85	3,00	1,00	3,00	0,55
Dependent variable: Hand – eye coordination [points]	Value of bilateral comparison (Kruskal-Wallis test) H= 11.022. p=0.004)						
	Independent variable: postnatal Apgar scale evaluation [points]						
	0–3	4–7		8–10			
	R: 18.889		R: 32.833		R: 33.885		
	0–3	0.101		0.154			
4–7	0.101		1.000				
8–10	0.154		1.000				
B. Memory versus postnatal Apgar scale evaluation							
Variable	Apgar scale postnatal evaluation	N	$\bar{x}$	Me	Min	Max	s
Memory [points]	0–3 points	9	1.61	1,50	1,00	2,50	0,49
	4–7 points	39	2.24	2,50	0,50	3,00	0,76
	8–10 points	13	2.42	2,50	0,00	3,00	0,84
Dependent variable: Memory [points]	Value of bilateral comparison (Kruskal-Wallis test) H=8.474. p=0.014)						
	Independent variable: postnatal Apgar scale evaluation [points]						
	0–3	4–7		8–10			
	R: 16.444		R: 32.205		R: 37.462		
	0–3	0.049		0.019			
4–7	0.049		1.000				
8–10	0.019		1.000				
C. Summary result versus postnatal Apgar scale evaluation							
Variable	Apgar scale postnatal evaluation	N	$\bar{x}$	Me	Min	Max	s
Summary result [points]	0–3 points	9	17.56	17,50	13,00	23,00	2,90
	4–7 points	39	21.09	21,50	9,50	25,00	4,25
	8–10 points	13	22.19	20,50	17,50	27,00	3,89
Dependant variable: Summary result [points]	Value of bilateral comparison (Kruskal-Wallis test) H=8.610. p=0.013)						
	Independent variable: postnatal Apgar scale evaluation [points]						
	0–3	4–7		8–10			
	R: 15.444		R: 32.705		R: 36.654		
	0–3	0.026		0.018			
4–7	0.026		1.000				
8–10	0.018		1.000				

especially noticeable Such differences were not noticed between postnatal Apgar scale evaluation, birth weight and area of hand-eye coordination (Table 7A, table 6C).

Discussion

Children born prematurely are not considered homogeneous group due to various factors such as birth weight of gestation time. Serious neuro-developmental disorders as severe as OUN ones are not frequent, however further development of children prematurely born depends on mutual relation between the immaturity level, existing complications and neurological malfunctions (broncho-pulmonary dysplasia, retinopathy of prematurity, intra-ventricular hemorrhage, periventricular leukomalacia) as well as environmental and socio-economic factors.<sup>8</sup>

In the light of above, it can be concluded that premature children are more prone to disorders in proper functioning and development. Those disorders can affect both psychical and physical child’s development and they can produce the disorders of various degree: from almost unnoticeable to very recognizable ones.<sup>9</sup> Izabela Marczykowska and Wioletta Koczaja-Styka in their paper described risk factors and consequences of prematurity.<sup>10</sup> The results of multiannual observations of extremely immature newborns published by world neonatological centers show the significance of long-term observation of this group of patients.<sup>11</sup>

The motoric and psycho-social development in regard to school readiness in 61 premature children aged 5-8 was evaluated in presented own research. Statisti-



cal significance was obtained between postnatal Apgar scale evaluation and summary with the use of questionnaire in the range of the following areas: big motorics, hand-eye coordination, memory. The lower Apgar scale evaluation, the lower result in big motorics ( $p=0.013$ ) (Table 7C). There are many publications concerning school readiness of premature children in various areas. Lina Brostrom et al. conducted the evaluation of 80 premature children, age 6, not diagnosed with Cerebral Palsy. In order to perform movement evaluation the authors used simplified version of neurological examination Touwen Infant Neurological Examination as well as Movement Assessment Battery for Children Second Edition (MABC-2), Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV), the Strengths and Difficulties Questionnaire (SDQ) and Five to Fifteen Questionnaire. After the analyses of the results, the researchers concluded that despite absence of Cerebral Palsy, premature children are prone to small neurological disorders that can disrupt motorics, cognitive abilities and behavior.<sup>12</sup>

Hsu CT et al. evaluated the correlation between the birth weight and psycho-motoric development of premature children in Taiwan. The authors researched 1791 premature children born 2007-2011 with birth weight under 1500g. To evaluate psycho-development they applied Bayley Scales of Infant Development-II (BSID-II) while the rest of data such as weight, occipito-frontal circumference, gender, co-existing illnesses were derived from medical documentation. The research proved the relation between lower birth weight corrected in age of 6, 12 and 24 months and low neuro-developmental results. What in turns, confirms the influence of unfavorable factors that can disrupt and affect motoric and psycho-social development of premature children.<sup>13</sup>

Multiplicity of complications due to prematurity has to be considered the major negative factor. The most frequent are: Cerebral Palsy, sight, hearing and speech disorders, mental retardation, retinopathy of prematurity (Tab 3A) which significantly influence further motoric and psycho-social development of a child.<sup>14</sup> Personal questionnaire (Table 3A) confirmed ballast of unfavorable perinatal events and risk of hearing loss (Table AB). Ream MA et al. observed 145 premature children beginning the compulsory education and compared them with their full-term peers. The authors describe consequences and after-effects of premature delivery emphasizing the occurrence of neurological disorders in premature children and their correlation with later cognitive and social ones.<sup>15</sup>

Our research confirms statistical significance between big motorics, memory, summary and postnatal Apgar scale evaluation as well as between birth weight and hand-eye coordination. The lower the Apgar scale evaluation, the lower result in above mentioned ar-

eas. This relation confirms the relevance of both Apgar scale and birth weight in the context of course and psycho-somatic development in researched group of children. Oudgenoeg-Paz O. et al. widely analyzed literature about prematurity influence, low birth weight on the level of motorics and cognitively in premature children. The conclusions confirm the significance of level of motoric development in the first year of life and later cognitive abilities in premature children with low birth weight.<sup>16</sup>

Magdalena Chrzan-Dętkoś and Marta Bogdanowicz researched 99 premature pre-school children, hospitalized after birth in ICU in two Gdańsk hospitals in order to evaluate their psycho-kinetic development. The children were delivered in 32 week (in average), an average birth weight was 1776 g., an average Apgar scale evaluation – 5,56 points. The authors used Columbia Mental Maturity Scale, chosen sub-test of Terman-Marrill Scale. To evaluate cognitive development they applied Orientative DSM Scaled for Girls and BOYD elaborated on the base of CBCL 1,5-5 Questionnaire. The results indicate bigger cognitive and emotional difficulties of premature children. Those difficulties were especially noticeable in children born before 32nd week of pregnancy, with very small birth weight (1500g.).<sup>17</sup> This research can be also useful in assessment of school readiness.

Perez-Rochet et al. performed the analyses of premature children in regard to school maturity. They researched children with low birth weight and subsequently assessed their abilities to learn at school. They conducted the full ophthalmological examination and used standard visual test of perceptive abilities as well as visual abilities test. The parents filled the questionnaire concerning the learning results of children. The authors observed that visual deficiencies and motoric disorders create significant difficulties in early school learning process of math and reading for premature children.<sup>18</sup>

Hand-eye coordination enables children to perform activities requiring the simultaneous usage of hand and eye. Such coordination is necessary to perform various activities such as: writing, drawing, physical exercises. In pre-school and early school children the disorders in this area are shown by small precision of movements and difficulties with performing simple orders. Bayley Motor Scale, Peabody Development Motor Scale, Griffiths Mental Development Scales are used in pediatrics to evaluate this coordination.<sup>19</sup>

Premature, pre-school children with low birth weight show the disorders in hand-eye coordination, what was confirmed in our research (Table 6C) by analyses of questionnaire and research results (Table 3E).

Surka et al. evaluated and compared full-term peers with Cerebral Palsy children with spastic hemiplegia of

prematurity in regard to hand-eye coordination. The research was conducted by reaching and garbing some object setup in one position and then placing it in proper place and proper position. Visual reactions were recorded with the use of device following eyes mounted on the head of the patient while movements of shoulders with the help of movement recorder (120Hz). The researchers noticed the delayed time of perception during planning phase and movement performance in regard to control group. Cerebral Palsy children had higher frequency of eyeball movement, longer reaction time (RT and movement time (MT)). In spite of the fact that the researched group consisted of Cerebral Palsy children with spastic hemiplegia of prematurity, it does not negatively influence the hereby discussion, as it is well known that those children can attend regular school. The authors, however, emphasize the role of therapy focusing on an improvement of hand-eye coordination, as it can increase their motoric efficiency.<sup>20,21</sup>

Ribeiro CD et al. observed and described hand-eye coordination disorders in premature children aged 1-3 with low birth weight and low Apgar scale evaluation. The authors applied own protocol with socio-economical classification and Denver Developmental Screening Test (DDST-II). There was significant correlation between prematurity, low Apgar scale, birth weight and adaptive and social opportunities, which were considerably lowered.<sup>22</sup>

Results and observations described above derived from own research and researches done by other authors confirm the necessity to conduct screening tests of premature, pre-school children to conduct early diagnosis and compensate developmental disorders what will make school preparation process better and more efficient.

## Conclusions

1. The results of the questionnaire on the indicative study of motor and psychosocial development in terms of school readiness are differentiated by the post-natal Apgar score (in the areas of child's functioning – high motor skills, visual-motor coordination, memory and total score), as well as birth weight (in terms of eye-and-eye coordination).
2. The results of the study confirm the prognostic importance of the Apgar scale as to the psychomotor development in the examined group of children.

## References

1. Obłozą B, Raba G, Fudali-Walczak M. Organisation and financing of preterm baby care system. *Prz Med Uniw Rzeszow Inst Leków*. 2015;13(3):279–289.
2. Dytrych G. Analysis of motor development of premature born children with low body weight rehabilitated with the Vojta method. *Neurol Dziec*. 2009;5:41–48.
3. Borszewska-Kornacka MK. Kompendium wiedzy o wcześniaku. Comprehensive review of prematurity. *Stand Med/Pediatrics*. 2013;10:597–611.
4. Bagnowska K. Factors affecting the efficacy of rehabilitation NDT-Bobath children born prematurely. *Nowa Pediatra*. 2014;2:63–71.
5. Durlak W, Klimek M, Kwinta P. Regional lung ventilation pattern in preschool children with bronchopulmonary dysplasia is modified by bronchodilator response. *Pediatr Pulmonol*. 2017; 52(3):353–359.
6. Radgowski W. Opieka okołoporodowa na oddziałach położniczych - świadczenia standardów świadczeń zdrowotnych. *Kontrola Państwowa*. 2017;62:50–66.
7. Oblacińska A, Jodkowska M. ABC badań bilansowych w pediatrii. Bilans zdrowia dzieci w wieku 5 lat oraz dzieci objętych rocznym obowiązkowym przygotowaniem przedszkolnym. *Med Prakt Pediatr*. 2014;6:92–102.
8. Woynarowska B. *Profilaktyka w pediatrii*. Warszawa:P-ZWL;1998.
9. Klimek M, Nitecka M, Dutkowska G, Gilarska M, Kwinta P. Temperament traits in 4-year-old children born prematurely – may they suggest a threat for mental functioning. *Psychiatr Pol*. 2018;52(2): 371–386.
10. Twilhaar ES, Wade RM, de Kieviet JF, van Goudoever JB, van Elburg RM, Oosterlaan J. Cognitive Outcomes of Children Born Extremely or Very Preterm Since the 1990s and Associated Risk Factors A Meta-analysis and Meta-regression. *JAMA Pediatr*. 2018;172(4):361–367.
11. Marczykowska I, Koczaja-Styka W. *Opóźniony rozwój mowy na tle skrajnego wcześniactwa – studium przypadku*. Rzeszów: Wydawnictwo Uniwersytetu Rzeszowskiego, Głos – Język – Komunikacja; 2017;4:164–181.
12. Maggi EF, Magalhães LC, Campos AF, Bouzada MC. Preterm children have unfavorable motor, cognitive, and functional performance when compared to term children of preschool age. *J Pediatr (Rio J)*. 2014; 90(4):377–383.
13. Broström L, Vollmer B, Bolk J, Eklöf E, Ådén U. Minor neurological dysfunction and associations with motor function, general cognitive abilities, and behaviour in children born extremely preterm. *Dev Med Child Neurol*. 2018; 60(8):826–832.
14. Hsu CT, Chen CH, Lin MC, Wang TM, Hsu YC. Correction: Post discharge body weight and neurodevelopmental outcomes among very low birth weight infants in Taiwan: A nationwide cohort study. *PLoS One* 2018; 13(5): e0198310.
15. Ferreira RC, Mello RR, Silva KS. Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. *J Pediatr (Rio J)*. 2014; 90(3):293–299.
16. Ream MA, Lehwald L. Neurologic Consequences of Preterm Birth. *Curr Neurol Neurosci Rep*. 2018;16,18(8):48.
17. Oudgenoeg-Paz O, Mulder H, Jongmans MJ, van der Ham IJM, van der Stigchel S. The link between motor and cognitive development in children born preterm and/or with

- low birth weight: A review of current evidence. *Neurosci Biobehav Rev.* 2017;80: 382-393.
18. Chrzan-Dętkoś M. Bogdanowicz M. Cognitive and emotional development of preterm children in kindergarten age. *Pediatr Pol.* 2009;11(1),84 (6):517-523.
19. Perez-Roche T, Altemir I, Giménez G, et al. Effect of prematurity and low birth weight in visual abilities and school performance. *Res Dev Disabil.* 2016;59:451-457.
20. Kostiukow A. Malak R. Rostkowska E. Samborski Wł. Motor coordination tests as a diagnostic tool in number of diseases. *Horyzonty współczesnej fizjoterapii.* Poznań: Wyd. WSEiT; 2016:17-28.
21. Surkar SM, Hoffman RM, Davies B, Harbourne R, Kurz MJ. Impaired anticipatory vision and visuomotor coordination affects action planning and execution in children with hemiplegic cerebral palsy. *Res Dev Disabil.* 2018; 80:64-73.
22. Ribeiro CD, Pachelli MR, Amaral NC, Lamônica DA. Development skills of children born premature with low and very low birth weight. *Codas.* 2017; 30,29(1).



## ORIGINAL PAPER

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# Physical activity in postmenopausal women

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### Abstract

**Introduction.** Menopause is the time when the female body goes through substantial endocrine changes resultant from the gradual phasing out of the reproductive activity of the ovaries. Consequently, post-menopausal women face some perimenopausal symptoms. These symptoms affect everyday physical and psychological functioning to various extent, and result in certain limitations.

**Aim.** The aim of this paper was to study which limitations are most difficult for postmenopausal women, and how menopause symptoms affect women's physical activity and satisfaction with life, as these are important components of quality of life.

**Materials and methods.** The study involved 60 postmenopausal women. We used our own questionnaire.

**Results.** We did not find the remaining relationships enumerated in research questions: the impact of menopausal syndromes on the frequency of physical activity, on its intensity, and on satisfaction with life, nor with the impact of subjective health on intensity of physical effort.

**Conclusions.** We confirmed the relationship between intensity of physical effort and satisfaction with life and the relationship between subjective assessment of one's health and the frequency of physical activity.

**Keywords.** menopause, postmenopause, physical activity

### Introduction

The World Health Organization (WHO) defines menopause as a particular moment in a woman's life when she experiences her last menstrual bleeding, after which there is no menstruation for 12 consecutive months and there are no pathological reasons for this state.<sup>1</sup> Therefore, menopause is a permanent end of the menstrual cycle resulting from the ceased activity of the gonads. It is

a natural process in women between their reproductive age, when they are capable of conceiving, and entering older age. The menopause usually happens between the 40<sup>th</sup> and 60<sup>th</sup> year of age, while the mean age for women for their last menstrual bleeding is 50 years for Poland.<sup>2</sup>

In contrast to *physical activity*, a notion whose essential meaning is the sheer movement done when working, training or other physical effort, the *physical*

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 13.07.2018 | Accepted: 23.09.2018

Publication date: December 2018

*ability* denotes a set of attributes of the functioning of one's body which a person undertaking physical activity wished to gain. Physical ability is therefore an aim in the sphere of physical functioning of the body, and physical activity is the means to achieve this aim. In menopause and its postmenopausal consequences it is the physical ability aimed at good health that is essential.<sup>3</sup>

For women undergoing menopause or those who have just undergone it, the physical activity is a particularly essential and effective way to limit the consequences of the climacterium. Doing physical activity prevents diseases in healthy individuals and helps fighting syndromes in patients who have clinical symptoms of illnesses. Systematic physical activity in the form of exercise, sportive activities, cycling, mountain hikes or amateur sport has positive impact on body function, and decreases the risk of developing chronic illnesses.<sup>4,5</sup> In contrast, hypokinesia (decreased bodily movement) results in decreased physical function and physical ability, consequently influencing general health and quality of life.

The aim of the study was to assess physical activity in postmenopausal women through determining the frequency, intensity and forms of physical activity in the studied female population, and to determine the relationship between subjective physical and psychological wellbeing and the model of physical activity they had. The aim of the study was also to determine the relationship between the degree of physical activity and positive subjective quality of life in postmenopausal women.

**Material and method**

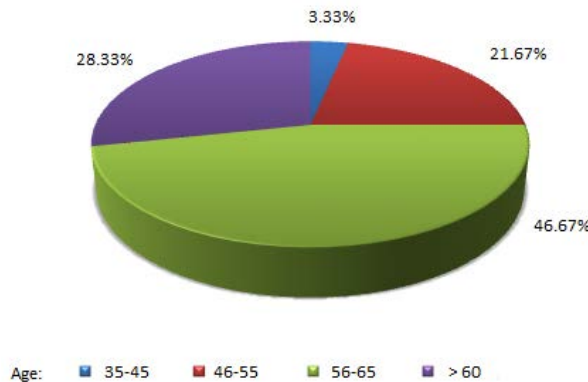
In June 2018, we conducted anonymous survey in the Health Resort Wysowa ("Uzdrowisko Wysowa"). We asked women who were spending their holidays in the resort to fill out our questionnaire. Each of the subjects expressed informed consent to participate in the study and was informed on the course of the study and on the way to fill out the questionnaire.

**The study population**

The study involved 94 women going through various stages of the menopause. For technical and politeness reasons, we had not been able to conduct a preliminary identification of the women at the resort and to choose the postmenopausal women only. Therefore, we handed out the questionnaires to all the women. The questionnaire was constructed in a way to enable all respondents to complete it, regardless of which the stage of the menopause they were at, or whether they were before the menopause. The basic information about the age of holidaymakers had revealed that many of them might have been in the postmenopausal age. We received 95 completed questionnaires, and we had to reject one as answers to some questions were missing. Finally, we obtained 60 questionnaire from postmenopausal women,

20 questionnaires from perimenopausal women, and 14 from women whose menopausal changes had not started yet. Because of the subject of the study and the research questions, for the purpose of further analysis we qualified only the 60 questionnaires from postmenopausal women.

Figure 1 presents the age of the postmenopausal females divided into categories.



**Fig. 1.** Age of the postmenopausal females divided into categories

None of the respondents was younger than 35 years, so Figure 1 does not provide for this age group. Most of the respondents – almost half of the group (46.67%) were women aged 56–65 years. The group of the oldest respondents, 65 years or older, was significantly smaller (28.33%). Approximately every fifth respondent was 46–55 years old. The age of only two (3.3%) of postmenopausal respondents was between 35–45 years. The scarce number of youngest respondents is understandable, as the prevalence of menopausal changes and lack of menstruation is usually insignificant in women younger than 46 years.

The literature divides the time since the first menopausal syndromes until the moment menstrual periods stop permanently into two stages: the early stage, which starts at approximately 42 years of age, and the later stage, beginning approximately at 46 years of age, at which point the likelihood of the ovaries permanently ceasing their function and the permanent stop of menstrual periods increases significantly, thus marking a woman's reaching the postmenopausal age.<sup>6</sup> The answers to questions on respondents' age reflected the age limit of 46 years defined in the literature: the group of youngest respondents aged 35–46 years was the smallest (3.33%), while in the age group that followed, with subjects aged 46–55 years, the number of post-menopausal respondents rose significantly (to the level of 21.56%).

**Methods**

We used the diagnostic survey method. The research tool was a questionnaire, comprising of 16 questions.

There were 10 closed-ended questions and 6 semi-open-ended questions, where the respondents could provide their own answers. The semi-open-ended questions allowed for an unlimited choice of multiple responses, while in the closed-ended questions respondents were asked to choose one response only. In four questions, the respondents were asked to choose the degree of intensity of a phenomenon. Here, we used a five point scale: 1 – meant the lowest intensity, 2 – moderate intensity, 3 – average intensity, 4 – high intensity, and 5 – highest intensity.

The questionnaire contained basic questions on respondents' age and the phase of the climacterium. We used the obtained information to draft the characteristics of the study population. The following questions concerned the current subjective physical and psychological wellbeing, health, the symptoms of menopausal change and their severity. The respondents were also asked to provide information on how often and how intensively they did physical activity, to assess results of physical activity, and define the reasons why they started physical activity or increased its intensity. The questionnaire concluded with the question on subjective quality of life.

### Statistical analysis

We calculated the Pearson correlation coefficient to determine correlation strength between studied variables, presented in the research questions of this study. Correlation strength was determined according to the following classification:

#### Strength of relationship

under 0.2 – very weak correlation (practically no relationship)

0.2–0.4 – weak correlation (visible relationship)

0.4–0.6 – moderate correlation (significant relationship)

0.6–0.8 – strong correlation (strong relationship)

0.8–0.9 – very strong correlation (very strong relationship)

0.9–1 – practically full relationship

For our calculations of correlation coefficient for individual variables we used responses the subjects provided to our questions from the survey. All the questions involved answers given on a scale. We designed a system of points for the scale. Four of the questions involved a five-point scale, so we designed an identical system of points from 1 to 5, convergent with the individual points on the scale: the number “1” corresponded to the lowest value of the variable, while the number “5” corresponded to the highest value of the variable. For the fifth variable, we designed a reversed four-point scale from 1 to 4, where 1 was given to the highest negative value given to the question, while 4 was given to the

answer on the opposite range of the scale. To calculate individual variables, we used answers for the following questions:

1. the variable of “satisfaction with life” - answers to question no. 16. The question was “How would you assess your satisfaction with life on scale from 1 to 5? 1 denotes poor satisfaction, and 5 denotes great satisfaction”. Points from 1 to 5 corresponded with values on the scale, and the greatest number of points was given to the greatest intensity of the phenomenon presented in the question.
2. the variable “frequency of physical activity” – answer to question no. 7. The question was “How on the scale from 1 to 5 would you best describe the frequency of your physical activity (understood as exercise, sport, cycling etc.)? 1 denotes rare activity, and 5 denotes very frequent activity”. The greatest number of points was given to the greatest intensity of the phenomenon presented in the question.
3. the variable “intensity of physical effort” – we used answers to question no. 9. The question was: “How on the scale from 1 to 5 would you describe the intensity of effort you put into your total physical activity? 1 denotes little effort, and 5 denotes very intensive effort”. Points from 1 to 5 corresponded with values on the scale, and the greatest number of points was given to the greatest intensity of the phenomenon presented in the question.
4. the variable “assessment of health” – we used answers to question no. 6. The question was “How on the scale from 1 to 5 would you describe your current health? 1 denotes poor health and frequent infections, and 5 denotes lack of chronic health problems and only rare infections?” Points from 1 to 5 corresponded with values on the scale, and the greatest number of points was given to the greatest intensity of the phenomenon presented in the question.
5. the variable “severity of menopausal syndromes” – we used answers to question no. 4 (it concerned the severity of menopausal symptoms enumerated in question no.3): “How severe are the syndromes enumerated in point 3?”. For answers to this question we created a scale from 1 to 4, where, in contrast to the other variables, the greatest number of points was given to the answer which corresponded with the slightest intensity of the phenomenon. This is why the values of this variable are inversely proportional in relation to the remaining variables.

### Results

A significant proportion of the studied women believed that the easiest and the least straining form of physical activity was a walk in the fresh air. Many respondents also did exercise of higher intensity: half of the respon-

dents reported regular cycling, and a quarter reported doing Nordic Walking, a more intense walk or march with sticks held in hands. Intense physical activity or activity that required physical endurance were less popular among our respondents: 16.67% respondents chose swimming, and 13.33% chose mountain hiking. Less than 10% respondents chose physical activities which involved the whole body or which required significant energy loss: aerobics (6.67%), pilates (6.67%), yoga (1.6%) and running (3.33%). Only one person's physical activity had the form of engaging in sports disciplines (1.67% of the study population) - here, the discipline was skiing. None of the respondents went to fitness classes. Every tenth respondent chose the answer "other" in the questionnaire, and provided the information on the type of physical activity: three respondents (5% of the total study population) did spine exercise (one on the cervical spine, two others the "healthy spine" set), one respondent mentioned gardening, another mentioned exercise with sports equipment, and one mentioned skiing.

Most of our respondents did physical activity with moderate frequency - this corresponded with "3" on the answer scale (almost 40% of women). The second largest group did physical activity rarely (20%). 30% of respondents chose frequent and very frequent physical activity (15% in each group). Very frequent, frequent and moderate activity was reported by a total of 70% respondents. Almost 14% of respondents described their physical activity as occasional.

Most of the women chose physical activity of medium and moderate intensity of effort: 35% and 26.67% of answers in these two categories, respectively. 8% women chose low intensity. Intensity of the three lowest categories (points 1 to 3) was declared by a total of 70% respondents, a significant proportion in comparison to the remaining group. Everyday activity of high or very high intensity effort was reported by 23.33% and 6.67% of respondents, respectively.

Almost 37% of respondents admitted they were did not do physical activity regularly. Their physical activity therefore has to be considered to be incidental and unsystematic. Every third respondent reported always having been involved in some activity. Every fifth respondent (20%) started regular physical activity shortly before menopause, as an element of preparation for a time of violent hormonal changes. Only 8.33% respondents chose the stop of menstrual periods as the starting time for doing physical activity. 6.67% respondents started systematic physical activity during menopause.

For the significant majority of respondents (85%) menopausal changes or their effects were not the reason for beginning physical activity. Only 15% respondents reported that their decision to start physical activity was directly related to the necessity of preparing their bod-

ies for the hormonal distortions of the menopause or to the necessity to decrease the severity of menopausal syndromes.

For the majority of respondents, menopausal changes or their negative effects were not the reason to increase the intensity of the activity or its frequency - only 18.33% respondents chose a positive answer here, as compared to 81.67% negative answers.

More than a half of the respondents were motivated for activity by health related reasons. They wanted to improve their subjective wellbeing, or they had to counteract the effects of disorders in which physical activity is essential. Improving physical fitness (45%) and improving physical ability (43.33%) were important for the respondents. The desire to improve one's body shape was slightly less often, but still relatively often reported (30%). Reduction of body mass, both for health and for looks, was reported as priority by every third respondent. Almost 24% respondents reported the need for relieving stress. Slightly fewer respondents (20%) reported that they did physical activity because they liked it and because they enjoyed active leisure. For 8.33% respondents the reason for physical activity was boredom and a need to fill up their time, while the desire to test oneself was the motivation for 6.67% respondents. One person chose the option of providing her own answer. She wrote that she did a lot of walking, because she did not want to resign from physical activity, and did not feel strong enough to do activities different than walking.

A significant number of women noticed positives of doing physical exercise both in the areas of physical functioning and in the psychological sphere. More than 46% respondents noticed that their physical abilities improved, and 45% experienced positive changes in their psychological wellbeing and in their mood. 36% of respondents improved their physical fitness. Every third woman experienced positive changes in the skeletal system, manifested in reduction of spine and limb pain. As many as 30% respondents gained higher joy of life. Every fourth respondent reported body mass reduction. Similarly, one fourth of respondents experienced increased self-esteem and beneficial effects of physical activity on health. Only 20% experienced increase in quality of sleep and only 18% observed positive effects in their figures. Two respondents did not notice any positive effects of physical exercise (3.33%) - they informed us of that by writing their own answers in the "other" section; while one of them added a commentary that her physical activity is too rare for any improvement in any of the fields to take place.

Thanks to physical activity, our female respondents most often experienced improvement in the functioning of the skeletal system. More than half of them noticed relief in spinal pain, and 40% experienced relief in limb joints. Other health areas improved less often.

Every fifth respondent reported less frequent headaches and dizziness. Improvement in diabetic tests was reported by 18% respondents, and the beneficial effect of physical exercise in the cardiovascular system was observed in 15% respondents. Slightly fewer respondents (13.3%) had better cholesterol levels. Two respondents (3.33%) gave their own answers, pointing to the overall better health. Every fifth postmenopausal respondent, however, did not experience any beneficial effects of physical activity they did.

The majority of the study population females were satisfied with life (43%). There were also respondents who were very satisfied with life (16.47%). Every fifth respondent was averagely happy with life. In the three group of women, who chose 3, 4 or 5, or averagely satisfied, satisfied or very satisfied, to assess their satisfaction with life, there was a total of 88.33% respondents. Every tenth woman was moderately satisfied with life and only one person had little satisfaction with life (1.67%).

#### **Relationship between frequency of physical activity and satisfaction with life**

The study found that the correlation coefficient between frequency of physical activity and satisfaction with life of postmenopausal women was  $r=0.14$ , which denotes weak correlation. This means that there was practically no relationship between the two variables. We did not find any confirmation between the potential increase of frequency of physical activity and the level of satisfaction with life they declared, or between a decrease in frequency of physical activity and decrease in satisfaction with life.

#### **Relationship between intensity of physical effort and satisfaction with life**

The study found a relationship between intensity of physical activity of the postmenopausal respondents and their satisfaction with life. The correlation coefficient was  $r=0.32$ . This denotes a weak correlation, yet there is a clear relationship between the two variables. This means that there is a clear relationship between declared intensity of physical effort and satisfaction of life among postmenopausal women. The relationship can be thus expressed: the more intense the physical activity of the studied respondents, the greater satisfaction with life.

#### **Relationship between severity of menopausal syndromes and the frequency of physical activity**

We found that the correlation coefficient between the severity of menopausal syndromes and the frequency of physical activity in studied women was  $r=0.058$ , which denotes a very weak correlation. Therefore, there was no relationship between the two variables. This means that for the studied population we cannot formulate a thesis: the more severe the menopausal symptoms, the poorer engagement in physical activity. Similarly, we cannot formulate a reverse thesis: the more frequent

the physical activity, the less severe are the menopausal symptoms.

We need to stress that to calculate correlation between the two variables, for the first variable “severity of menopausal symptoms” we used a reversed scale of points, therefore an increase in the value would be inversely proportional to the values of the other variable, i.e. the frequency of physical activity.

#### **Relationship between severity of menopausal symptoms and intensity of physical effort**

We did not find any relationship between the severity of menopausal symptoms and intensity of physical effort of the studied women. The correlation coefficient between the two variables was  $r=0.080$ , which denotes a very weak correlation.

#### **Relationship between the severity of menopausal symptoms and satisfaction with life**

We did not find any relationship between severity of menopausal symptoms and satisfaction with life of the studied women. The correlation coefficient was  $r=0.054$ , which denotes very weak correlation.

#### **Relationship between subjective health and frequency of physical activity**

We found a relationship between subjective health of the studied postmenopausal women and frequency of their physical activity. The correlation coefficient for the two variables was  $r=0.39$ . This denotes a weak correlation, yet this value of correlation is referred to as visible correlation. In fact, had the value been higher by 0.1 point, the correlation would be referred to as moderate. There is therefore statistically significant relationship between the declared subjective health among postmenopausal women and the frequency of their physical activity. We can therefore formulate the following thesis: the better the postmenopausal respondents assessed their health, the more frequent was their physical activity.

#### **Relationship between subjective health and intensity of physical effort**

We found no relationship between subjective health of the studied postmenopausal respondents and their physical activity. For this pair of variables, the correlation coefficient was  $r=0.19$ , a value denoting a very weak correlation. Therefore we cannot formulate a following statement: the better the assessment of subjective health of postmenopausal respondents, the more intensity of their physical effort.

It has to be noted, however, that we cannot decide about explicit lack of relationship between both variables: had the value of correlation coefficient been 0.1 higher, the relationship would have been confirmed. This means a tiny difference; and as the systems for defining correlative relationships is to certain extent arbitrary, in a different system of classification this value might have been considered to be a significant correlation.



### Relationship between subjective health and satisfaction with life

We did not find relationship between subjective health of postmenopausal women and their satisfaction with life. The correlation coefficient was low –  $r = 0.079$ , which explicitly denotes a very weak correlation. We therefore cannot formulate a statement: the better the subjective health of postmenopausal women, the better their opinion of the life and their satisfaction with it.

### Discussion

We found no correlation between severity of menopausal symptoms and frequency of physical activity of studied women. In postmenopausal women, lack of correlation between these two variables may be a positive phenomenon, as there is a scientifically confirmed relationship between psychological mindset and menopausal symptoms and their severity.<sup>7,8</sup> It is possible to put forward a thesis that lack of correlation between severity of menopausal symptoms and physical activity in the studied population is related to the attitude of the respondents.<sup>9</sup> The public sphere offers much floor to the issue of menopause, and women entering the menopausal phase have an easy access to educational materials. These materials present issues related to the menopausal period – thematic publications (free brochures and books), television and the Internet (internet portals and discussion forums where women can share their experiences) are rich sources of reliable information. There are information campaigns on the issues of the menopausal period, its course and symptoms, which means that Polish women are better prepared for the menopausal phase.<sup>10</sup> The knowledge on the process of menopause eliminates the element of negative surprise with unsettling or bothersome symptoms, and may constitute one of the reasons for lack of correlation between severity of menopausal symptoms and physical activity of our respondents, who, having gained knowledge on the importance of physical activity during menopause, may try to undertake physical activity without regard to the felt menopausal symptoms. In such a case, lack of relationship is advantageous, since it points to resigning from linking physical activity to current physical or psychological wellbeing. This opens up the opportunity for improvement of the functioning in both of these spheres by physical activity. The beneficial impact of physical activity has been numerously proven by studies on a variety of studied populations.<sup>11,12</sup> It is still worth to stress that our study did not analyze the relationship between the severity of menopausal symptoms and the sheer fact of undertaking physical activity. Rather, the focus of the second variable was only the frequency of physical activity in postmenopausal women.

Similar interpretation of results is possible for the lack of relationship between the severity of menopausal

symptoms and the intensity of physical effort. The relationship between both factors is based on inverse proportionality, therefore lack of correlation between them allows us to state that in the studied group of postmenopausal women the lower intensity of physical effort was not the result of severity of menopausal symptoms.

As we did not find any correlative relationships in any of the situations, where one of the variables was the severity of menopausal symptoms, in the light of the available studies we may come to a conclusion that the studied women might have used a psychological defence strategy, where they counteracted states in which severity of the symptoms could limit the ability to undertake physical activity.<sup>9</sup> For many women, this might have been a conscious mechanism, an action taken on the basis of information from technical and lay sources that discuss the importance of physical activity in preparing for the menopausal period and later maintaining good physical fitness<sup>11,12</sup>; or on the basis of materials which stress the importance of physical activity in striving for improvement of health and in relieving the effects of menopausal symptoms.<sup>7</sup> In the light of the above, it does not seem surprising that we did not find relationship between severity of menopausal symptoms and the satisfaction with life in our respondents. As the process of menopausal changes leads to a partial loss of control over one's body and brings numerous disadvantageous and unpleasant symptoms,<sup>7,10</sup> the studied population may have used a psychological defence mechanism against the negative results of menopause on their psychology and their subjective satisfaction with life.

We found that in the studied population of postmenopausal women, the improvement caused by physical activity related most importantly to the physical fitness (over 46%), mood and psychological wellbeing (45%), physical fitness (over 36%), that is in the areas which have been proven to be positively affected by physical activity by numerous studies on wider population groups.<sup>13,14</sup> Fewer respondents, however, reported improvement of functioning in areas closer related to the results of hormonal distortions, such as disorders in the skeletal system (33.3%), sleep disorders (20%) or body mass increase (over 26%). It is still important to remember that the study was conducted on the basis of respondents' self assessment, and there was no element of verification of this self assessment by an independent party (healthcare specialists).

Typical menopausal symptoms seem to function in the consciousness of many postmenopausal women as a temporary phenomenon. This may lead them to develop a task oriented attitude and to perceive menopause as a normal obstacle to overcome.<sup>9,10</sup> The situation seems different in the case of subjective health assessment, especially if the negative health symptoms were confirmed by objective medical tests. The research we

conducted for the purpose of this study found that there was a relationship between subjective health and the frequency of physical activity among the studied postmenopausal women. The correlation coefficient was  $r=0.39$ , therefore the strength of correlative relationship is significant. This value means that the better subjective health of studied women, the higher frequency of physical activity. In turn, the worse subjective health, the less frequent the physical activity. The result of the study seems to have justified grounds, as in the course of various diseases there are medical contraindications for various type of activity or activity of various intensity. On the other hand, the respondents expressed their own assessment of their health, which means that a considerable degree of subjectivity must not be excluded, as well as considerable impact of fear and anxiety towards doing physical activity, not necessarily related to objective medical grounds.

For the two variables “subjective health” and “intensity of physical effort” we did not find any relationship. The correlation coefficient was  $r=0.19$  and only 0.01 point was missing for the correlative relationship to be found. The lack of correlation means that poor subjective health did not mean reduction of intensity of physical exercise. Taking decisions on physical activity and on its intensity independently of one’s subjective health seems to be a positive phenomenon, in line with doctors’ recommendations. Doctors usual advice to their patients suffering from various ailments is to do as much safe exercise as possible, in order to improve general wellbeing and as a tool to accompany treatment process.<sup>5,14</sup> The type and the intensity of physical exercise in case of accompanying diseases must always be designed in accordance with doctor’s recommendations.<sup>15</sup>

Although there is no direct relationship between subjective health and intensity of physical effort in the study population, it is worth to notice that studied women usually chose physical activity of lowest intensity, i.e., walking. This activity was chosen by 70% of respondents, probably due to its simplicity. Even though the relevant question allowed for choosing any number of answers, most of enumerated activities did not reach more than 25% of choices, especially the more intense ones. The exception was cycling, chosen by 50% women, most probably also due to the fact that the bicycle is a very practical means of transport.

It is important that in the course of the study we did not find any relationship between the subjective health and satisfaction with life of the studied postmenopausal women. This may be a proof for women using complex psychological defence mechanisms when faced with crisis situations.<sup>16,17,18</sup> More than 43% of women had high satisfaction with life, and almost 17% had very high satisfaction with life, which may again prove that studied postmenopausal women had certain psychological re-

sistance to the difficulties of menopause, its symptoms and consequences. Another argument for this thesis would be the fact that as many as 65% of respondents declared that even though they experienced menopausal symptoms, they could manage them quite well.

In the light of the above the answer to the fundamental research question of this paper seems interesting. We did not find relationships between the frequency of physical activity and satisfaction with life of the studied postmenopausal women, but we found correlations between intensity of physical effort and satisfaction with life. This result is similar to other studies on postmenopausal women, who noted higher health benefits from the quality of physical exercise (reflected by the intensity of physical effort), and not just from its frequency. This was found for instance in studies on prevention and treatment of osteoporosis, where training of medium intensity based on high impact exercise was more beneficial than more frequent exercise of lower intensity.<sup>19,20</sup> Better physical fitness, physical ability and subjective wellbeing achieved in physical activity has in turn direct effect on satisfaction with life and is an important component of quality of life.<sup>21,22</sup> The studied population of women had a tendency to do exercise of medium (35%), high (23,33%) or moderate (26.67%) intensity.

Our results show how important is the psychological aspect in the menopausal and postmenopausal period. Psychological resilience, healthy distance to menopausal symptoms, ability to cope with stress and the skill to deal with obstacles make the cost of going through the stormy period of menopausal change smaller, and help to find health and mental balance in the new stage of life.<sup>23,24</sup> An optimistic approach towards menopause and the process of ageing results in cultivating desirable behaviours, such as taking good care about health, doing relevant medical tests, healthy lifestyle and physical activity, which has important impact on general physical and psychological wellbeing.<sup>25,26</sup>

## Conclusion

We confirmed the relationship between intensity of physical effort and satisfaction with life and the relationship between subjective assessment of one’s health and the frequency of physical activity.

## References

1. Jagła D, Korzeniowska K, Pawlaczyk M. Skóra kobiet w okresie menopauzy. *Farmacja Współcz.* 2012;5:83–87.
2. Koligat D, Paczkowska A, Michalak M. et al. The prevalence of depression and anxiety in women during menopausal transition. *Pol Prz Nauk Zdr.* 2015;3:159–163.
3. Caspersen CJ, Powell KE, Christenson GM. Physical Activity, Exercise, and Physical Fitness: Definitions and Distinctions for Health-Related Research. *Public Health.* 1985;100:126–131.

4. Podbielska M. Influence of physical activity on the quality of life of healthy adults – preliminary remarks. *Acta Bio-Optica et Informatica Medica Inżynieria Biomedyczna*. 2014;20(2):128–132.
5. Sheila D, Kelley PG, Brittney SL, Carrie KG. Physical Activity and Physical Function: Moving and Aging. *Obstet Gynecol Clin North Am*. 2018;45:723–736.
6. Steiner AZ. Przewidywanie wieku wystąpienia menopauzy: hormonalne, rodzinne i miesięczkowe czynniki determinujące. *Menopausal Medicine*. 2011;19:1–5.
7. Fu SY, Anderson D, Courtney M. Cross-cultural menopausal experience: comparison of Australian and Taiwanese women. *Nurs Health Sci*. 2003;5:77–84.
8. Yisma E, Eshetu N, Ly S, Dessalegn B. Prevalence and severity of menopause symptoms among perimenopausal and postmenopausal women aged 30–49 years in Gulele sub-city of Addis Ababa, Ethiopia. *BMC Women's Health*. 2017;124:1–8.
9. WHO. Mental health aspects of women's reproductive health: a global review of the literature. *World Health Organization*. 2009:79–86.
10. Markwitz-Grzyb N. Women and the sources of solutions to the problems caused by menopause. *Now Lek*. 2012;81:197–202.
11. Wiśniewska A, Napierała M, Pezala M, Zukow W. Wpływ aktywności fizycznej na psychomotorykę kobiet w okresie menopauzy. *Journal of Health Sciences*. 2014;4:257–272.
12. Dąbek A, Adamiec A, Rekowski W, Czyżewski P. The influence of physical activity on climacteric symptoms. *Post Reh*. 2016;12:7–32.
13. Borker S, Venugopalan PP, Bhat SN. Study of menopausal symptoms, and perceptions about menopause among women at a rural community in Kerala. *J Midlife Health*. 2013;4:182–187.
14. Reiner M, Niermann C, Jekauc D, Woll A. Long-term health benefits of physical activity – a systematic review of longitudinal studiemi. *BMC Public Health*. 2013;13:813.
15. Aparicio-Tin FE, Farris M, Courneya KS. Predictors of physical activity at 12 month follow-up after a supervised exercise intervention in postmenopausal women. *Int J Behav Nutr Phys Act*. 2015;12:55.
16. Pertyński T, Stachowiak G. Menopauza — fakty i kontrowersje. *Endokrynol Pol*. 2006;57:525–534.
17. Stadnicka G, Iwanowicz-Palus GJ. Wpływ wizerunku własnego ciała na objawy okołomenopauzalne u kobiet. *Gerontol Pol*. 2017;25:28–33.
18. Elavsky S. Physical activity, menopause, and quality of life: the role of affect and self-worth across time. *Menopause*. 2009;16:265–271.
19. Ćwirlej A, Wilmowska-Pietruszyńska A. Znaczenie aktywności fizycznej w profilaktyce osteoporozy. *Prz Med. Uniw Rzesz*. 2008;2:111–115.
20. Caputo EL, Costa MZ. Influence of physical activity on quality of life in postmenopausal women with osteoporosis. *Rev Bras Reumatol*. 2014;54:467–473.
21. Chang TJ, Ting YT, Sheu SL, Chang HY. Effects of tai chi in postmenopausal women with osteoporosis: a systematic review. *Hu Li Za Zhi*. 2014;61:75–84.
22. Trzebiatowski J. Jakość życia w perspektywie nauk społecznych i medycznych – systematyzacja ujęć definicyjnych. *Public Health*. 2011;46:25–31.
23. Graziottin A, Serafini A. Depression and the menopause: why antidepressants are not enough? *Menopause Int*. 2009;15:76–81.
24. Baker A, Sirois-Leclerc H, Tulloch H. The Impact of Long-Term Physical Activity Interventions for Overweight/Obese Postmenopausal Women on Adiposity Indicators, Physical Capacity, and Mental Health Outcomes: A Systematic Review. *J Obes*. 2016;2016:6169890.
25. Van Gemert WAM, Schuit AJ, Van der Palen J. et al. Effect of weight loss, with or without exercise, on body composition and sex hormones in postmenopausal women: the SHAPE-2 trial. *Breast Cancer Res*. 2015;17:120.
26. Sternfeld B, Dugan S. Physical Activity and Health During the Menopausal Transition. *Obstet Gynecol Clin North Am*. 2011;38:537–566.



## ORIGINAL PAPER

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# Evaluation of the knowledge of the issues related to human papillomavirus infections within young women

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## Abstract

**Introduction.** Human papillomavirus infections are frequent in on average 9% to 13% of the female population, and the risk of infection throughout life exceeds 50%. The HPV virus causes changes in the mucous membranes and the skin of the genital area in both women and men.

**Aim.** This paper presents epidemiology, prophylaxis, diagnostics and treatment of HPV and cervical cancer infections. In addition, the knowledge of issues related to human papillomavirus infection among young women was assessed.

**Materials and methods.** The diagnostic survey method was used to carry out the research. The research tool was a questionnaire of own authorship consisting of 41 questions. The research group consisted of 240 women. The research was carried out from June to September 2016 at the Chodźki Medical Center and the Luxmed facility in Lublin.

**Results.** There is a relationship between the education of the respondents and their knowledge about the human papillomavirus infection. The studies did not show a significant relationship between the self-esteem of the studied women and whether they were vaccinated against the HPV virus (Chi-square = 0.362,  $p = 0.547$ ).

**Conclusions.** The general level of knowledge on issues related to human papillomavirus infection among young women is at the secondary level. A higher level of general knowledge was shown by women with better education, related to the medical and biological sciences. The self-assessment of the respondents coincides with the general knowledge, based on detailed questions, on issues related to HPV infection. Promoting knowledge about HPV infection is unsatisfactory

**Keywords.** HPV virus, human papillomavirus, cervical cancer

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 13.07.2018 | Accepted: 13.09.2018

Publication date: December 2018

## Introduction

Human papillomavirus infections are frequent, an average of 9% to 13%, and the risk of infection throughout life exceeds 50%.<sup>1</sup> HPV causes changes in mucous membranes and the skin of the genital area in both women and men. These can be mild as well as pre-cancer and cancer. There are three stages of infection: a clinically overt phase, a subclinical phase, a latent phase.<sup>2</sup> Mostly HPV infection occurs during sexual contact. This is the most common sexually transmitted infection. Vertical transmission from mother to fetus during vaginal birth is also possible. The risk factors for viral infection also include a large number of sexual partners as well as their frequent change and early initiation of sexual intercourse.<sup>2</sup> The development of cervical cancer is associated with infection with high-pathogenic types of human papillomavirus. It is one of the most frequent cancer malignancies in women. However, you can effectively prevent its development. The simple and cheap methods of its detection include performing regular cytological examination. It is a basic tool for the detection of precancerous and cervical cancer.<sup>3,4</sup>

Introduction of primary prophylaxis, which is vaccination against HPV, effectively prevents both the persistence of infection with the human papillomavirus and the formation of pre-cancerous changes on the cervix. Vaccines do not protect against all types of virus, therefore it is very important to continue screening programs.<sup>5</sup> HPV (Human Papilloma Virus) belongs to the family of Papovaviridae viruses. Almost 200 types of this virus are known so far. About 40 of them are so-called genital types. They show affinity for mucous membranes as well as epithelial cells of the skin. Among human papilloma viruses, we distinguish high and low-carcinoma types.<sup>6,7</sup> Human papillomavirus infection is one of the most common sexually transmitted infections, both in the world and in Poland. Human pregnant women and people with immunosuppression are particularly vulnerable to human papillomavirus infection.<sup>8,9</sup> About 50% of people who are sexually active are infected with genital HPV types. They can cause infections in the epithelium without causing inflammation and the spread of infection to other organs. Not every infection must cause clinical symptoms. The virus may remain in the latent phase. Quite often it also comes to spontaneous cure.<sup>10,11</sup> HPV virus is ubiquitous and easy to infect. Most often it comes to a person during the first sexual encounters. It can also be infiltrated through saliva, which may contribute to the development of head and neck cancer (cancer of the lip, mouth, salivary glands, tonsils, pharynx, paranasal sinuses, soft neck tissues and the outer ear region). Virus infection can also be associated with hospital and cosmetic procedures that pave the way for infection or insufficient hygiene. The presence of infection leaves no immunity, that is why

reinfection is possible.<sup>12-14</sup> To prevent HPV infection include educating both women and men about the risks and consequences of infection, as well as vaccinations against genital HPV types.

Infections with microorganisms or chronic and recurrent vaginal inflammations should be diagnosed and treated as soon as possible because they can contribute to HPV infection.<sup>15,16</sup> Two vaccines are present on the market: quadrivalent and two-valent. Vaccination is prophylactic. It is not able to eliminate the existing infection and pathological changes.<sup>17</sup> Infection with human papillomavirus usually proceeds asymptotically. In severe cases, local symptoms such as pruritus or discharge occur. The HPV virus has the ability to avoid being recognized by the body's immune system. This makes it difficult to diagnose. The infection is local.<sup>8,18</sup> Mild diseases caused by human papillomavirus infection include: condylomata acuminata, skin warts, laryngectomy of the larynx and respiratory tract. Genital warts occurring in the genital area in over 90% of cases are caused by HPV types 6 and 11. These changes can also be caused by other types of virus. They are difficult to treat and very often convert. In most cases, the resulting warts do not undergo any changes for a long period of time. Some people develop new ones that are located in a different place than the previous ones and have different sizes. In about 5-20% of patients, spontaneous regression is possible.<sup>3,5</sup> The formation of dermal warts is caused by stimulation of epidermal cells to proliferation. They can be located in different places. The incubation period for an infection ranges from a few to a dozen or so weeks. Changes may undergo spontaneous regression.<sup>11,19</sup>

The cancers and precancerous conditions associated with human papillomavirus infection include: cervical cancer, vulvar cancer, vaginal cancer, penile cancer, anal cancer, and head and neck cancer. HPV viruses are responsible for approximately 5.2% of all malignant tumors. In the case of the cervix it is a factor in the occurrence of cancer in more than 90%.<sup>11</sup> Treatment of HPV infection can be ineffective. Sometimes the body's immune system fights the virus itself. Spontaneous healing does not leave resistance, therefore it is possible to re-infect with the virus of the same type as before. In the case of persistent infection, it is not possible to eradicate HPV, due to the fact that medicine does not have any medicine that could destroy it. The only way to overcome the infection is immunomodulatory treatment. This treatment strengthens the immune response of the body, which helps to control the HPV infection. Even if this form of therapy does not help to get rid of the virus from the body, it has been proven that it effectively protects against the occurrence of lesions. We can also treat HPV-induced lesions by limiting ourselves to symptomatic treatment, which usually consists in removing lesions.<sup>20,21</sup>

Aim

The aim of the study is to assess the knowledge of issues related to human papillomavirus infection in a group of randomly selected young women. The issues of vaccination against human papillomavirus and sources of HPV infection were raised.

Materials and methods

The diagnostic survey method was used to carry out the research. The research tool was a questionnaire of own authorship consisting of 41 questions. The obtained results were subjected to statistical analysis based on chi-square tests, assuming  $p < 0.05$  as statistically significant. The results are presented in tables and figures. The analysis of the results was carried out using the IBM SPSS Statistica statistical package. Research for the purposes of this work was carried out from June to September 2016. The research was voluntary and anonymous. The survey was conducted among 240 women in Lublin at the Chodźki Medical Center and in the Luxmed facility.

Results

The study included 240 randomly selected young women between the ages of 19 and 29 years. The average age of the respondents was 24.19 (the youngest was 19 years old, the oldest was 29). Over half of the respondents (65%,  $n = 156$ ) were between 19 and 24 years old, the others (35%,  $n = 84$ ) were between 25 and 29 years old. The vast majority of respondents started intercourse (84.2%,  $n = 202$ ). 15.8% ( $n = 38$ ) of the respondents did not start their intercourse yet. The average age of sexual initiation was 18.96 years. Most of the surveyed women did not give birth yet (79.2%,  $n = 190$ ). 20.8% ( $n = 50$ ) of the respondents released offspring. The vast majority of respondents (85.4%,  $n = 205$ ) were already at the gynecological visit. 14.6% ( $n = 35$ ) of the respondents were not present at the gynecologist. More than half of the respondents (66.7%,  $n = 160$ ) had cytology performed in their own studies. 33.3% of women ( $n = 20$ ) did not have this test. Vaccination against HPV was carried out only by 5% of respondents ( $n = 12$ ). 95% of the surveyed women ( $n = 228$ ) were not vaccinated. By far the most common (78.2%;  $n = 179$ ) reason for the lack of vaccination of women was the lack of knowledge about the existence of the vaccine. The next reason was the uncertainty about the effectiveness of this vaccine (7.4%,  $n = 17$ ) and its high cost (7.0%,  $n = 16$ ). The smallest percentage of respondents were not vaccinated for health reasons (3.9%,  $n = 9$ ) and convictions about vaccines (3.5%,  $n = 8$ ). Definitely the majority of respondents (90.8%,  $n = 218$ ) claimed that dissemination of knowledge about HPV infection is not sufficient. The opposite opinion was 9.2% ( $n = 22$ ) of the respondents.

The obtained results were subjected to statistical analysis based on chi-square tests. A 5% error of infer-

ence and associated significance level  $p < 0.05$  indicating a significant statistical relationship were adopted. The results are presented in tables and figures. The analysis of the results was carried out using the IBM SPSS Statistics statistical package.

The questionnaire contained 27 questions on the knowledge of issues related to human papillomavirus infection, therefore the women surveyed could get just that number of points. The average number of points scored by the respondents was 15.55 points (SD = 5.99). The minimum number of points received was 0, and the maximum was 27. Due to the number of points received by the respondents, they were divided into three groups: people with low level of knowledge, average level of knowledge and a high level of knowledge. (Table 1,2)

Table 1. The level of respondents' knowledge

Level of knowledge	n	%
Low knowledge (0-13 points)	78	32.5
Average knowledge (14-20 points)	104	43.3
Knowledge (21 -27 points)	58	24.2
Totality	240	100.0

Table 2. Dependence between age, actual knowledge plate of the surveyed women

Age	Level of knowledge		
	Low knowledge	Average knowledge	Knowledge
19-24	49	63	44
	31.4%	40.4%	28.2%
25-29	29	41	14
	34.5%	48.8%	16.7%
Chi-square=4.065; p=0.131			

As a result of the statistical analysis, it was found that more women in the younger age group had high knowledge of HPV. In both age groups, the majority of respondents had average knowledge. (Table 3)

Table 3. Relationship between education and the actual level of knowledge of the surveyed women

Education	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Basic / vocational	18	12	0
	60.0%	40.0%	0%
Average / higher	60	92	58
	28.6%	43.8%	27.6%
Chi-square=16.352; p<0.001*			

People with higher / secondary education statistically more often characterized the average and high level of knowledge than those with basic / vocational education. Interestingly, no one with basic or vocational education had a high level of knowledge.

There is a relationship between the education of women surveyed and their knowledge. Women with education related to medical and biological sciences had much more knowledge about HPV infection. Only 9.7% of respondents had low knowledge. Women who had no education related to medico-biological sciences had this knowledge lower. (Table 4)

**Table 4.** Relationship between education related to medico-biological sciences and the actual level of knowledge

Did you educate yourself with medico-biological sciences?	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Yes	7	23	42
	9.7%	31.9%	58.3%
No	71	81	16
	42.3%	48.2%	9.5%
Chi-square=69.184; p<0.001*			

There is no statistical relationship between the fact of coexistence and the level of knowledge. Both women who have begun intercourse, as well as those who have not started it yet, mostly have average knowledge.

**Table 5.** Relationship between the place of residence of the respondents and the level of knowledge

Place of residence	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Village	24	19	13
	42.9%	33.9%	23.2%
A city below 100,000 residents	45	57	26
	35.2%	44.5%	20.3%
A city over 100,000 residents	9	28	19
	16.1%	50.0%	33.9%
Chi-square=11.553; p=0.021*			

Statistically, more women living in the countryside have a low level of knowledge. Most women living in cities have average knowledge. (Table 5) In a difficult / average financial situation, the approximate number of women has low knowledge. Only 16.1% of women have high knowledge. In the case of women with a good or very good material situation, this percentage is twice as high, and low knowledge has 24.1% of respondents.

In both cases, the most women have average knowledge, and the least high. Among women who gave birth is more than four times smaller percentage of respondents with high knowledge than women who did not give birth. There is no significant statistical relationship between the knowledge of the surveyed women and the fact whether they were already at the gynecological visit. In both cases, the highest number of respondents has average knowl-

edge, and the lowest. Whether a woman had a cytological examination does not significantly affect the level of her knowledge. In both cases, the majority of women were characterized by an average level of knowledge, and the smallest percentage of respondents had high knowledge. The statistical surveys carried out did not show any dependence ( $p>0.05$ ) between the level of knowledge of the respondents and whether they were vaccinated against the HPV virus. In both cases, most women had average knowledge. Statistical research has shown that women who were subject to HPV infection during the education have a definitely higher level of knowledge than women whose subjects were not discussed during the study. In women with only 7.7% of these issues, they have low knowledge. In women whose topics have not been raised high knowledge has only 8.7%. (Table 7)

**Table 6.** Relationship between the time of delivery and the level of knowledge

Did you give birth?	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Yes	21	26	3
	42.0%	52.0%	6.0%
No	57	78	55
	30.0%	41.1%	28.9%
Chi-square=11.474; p=0.003*			

**Table 7.** The relationship between the level of knowledge and the subject of HPV infection during the education of subjects was discussed

Do you have any issues related to HPV infection during your life?	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Yes	7	39	45
	7.7%	42.9%	49.5%
No	71	65	13
	47.7%	43.6%	8.7%
Chi-square=66.537; p<0.001*			

In both cases, the majority of respondents have knowledge on an average level. Only 13.6% of women who say that spreading knowledge about HPV infection is sufficient has high knowledge. However, this is a smaller percentage than for women who believe that the promotion of knowledge is insufficient (Table 8).

There is a statistical relationship between the self-assessment of knowledge about HPV infection and its actual level. Women who assess their knowledge on good or very good really have a high knowledge. Over half of the respondents who recognized that their knowledge is average has an average level of knowledge. One-third of the respondents who rated their knowledge as poor have low knowledge. (Table 9)

**Table 8.** Relationship between the level of knowledge and the impression of the respondents on the propagation of knowledge about HPV infections

In your opinion, is spreading knowledge about HPV infection sufficient?	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Tak	4	15	3
	18.2%	68.2%	13.6%
Nie	74	89	55
	33.9%	40.8%	25.2%
Chi-square=6.090; p=0.048*			

**Table 9.** Relationship between the self-assessment of the level of knowledge and factual knowledge

How do you rate your knowledge about HPV?	Level of knowledge		
	Low knowledge	Average knowledge	High knowledge
Bad	49	26	3
	62.8%	33.3%	3.8%
Average	26	67	23
	22.4%	57.8%	19.8%
Good/very good	3	11	32
	6.5%	23.9%	69.6%
Chi-square=105.199; p<0.001*			

The highest level of knowledge is given to women who receive information about HPV from professional literature or from a doctor or nurse. The lowest level of knowledge has been surveyed, which the media chose as the source of information. Women whose main source of information is the Internet and family and friends mostly have average knowledge. (Table 10)

**Table 10.** Relationship between the source of knowledge and the level of knowledge

Sources of knowledge	Level of knowledge			Chi-square
	Low knowledge	Average knowledge	High knowledge	
Internet	54	80	32	8.260 p=0.016*
	32.5%	48.2%	19.3%	
Media (radio, magazines, television)	26	25	4	13.292 p=0.001*
	47.3%	45.5%	7.3%	
Family, friends	10	15	4	2.045 p=0.360
	34.5%	51.7%	13.8%	
Doctor, nurse / professional literature	8	19	33	43.027 p<0.001*
	13.3%	31.7%	55.0%	

There is no statistical relationship between the material situation of the women surveyed and whether they were vaccinated against the HPV virus. In both cases, the approximate percentage of respondents received vaccination. There is no statistical dependence between whether during the training of the surveyed

women there were topics related to HPV infection and whether they were vaccinated against the human papillomavirus. In both cases, the number of respondents was approximated. No woman with primary or vocational education assessed her knowledge as good or very good. One fifth of women with secondary or higher education found their knowledge good / very good. The rest assessed her as bad or average. More than half of the respondents whose education is related to medical and biological sciences assessed their knowledge as good or very good. Almost all respondents whose education was not associated with medico-biological sciences recognized that their knowledge is bad or average.

**Table 11.** Relationship between self-knowledge and the fact of being vaccinated

Have you been vaccinated on HPV?	Self-assessment of knowledge	
	Bad / average	Good / very good
Yes	11	1
	91.7%	8.3%
No	183	45
	80.3%	19.7%
Chi-square=0.362; p=0.547		

**Table 12.** The relationship between self-assessment of knowledge and that during education were discussed topics related to HPV infection

Did you discuss topics related to HPV infection during your education?	Self-assessment of knowledge	
	Bad / average	Good / very good
Yes	51	40
	56.0%	44.0%
No	143	6
	96.0%	4.0%
Chi-square=55.589; p<0.001*		

The research did not show the relationship between the self-esteem of the knowledge of women surveyed and the fact whether they began to live together. In both cases, the majority of respondents rated their knowledge as bad or average. Regardless of the place of residence, the surveyed women mostly assessed their knowledge as bad or average. Both women who had a cytology test and those who never had cytology assessed their knowledge about HPV virus comparatively. The studies conducted did not show a significant relationship between the self-esteem of the surveyed women and whether they were vaccinated against the HPV virus. In both cases, the vast majority judged their knowledge as bad or average. (Table 11)

Almost all women who were never touched on topics related to HPV during their education assessed their knowledge as bad or average. Only 4% of the respondents have rated themselves good or very good.



It is ten times lower self-esteem than the respondents who were subject to these topics during the education (Table 12).

## Discussion

In the conducted research, 84.2% of the respondents started life and the average age of sexual initiation was 18.96 years. In studies carried out by Kempieńska, the average age of sexual initiation was 17.05 years.<sup>22</sup> According to studies by Filipp, the average age of women and men in the first relation in Western Europe is 17-18 years, and in Eastern Europe around 20.<sup>23</sup> Izdebski in his book claims that the average age of sexual initiation of Polish women is 18.7 years, which is very similar to the results of own research.<sup>24</sup>

The human papillomavirus belongs to the family of Papovaviridae viruses. There are high and low-carcinoma types. High ankyra types are responsible for approximately 70% of cervical cancer cases. Low-carcinoma types are responsible for the formation of condylomata acuminata and non-malignant warts.<sup>25</sup> Own research shows that 77.5% of respondents know what disease can be caused by HPV infection with high oncogenic risk. 2.9% associated this virus with ovarian cancer and 1.3% with breast cancer. 18.3% of respondents did not know the answer to this question. Greater knowledge (91.2%) about the high oncogenicity virus had young women examined by Stefanek and Durke.<sup>26</sup> In own studies, less than half of respondents (39%) answered a question about HPV with low oncogenicity, that it caused papillary lesions and condylomata acuminata. 32% of women did not know what the correct answer was. One quarter of them said that it contributes to the occurrence of inflammation. 5% responded that infection with this virus causes discharge.

Human papilloma virus is the most common infection that is sexually transmitted. Own research shows that half of the women surveyed (49.6%) know that HPV can infect women and men. In the Mastalerz-Migas et al. research, in which 168 women aged between 16 and 30 took part, the percentage is slightly smaller (45.2%).<sup>27</sup> Also, a similar percentage of young women (60.5%) gave such an answer from a study conducted by Jurczak and colleagues.<sup>28</sup> Although the infection of the human papillomavirus in most cases is asymptomatic, it is possible to detect it. For this purpose, tests for the presence of viral DNA are performed. Own research shows that almost half of the respondents know about this possibility and know how the material for this research is collected. 7% of women surveyed claim that there is no possibility of detecting HPV infection. 18% of respondents believe that this infection is detected by taking blood for testing. No literature was found that would raise a similar problem among the respondents. Condom use during sexual intercourse can effectively

reduce the risk of HPV infection. According to our own research, more than three quarters (77.5%) of respondents agree with this claim. In the study of Szykuła et al., verifying the knowledge of nursing students on the prevention of cervical cancer, the majority of this opinion is the majority, as many as 91% of the respondents.<sup>29</sup> In the author's studies, a small (4.6%) part of the surveyed women believes that the use of condoms cannot protect against virus infection. This result is similar to that of Szykuła et al.<sup>29</sup>

A frequent change of sexual partners increases the risk of human papillomavirus infection. This infection can lead to the development of cervical cancer. According to own research, the majority (82.1%) of respondents know that there is a relationship between frequent change of sexual partners and the risk of HPV infection. Similar results were obtained by Szykuła et al. where over 90% of respondents answered correctly.<sup>29</sup> According to the studies by Stefanek and Durke, the vast majority (75%) of women understand the negative impact of frequent change of sexual partners on the risk of infection.<sup>26</sup> Research by Baran et al., which was carried out to check the knowledge of women from the Podkarpackie region, shows that only a quarter of respondents know about it.<sup>30</sup> In own research, 80% of respondents believe that the infection occurs during sexual intercourse. In the study Szykuła et al., respondents gave slightly less respondents (64%).<sup>29</sup>

Vaccination against HPV is one of the primary prevention of cervical cancer. In Poland, it is recommended for girls who have not yet started sexual intercourse. In our country, vaccinations in most regions are not refunded by the NFZ, but are on the list of recommended vaccinations. Only some of the richest municipalities can afford to introduce a preventive vaccination program, which is reimbursed by the authorities. Vaccination against human papillomavirus is expensive and only a full refund would provide general access to it. However, widespread vaccination of girls is already introduced in most European Union countries (eg Belgium, France, Germany).<sup>29</sup> In own studies, the number of vaccinated women is only 5%. These results are comparable to those of other authors. Gotlin and Szykuła, studying nursing students at the Warsaw Medical University aged 20-26, stated that only 1% of the respondents were vaccinated.<sup>31</sup> And according to the research of Mastalerz-Migas and colleagues, only 2.4% of respondents used the possibility of vaccination. In our own studies, the main reason for not being vaccinated was ignorance of the existence of a vaccine against HPV. Due to ignorance, as many as 78.2% of respondents did not get vaccinated. Contrary to appearances, the high price of the vaccine was not an important reason, as only 7% of respondents gave such a response. In own research, similarly to the studies of Gotlin and Szykuła

et al. the vast majority of respondents knew that these vaccinations are not mandatory in Poland.<sup>31</sup>

Cytological examination is the basic prophylactic examination. It allows to detect precancerous conditions and early forms of cervical cancer. The cytology should be carried out at least once every three years, preferably every year. The Polish Gynecological Society recommends that the first cytological examination should be performed no later than three years after the beginning of sexual intercourse. Our own research showed that one-third of the respondents never had a cytological examination. This may be due to the young age of the respondents and lack of coexistence (15.8%). Comparing the level of knowledge of this group to women who had cytology, there was no difference in their knowledge of infections caused by human papilloma virus and cervical cancer prophylaxis. In the paper written by M. Wyderke, all the respondents had this test done.<sup>33</sup> According to own research, the vast majority of respondents (85.4%) knew what cytological examination is. In research conducted by M. Wyderke this knowledge is slightly lower and amounts to 76%.<sup>33</sup> And in the studies of Lewandowska et al., almost all of the respondents are aware of what this study is.<sup>44</sup> Błazucka and Cieślak examined the knowledge of first-year nursing students at the Warsaw Medical University.<sup>35</sup> They showed that knowledge about the use of cytological examination as a study for cervical cancer is also high.

Own research showed that 67.5% of respondents know what is the collection of cytological smear. In M. Wyderke's<sup>33</sup> research, the percentage of correct answers is much higher and amounts to 82%. The influence on higher knowledge may have the fact that the author researched women in a larger age range. In the study, Szykuły et al., conducted on students of the first and third year of nursing, the result was comparable with own research and amounted to 63%.<sup>29</sup> The majority (86.3%) of examined women know how often a cytological examination should be performed. It is the same in the studies of Lewandowska et al., where 72% of respondents have the correct knowledge on this topic.<sup>34</sup>

In the conducted own research, half of the respondents (52.9%) answered the question of when to perform cytology, correctly answered that no later than 3 years from the beginning of sexual intercourse. Almost 23% of respondents stated that this period should not exceed 3 years from the appearance of the first menstrual period. 7.5% of women felt that this test should be done only after the birth of the first child. In the study, Szykuły et al., the largest group (94% of third-year students and 76% of first-year students) admitted that the first cytological examination should be performed after starting sexual intercourse.<sup>29</sup>

The vast majority, 87.9% of the surveyed women know at what age according to the Population Preven-

tion and Early Cervical Cancer Screening Program, cytological tests are covered by the refund. In the studies of Mastales-Migas et al., the majority of women correctly answered this question (70.3%), and in Leszczynski studies almost all of the respondents (91%).<sup>32,36</sup>

The colposcopic examination aims to verify the incorrect results of cytological tests. It is based on enlarging the cervix. According to own research, a very small group of women (41.7%) know what colposcopy is. 14.6% of the respondents mistook this biopsy study and answered that it involves taking a segment of the cervix. In studies by Szykuły et al. over half of third year students and one third of the first year gave the correct answer. In our own research, only half of the respondents (50.4%) knew when to perform a colposcopic examination.<sup>29</sup>

When asked about the symptoms of cervical cancer, the majority of respondents (43.8%) answered that in the initial stage the cancer did not show any symptoms. 29.6% of the respondents answered that in the early stage there is bleeding between the menstrual periods and abdominal pain. Over a quarter (26.7%) of women did not know the answer to this question. In the studies of Lewandowska et al., more than half of the respondents replied that in the initial stage the cancer may develop asymptotically and 20% could not answer this question.<sup>34</sup>

The analysis of own research shows that the vast majority (82.9%) of respondents know that cervical cancer detected in the early stage is curable. According to studies by Lewandowska et al, this is the knowledge of 62% of respondents, and almost a quarter thinks that it is not curable. In own research, this percentage is much smaller (5.8%).<sup>34</sup>

Own research shows that the most common source of knowledge on issues related to HPV infection is the Internet (69.2%). The second source mentioned by respondents (26.7%) was medical personnel and specialist literature. In the studies conducted by Iwanowicz-Palus et al., The gynecologist (25.9%), as well as the media (20%) and literature (21.8%), were most frequently interviewed as the source of knowledge.<sup>37</sup>

Own research has shown that knowledge of issues related to human papillomavirus infection is on an average level (43.3%). 24.2% of the respondents had a good level of knowledge, and 32.5% of the surveyed women on the low level. Chorążka and colleagues assessed the students of the Medical University of Lodz and the University of Lodz as insufficient in their research.<sup>38</sup> A significant proportion of women surveyed were not vaccinated against HPV. She did not know at all about the existence of such a vaccine. The examined women do not know when and how vaccination is done. They are aware, however, that it does not exempt people from regularly undergoing preventive examinations. Con-

trary to appearances, women who were vaccinated did not have much knowledge at all. According to almost all women (90.8%), spreading knowledge about HPV is inadequate. Young women should be educated about human papillomavirus and made aware of the possibility of vaccination and the benefits that follow.

## Conclusions

A small number of women were vaccinated against HPV. The main reason for the lack of this type of prophylaxis was the declared lack of knowledge about the existence of the vaccine. The self-assessment of the respondents coincides with the general knowledge, based on detailed questions, on issues related to HPV infection. The general level of respondents' knowledge is at the medium level. A higher level of general knowledge was shown by women with better education, related to medical and biological sciences, coming from larger cities, with a better financial situation. A higher level of knowledge has been demonstrated by subjects in which subjects related to human papillomavirus infection were raised during the education. At the same time, almost all respondents admitted that the dissemination of knowledge about these infections is unsatisfactory.

## References

1. Wysocki J, Bidziński M. Długotrwała skuteczność czterowalentnej szczepionki przeciwko ludzkim wirusom brodawczaka (HPV) w obserwacji 5-letniej. *Med prakt.* 2007;4:(50):32-36.
2. Grześ B, Heimrath J, Sozański L, Hercuń K. Skuteczność czterowalentnej szczepionki przeciwko HPV-Silgard w zapobieganiu i leczeniu kłykcin kończystych okolicy zewnątrznych narządów płciowych u kobiet. *Onkol Pol.* 2007;10:(4):141-144.
3. Sikorski M, Majewski S. Zmiany chorobowe związane przyczynowo z zakażeniem HPV. *Przewodnik lekarza.* 2008;1:(103):234-245.
4. Słopiecka A. Behaviour among women In the scope of cervical cancer prevention. *Studia Medyczne.* 2013;29:(2):287-291.
5. Spaczyński M, Malkowska-Walczak B, Nowak-Markwitz E. Rola cytologii i testu DNA HPV w erze szczepionki antywirusowej. *Ginekol Pol.* 2007;78:696-700.
6. Domagała B. Wirus HPV-niewidzialny zabójca kobiet. *Świat Farm.* 2011;3:36-39.
7. Nowak-Markwitz E. Zakażenia wirusem brodawczaka ludzkiego (HPV) a rak szyjki macicy. *Zakażenia.* 2009;1:92-96.
8. Miśta S. Pierwotna profilaktyka raka szyjki macicy-szczepionka przeciwko zakażeniom wirusem HPV. *Klinika.* 2015;5:(19):5076-5081.
9. Korona K, Olejek A, Waksmański B. Profilaktyka infekcji HPV w stanach przednowotworowych i raka szyjki macicy. *Lekarz.* 2007;9:80-84.
10. Majewski S. Szczepienia przeciwko genitalnym typom wirusa brodawczaka ludzkiego (HPV) w profilaktyce raka szyjki macicy i innych nowotworów. *Pediatrics.* 2011;8:270-275.
11. Nowakowski A, Kotarski J. Kliniczne postacie zakażeń HPV. *Ginekol Pol.* 2007;9:709-714.
12. Majewski S, Sikorski M. Przełom w pierwotnej profilaktyce raka szyjki macicy i innych zmian związanych z zakażeniem HPV. *Przewodnik lekarza.* 2007;1:93.
13. Miśta S. Szczepionki przeciwko zakażeniom wirusem HPV dla nastolatek-przełom w profilaktyce raka szyjki macicy. *Klinika pediatryczna.* 2008;17:(1):251-258.
14. Szyfter K, Wierzbicka M. Rola wirusa brodawczaka (HPV) w nowotworach głowy i szyi. Postępy w chirurgii głowy i szyi. 2008;2:(7):41-50.
15. Poręba R. Komentarz do „Szczepienie przeciw wirusowi brodawczaka ludzkiego (HPV) u dzieci i młodzieży jako element profilaktyki raka szyjki macicy”. *Pediatr Pol.* 2012;87:637-644. *Pediatrics Polska.* 2013;88:340-346.
16. Trojańczyk M. HPV-szczepić czy nie szczepić? *Probl Hig Epidemiol.* 2012;93:(3):623-626.
17. Hirnle L. Zakażenia wirusem HPV-problem medyczny i społeczny. *Ginekol prakt.* 2009;4:(103):8-12.
18. Suwalska A, Owczarek W, Fiedor P. Przydatność kliniczna metod wykorzystywanych w diagnostyce zmian wywołanych zakażeniem wirusem brodawczaka ludzkiego. *Pol Merk Lek.* 36:(212):129-132.
19. Nowakowski A, Kotarski J. Kliniczne postacie zakażeń HPV. *Ginekol Pol.* 2007;9:709-714.
20. Mądry E. HPV-wirus o wielu twarzach. *Family Medicine & Primary Care Review.* 2009;3:702-704.
21. Macioch T. Zapobieganie chorobom zależnym od zakażenia HPV-aspekty kliniczne i ekonomiczne stosowania szczepień profilaktycznych. *Curr Gynecol Oncol.* 2010;8:(2): 69-81.
22. Kempieńska U. Przedwczesna inicjacja seksualna jedną z przyczyn zawierania małżeństw młodocianych. *Zeszyty Naukowe WSHE.* 2011;32:111-119.
23. Filipp E. Metody planowania rodziny u nastolatek. *Ginekol prakt.* 2005;13:46-59.
24. Izbebski Z. Seksualność Polaków na początku XXI wieku. Kraków: Wyd. UJ; 2012.
25. Domagała B. Wirus HPV-niewidzialny zabójca kobiet. *Świat Farm.* 2011;3:36-39.
26. Stefanek A, Durka P. Poziom świadomości kobiet na temat profilaktyki raka szyjki macicy. *Polski przegląd nauk o zdrowiu.* 2014;1:(38):29-38.
27. Mastalerz-Migas A. Wiedza i świadomość młodych kobiet w zakresie profilaktyki raka szyjki macicy. *Family Medicine & Primary Care Review.* 2011;13:(3):443-445.
28. Jurczak A. Analiza wiedzy młodzieży dotyczącej profilaktyki zakażeń wirusem brodawczaka ludzkiego. *Family Medicine & Primary Care Review.* 2012;14:(2):160-162.
29. Szykuła A. Wiedza studentek pielęgniarstwa n temat profilaktyki raka szyjki macicy. *Pielęgn Pol.* 2013;3:(49):157-161.

30. Baran W. Ocena wiedzy kobiet z Podkarpacia na temat profilaktyki raka szyjki macicy. *Przegl Med Uniw Rzesz Nar Inst Lek w Warszawie* 2013;3:311-318.
31. Gotlin J, Szykuła A. Wiedza i postawy studentów pielęgniarstwa Warszawskiego Uniwersytetu Medycznego wobec szczepień przeciwko wirusowi brodawczaka ludzkiego-HPV. *Przegl Med Uniw Rzesz Nar Inst Lek w Warszawie*. 2012;1:98-108.
32. Mastalerz-Migas A. Wiedza i świadomość młodych kobiet w zakresie profilaktyki raka szyjki macicy. *Family Medicine & Primary Care Review*. 2011;13:(3):443-445.
33. Wyderka MI. Wiedza badanych kobiet o profilaktyce raka szyjki macicy. *Pielęgn Pol*. 2008;4:(30):262-270.
34. Lewandowska A. Wiedza kobiet na temat profilaktyki raka szyjki macicy i raka piersi. *Onkol Pol*. 2012;15:(1):5-8.
35. Błazuka U, Cieślak H. Stan wiedzy studentek Warszawskiego Uniwersytetu Medycznego na temat zakażeń HPV i związanej z nim profilaktyki. *Pielęgn Pol*. 2016;1:(59):23-29.
36. Leszczyńska K. Wiedza kobiet na temat profilaktyki raka szyjki macicy. *Wiedza i dobrostan*. 2015;2:257-270.
37. Iwanowicz-Palus G. Wiedza i postawy kobiet wobec profilaktyki raka szyjki macicy. *Pielęgn XXI w*. 2010;3:(4):32-33.
38. Chorążka A, Bieńkiewicz A. Profilaktyka raka szyjki macicy w świadomości studentek. *Zdr Publ*. 2002;112:(3):340-344.



## ORIGINAL PAPER

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# Select aspects of long-term care provision based on opinions of direct informal caregivers

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## Abstract

**Introduction.** The deteriorating health of persons of advanced age necessitates that essential health care services are provided not only by networks of health care institutions but by informal caregivers as well.

**Aim.** The aim of this study was to assess select aspects of care provision for persons requiring long-term care on the basis of opinions shared by their direct informal caregivers.

**Materials and methods.** Surveys were administered to 982 individuals providing informal care for chronically ill persons or for those with disabilities. The survey was conducted in 2017. The questionnaire contained questions concerning the dysfunctions of chronically ill or disabled persons in their daily functioning and addressed related care problems.

**Results.** Over half of the informal caretakers in the study were over 50 years of age (52.5%), had completed secondary education (45.8%), and lived mainly in cities with populations under 50 thousand (63.4%). Reconciling care-related duties with one's own professional work or studies was a problem for 43.2% of caregivers. The care tasks which entailed the greatest difficulties for caregivers were washing intimate areas after urination (57.4%) and bowel movements (55.6%) as well as total body bathing.

**Conclusions.** In the opinion of over half of the surveyed caregivers, the activity posing the greatest difficulty for those providing care for persons partially or completely immobilized and possessing physiological dysfunctions (urinary or fecal incontinence) was the washing of intimate areas of the body.

**Keywords.** care problems, informal care, sick persons, persons with disabilities

## Introduction

The occurrence of both socio-cultural and demographic changes (increasing average lifespans and an aging society) observed in Poland in the past few decades has led to an increase in the demand for long-term care. Increasing

lifespans, however, do not always entail their being of high quality. The worsening health and functioning of seniors and the raised incidence rate of chronic afflictions that require long-term care contribute to greater demand for services that are medical, care-related, or social in nature.

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 5.07.2018 | Accepted: 7.10.2018

Publication date: December 2018

Long-term care encompasses the care and continued treatment of persons who are chronically ill, disabled, or advanced in age in their home environment or, in unique circumstances when the provision of home care is hindered or made impossible, in inpatient health care facilities. Long-term care is designated for persons who are bedridden and chronically ill, who suffer from significant deficiencies in self-care, and who require round-the-clock care and continuation of treatment.<sup>1-3</sup>

The growth rate of long-term care services is slower than both the rate at which society is aging and the rate at which the number of chronically ill and disabled persons is rising. This gives rise to a need for informal caregivers to provide care. Caregivers provide assistance with the execution of daily tasks, offer emotional support, and organize medical services and social aide. Chronic disease, regardless of its nature, interferes in all areas of human functioning and can affect both subjective and objective aspects of the caregiver’s life, lowering the quality thereof in many aspects.<sup>4-6</sup>

Aim of the study

The aim of the study was to assess select aspects of care provision for persons requiring long-term care on the basis of opinions shared by their direct informal caregivers.

Material and methods

Surveys were administered to 982 persons, of which 843 (85.8%) were women and 139 (14.2%) were men, all of whom provided care for loved ones afflicted by chronic disease or disabilities. The subjects surveyed represented 11 different localities throughout Poland. The study was conducted in 2017 by trained interviewers and ambassadors of the “Razem Zmieniamy Świat” foundation (*in English: Together We Change The World*), working in co-

operation with TZMO S.A. in Toruń, Poland under the nationwide program “Damy Radę” (*in English: We Can Do It*). The participation of the caregivers in the study was voluntary and their consent was made in writing. Purposeful random sampling was employed. With this sampling method, it was possible to select entities whose management agreed to the studies being performed; entities in which there was a possibility of non-problematically establishing contact with caregivers.

The research instrument was a survey designed by the authors. The validation thereof was conducted in one of the centers in which the study was carried out. Sociodemographic questions as well as questions referring directly to the issue under analysis were taken into consideration in the survey. For all categories of sociodemographic variables, percentages were calculated separately in relation to the number of men and women participating in the study (Table 1). Intersexual differences between the categories of sociodemographic variables describing the population of men and women were assessed via a  $\chi^2$  test in the form of a G function.<sup>7</sup>

Due to the lack of statistically significant differences between the sociodemographic variables describing the population of men and women, the results of the main part of the survey have been presented in percentages where all persons included in the study, regardless of sex, equal 100%.

The questions contained in the principle part of the survey included issues concerning dysfunction in the daily functioning of chronically ill or disabled persons, care-related problems, and the possibilities of providing such persons with care. The questions concerned the caregivers’ subjective evaluation of the independence of those chronically ill or disabled persons under their care as well as their dysfunctions in daily functioning, including the

Table 1. Characteristics of the study population

Sociodemographic traits	Category	Total (n=982)		Women (n=843)		Men (n=139)		G Function
		n	%	n	%	n	%	
Age	up to 24	21	2.1	17	2.0	4	2.9	3.19 <sup>#</sup>
	25-30	34	3.5	26	3.1	8	5.7	
	31-40	104	10.6	88	10.4	16	11.5	
	41-50	307	31.3	268	31.8	39	28.1	
	over 50	516	52.5	444	52.7	72	51.8	
Education	primary	36	3.7	27	3.2	9	6.5	5.37
	trade	288	29.3	245	29.1	43	30.9	
	secondary	450	45.8	396	46.9	54	38.9	
	tertiary	208	21.2	175	20.8	33	23.7	
Place of residence	village	188	19.1	153	18.1	35	25.2	4.01
	town up to 50k	623	63.4	542	64.3	81	58.3	
	city 51-500k	141	14.4	121	14.4	20	14.4	
	city over 500k	30	3.1	27	3.2	3	2.1	

<sup>#</sup> Statistically insignificant differences between the categories of sociodemographic variables describing the population of women and men; ( $\chi^2$  test in the form of a G function)

severity of their urinary or fecal incontinence. Additionally, respondents were asked about the most frequent problems encountered by caregivers, the duration of care for the chronically ill or disabled person under their care, and the care-related activities that caused the greatest difficulties for caregivers at the beginning period of their care duties. In the case of several survey questions, respondents were able to choose more than one answer, which is why the percentages do not add up to 100%.

Results

The data in Table 1 shows that over half of the informal caregivers who filled out the survey were over 50 years of age (52.5%), had completed a secondary education (45.8%), and resided mainly in towns with populations under 50 thousand residents (63.4%).

The assessment of the independence of the chronically ill or disabled (Figure 1), shows that the majority of such persons moved with the assistance of a cane, crutch, or walker (33.7%). Equally high is the percentage of immobilized or wheel-chair bound persons (23.7%). As many as 24.7% of the persons requiring care were completely bedridden.

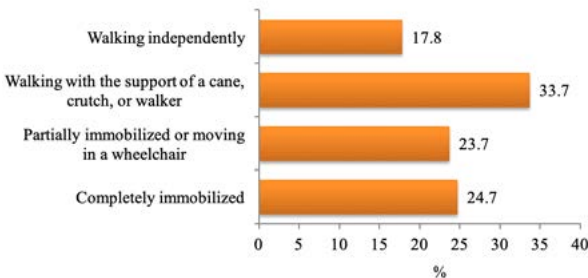


Fig. 1. Assessment of the independence of chronically ill or disabled persons

For 43.2% of caregivers, reconciling duties arising from the care of a chronically ill or disabled person with one’s professional duties or studies was a problem (Figure 2). Another significant problem proved to be domicile conditions, particularly apartment size (12.9%) and the distance separating the caregiver’s place of residence and the residence of the person requiring care (6.1%).

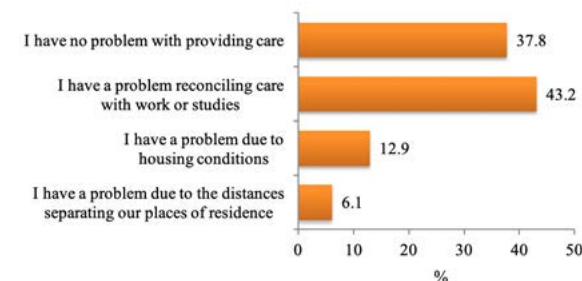


Fig. 2. Problems with providing care for a chronically ill or disabled person

Another important problem for informal caregivers was the urinary incontinence of those under their care (Figure 3). A slight degree of incontinence – characterized by minor leaking in between trips to the bathroom – affected 40% of persons, while moderate and severe degrees of urinary incontinence – the former occurring often and in significant volumes, the latter consisting in a complete lack of control over urination – affected 23.2% and 22.9% of persons, respectively.

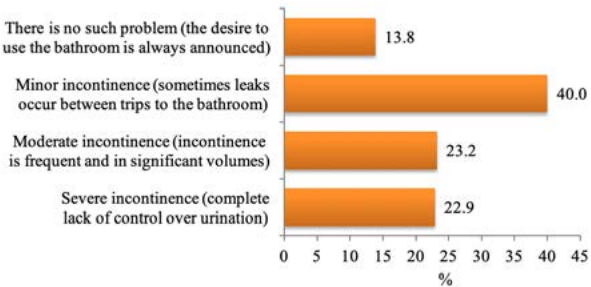


Fig. 3. Degree of urinary incontinence affecting persons requiring care

An equally significant problem proved to be fecal incontinence. A complete lack of control over bowel movements was reported by 27.8% of persons requiring care (Figure 4). For close to half of the caregivers surveyed (47.5%), difficulties related to fecal incontinence were an accidental occurrence, yet for another 27.4%, such difficulties were insignificant, for those under their care always voiced a need to have a bowel movement.

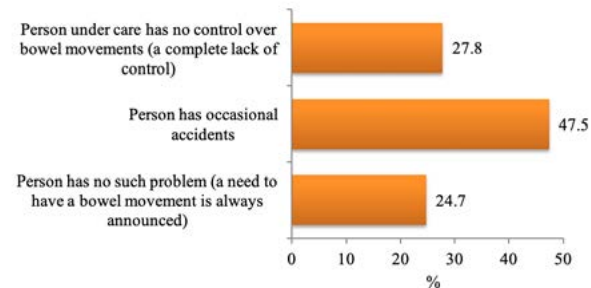


Fig. 4. Degree of fecal incontinence in persons requiring care

For 24.4% of the caregivers surveyed, the chronically ill or disabled person they cared for had been under their care for more than one 12 months, while for close to 60%, this time did not exceed 6 months (Figure 5). Care-related activities which caused caregivers the most problems during this time were washing intimate areas after urination (57.4%) and bowel movements (55.6%), followed by total body bathing (35.7%) and the washing of the person’s head (23.6%). The fewest difficulties were caused by oral hygiene maintenance (5.3%), the selection of proper absorbent underwear (6.2%), and changing bedding (7.4%).



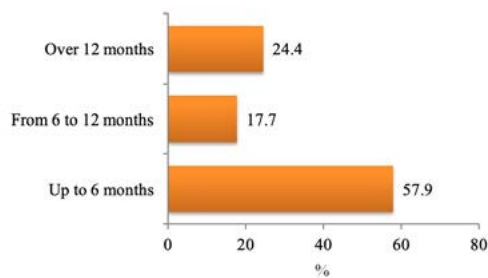


Fig. 5. Duration of care for chronically ill or disabled person

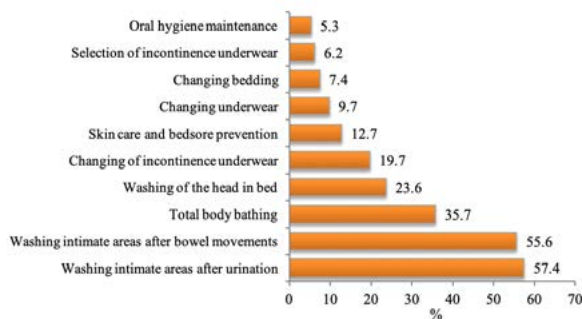


Fig. 6. Care-related activities causing the most difficulties for caregivers in the first 6 months of care

Informal caregivers’ knowledge about caring for chronically ill or disabled persons was acquired in similar percentages from nurses and physicians (Figure 7), with there being a slightly greater dependence on the former (65,6% vs. 64,5%). Respondents also indicated other sources as significant in terms of acquiring caregiving knowledge: unlicensed assistive personnel (29.9%), the Internet (22.7%), handbooks and professional medical books (18.9%). The least amount of interest was directed towards radio and television (5.3%).

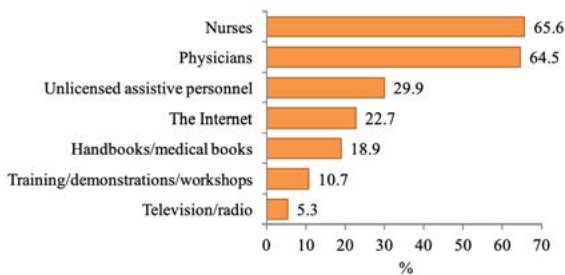


Fig. 7. Sources of knowledge about caring for chronically ill and disabled persons

Discussion

The deterioration in functioning that accompanies aging leads to a greater demand for various forms of care. The increase in the occurrence of chronic afflictions in the elderly and disabled as well as the increasing infirmity that is part of the aging process give rise to specific

health and care needs which, in consequence, leads to the elderly and disabled being more dependent on the assistance of others.<sup>8-12</sup>

One’s ability to care for oneself – one’s self-care efficiency – should be identified with independence in satisfying one’s basic life needs. These needs include movement, nourishment, control of physiological functions, and maintenance of personal hygiene.<sup>13,14</sup> The range of essential care is determined by one’s level of self-care efficiency, which in turn is contingent upon socio-economic factors, one’s age, and the degree to which one has lost independence, among other things. Results of Fidecki et al.’s study has shown that age and sex are significant factors in determining the functional fitness of seniors as well as one’s need for care.<sup>8</sup>

Analysis of the study data indicates a high degree of dependence in functioning (Figure 1). It shows that 57.4% of chronically ill or disabled persons were either persons dependent on the assistance of others, walking with either a cane, crutch, or walker, or persons partially immobilized moving around by means of a wheelchair. Subjects indicated that as many as 24.7% of the persons under their care were completely bedridden. In a study by Pruszyński et al., 77% of patients placed in care facilities displayed severe functional disability, 19.7% qualified as possessing moderate functional disability, while only 3.3 % did not display any functional disability.<sup>15</sup>

Caring for bedridden and chronically ill loved ones residing at home who do not require treatment inpatient care facilities poses a serious challenge for caregivers. However, due to existing health problems, these persons often require systematic and intensive care involving a primary care physician. Home-based care is significantly cheaper when compared to a stay in an long-term inpatient facility, and apart from such financial advantages, this form of care possesses a positive psychosocial dimension as it translates into a better state of being for the patient remaining at home while at the same time strengthening family bonds.<sup>16</sup>

Informal care of the chronically ill or disabled is usually taken up by family members. The problems encountered by direct caregivers are often very complex. Caregivers reported that it was most difficult to reconcile care-related duties with their own work or studies (43.2%) or with housing problems (12.9%) connected with the need to provide the person under their care with an extra room (Figure 2). Analysis of the housing situation of seniors conducted by Doroszkiewicz et al. confirmed the results reported above, as, from the 100 individuals surveyed aged 60 and above in the Geriatrics ward of the MSW Hospital in Białystok, a considerable majority resided with family before being transferred to the ward (46%).<sup>17</sup>

In many cases, when a senior requires constant care, one of the family members is forced to resign from work.



This is often not the result of a conscious, rational decision, but of a lack of alternatives. This is determined by cultural conditioning. Poland belongs to those countries which are extremely conservative with regard to care for seniors. The family was and still is perceived as the main care institution, and, in many circles, it is still believed that, in the situation described above, family members should sacrifice their professional ambitions to take care of the sick or disabled members of their family.<sup>18</sup>

In a study carried out by Sochy et al. concerning the quality of life of family members with terminally ill loved ones, it was shown that illness in the family affects the social and professional situation of those studied, generating a need to verify previously held life plans, which predominantly entailed decisions to shorten one's time of work.<sup>19</sup>

For most caregivers, the duration of care for chronically ill or disabled persons (Figure 5) did not exceed 6 months (57.9%). This relatively short period of caregiving, in combination with the physiological disorders of those needing care such as urinary or fecal incontinence (Figures 3 and 4), resulted in the fact that, even when such occurrences were reported as infrequent accidents, washing intimate areas after bowel movements (55.6%) or urination (57.4%) were reported (Figure 6) as activities causing the greatest difficulties in the initial period of care.

In the 2000 Norwegian study known as the *Epidemiology of Incontinence in the County of Nord-Trøndelag* (EPINCONT), the prevalence rate of urinary incontinence overall was 27.6%, reaching 10% for persons aged 20-25 and, for persons over 75, up to 40%.<sup>20</sup> This study concerned outpatient patients, not patients hospitalized due to this disease or long-term care home residents, where, according to estimates, up to 25% of care time is devoted to patients with urinary incontinence.<sup>21</sup>

Very similar results were obtained by Grochowska from 64 persons providing informal care for seniors over 65 years of age. This data shows that 28.13% of persons requiring care did not control urination, while 25% fulfilled their physiological needs in places not designated for this activity. Such a high percentage of persons in this group with physiological dysfunctions manifesting in urinary incontinence translated into a relatively high frequency of caregivers feeling burdened by care. Close to half of the surveyed caregivers (48.4%) at least sometimes felt burdened by care, one third (29.7%) – often, while one fifth (20.3%) reported never feeling burdened. Among those surveyed only one person (1.5%) always felt burdened by care.<sup>22</sup>

What were reported by caregivers as more minor care-related problems during the first 6 months of care were oral hygiene maintenance (5.3%), the changing of bedding (6.2%), and the changing of underwear (9.7%). As survey data shows, however, the selection of proper incontinence underwear in terms of size and absorben-

cy (6.2%) and the changing thereof (19.7%) also constitute significant problems (Figure 6).

The study results presented herein show that the greatest specialist support for those caring for the chronically ill and disabled was provided by nurses and physicians (Figure 7). This is a surprising yet positive finding, especially in the age of universal access to the Internet, which society considers the main source of knowledge – for caregiving information as well – and which was used by merely 22.7% of respondents. Perhaps this modest interest in the Internet as a source of information is related to the age of the caregivers (Table 1), of whom 1 in 2 was over 50 years of age (52.5%) and, as one may surmise, may have had problems with using a computer and/or the Internet. The fact that radio and television enjoyed the lowest level of interest as a source of caregiver knowledge (5.3%) is enlightening.

## Conclusions

1. The problems of direct informal caregivers responsible for persons requiring long-term care in the home environment arose both from the need to reconcile care duties with work or studies and from the short, less than 6 month period of caregiving.
2. In the opinion of half of the surveyed caregivers, while caring for persons partially or completely immobilized who possess physiological dysfunctions (urinary and fecal incontinence), the activity posing the greatest difficulty was the washing of intimate areas.

## Acknowledgement

The study was financed entirely by the “Razem zmieniamy świat” foundation in cooperation with TZMO S.A. in Toruń as part of the nationwide educational program “Damy Radę.” The authors would like to thank the ambassadors of the „Razem zmieniamy świat” foundation working in cooperation with TZMO S.A. in Toruń for help in carrying out the survey study.

## References

1. Kułagowska E, Kosińska M. Opieka długoterminowa w Polsce. Potrzeby, organizacja, bezpieczeństwo, jakość. Instytut Medycyny Pracy i Zdrowia Środowiskowego, Sosnowiec; 2014: 21-35.
2. Ziembicka DM, Marcinowicz L. Pielęgniarska opieka długoterminowa domowa – stan polskich badań naukowych. *Fam Med Prim Care Rev.* 2015;17(3): 232-236.
3. Nowak-Kapusta Z, Irzyniec T, Franek G, Drzazga B. Pielęgniarki i pielęgniarze opieki długoterminowej domowej. *Piel Pol.* 2017;3(65): 409-415.
4. Janowicz A. Rola opiekunów nieformalnych w opiece u kresu życia. Przyczynek do badań w ramach projektu European Palliative Care Academy (EUPCA). *Piel Zdr Publ.* 2014;4(2): 161-167.

5. Pyszkowska A, Naczyński M. Wsparcie społeczne, samoocena i jakość życia nieformalnych opiekunów osób starszych. *Społeczeństwo i Edukacja*. 2015;17(2): 265-276.
6. Kędra E, Borczykowska-Rzepka M, Wilusz J. Ocena jakości życia rodzin/opiekunów osób chorych na stwardnienie rozsiane dokonana w świetle przeprowadzonych badań. *Piel Pol*. 2017;3(65): 396-403.
7. Sokal RR, Rohlf FJ. Biometry. The principles and practice of statistics in biological research. W.H. Freeman and Co:San Francisco; 1969: 256-258.
8. Fidecki W, Wysokiński M, Wrońska I, Ślusarz R. Nieśprawność osób starszych wyzwaniem dla opieki pielęgniarskiej. *Probl Piel*. 2011;19(1): 1-4.
9. Zielińska A, Strugała M, Stachowska M. Ocena funkcjonowania czynnościowego, poznawczego oraz ryzyka rozwoju odleżyn, jako zasadniczych elementów w planowaniu zapotrzebowania na opiekę pielęgniarską u pacjentów w wieku podeszłym. *Probl Hig Epidemiol*. 2007;88(2): 216-222.
10. Kosińska M, Kułagowska E, Niebrój L, Stanisławczyk D. Obciążenie opiekunów osób zakwalifikowanych do opieki długoterminowej domowej. *Environ Med*. 2013;16(2): 59-68.
11. Grabowska-Fudala B, Jaracz K, Smelkowska A, Pniewska J, Buczkowska M. Obciążenie osób sprawujących opiekę nad osobami z chorobą Alzheimera. Wyniki wstępne. *Nowiny Lek*. 2013;82(1): 25-30.
12. Karczevska B, Bień B, Ołdak E, Jamiołowski J. Opiekunowie rodzinni osób starszych z otępieniem lub zaburzeniami poznawczymi w Polsce – czynniki ryzyka obciążenia opieką. *Gerantol Pol*. 2012;20(2): 59-67.
13. Ślusarz R, Beuth W, Książkiewicz B. Ocena czynnościowa chorych z krwotokiem podpajęczynówkowym. *Udar Mózgu*. 2008;10(2): 55-60.
14. Srugała M, Talarska D. Ocena sprawności podstawowej osoby w wieku podeszłym z wykorzystaniem katalogu czynności życia codziennego. *Fam Med & Care Rev*. 2006; 8: 332-35.
15. Pruszyński JJ, Cicha-Mikołaczyk A, Gębska-Kuczerowska A. Ocena wydolności czynnościowej i sprawności motorycznej osób przyjmowanych do pielęgniarskiego domu opieki w Polsce. *Przegl Epidemiol*. 2006;60: 331-338.
16. Markiewicz I, Cebulak M. Sprawność funkcjonalna pacjentów objętych domową długoterminową opieką pielęgniarską. *Probl Piel*. 2014;22(1): 42-51.
17. Doroszkiewicz H, Sierakowska M, Lewko J, Ostrowska A. Ocena stanu funkcjonowania pacjentów geriatrycznych wyznacznikiem zakresu opieki pielęgniarskiej. *Probl Piel*. 2014; 22(3): 258-264.
18. Jurek Ł. Polityka łączenia pracy zawodowej z opieką nad osobą starszą. *Acta Universitatis Lodziesis. Folia Oeconomica*. 2015;2(312): 95-110.
19. Socha B, Kutnohorska J, Zielińska M, et al. Ocena jakości życia członków rodzin pacjentów w terminalnym okresie choroby nowotworowej w warunkach domowych. *J Publ Health Nurs Med Resc*. 2011;2: 20-25.
20. Hannestad YS, Rortveit G, Sandvik H, Hunskaar S. A community-based epidemiological survey of female urinary incontinence: The Norwegian EPINCONT Study. *J Clin Epidemiol*. 2000;53: 1150-1157.
21. Tannenbaum C, DuBeau CE. Urinary incontinence in the nursing home: practical approach to evaluation and management. *Clin Geriatr Med*. 2004;20: 437-452.
22. Grochowska J. Poczucie satysfakcji oraz obciążenia obowiązkami nieformalnych opiekunów osób starszych w zależności od poziomu sprawności podopiecznych. *Med. Og Nauk Zdr*. 2014;20(1): 46-50.



## REVIEW PAPER

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# Provincial Commission for Adjudication of Medical Events as an alternative choice of indemnization of medical damage – functional and system analysis

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## Abstract

**Introduction.** Since January 1, 2012 a patient who suffered so-called medical damage has the right to choose between two alternative routes to compensate for medical damages, i.e. legal or extrajudicial.

**Aim.** To present the consequences of the out-of-court compensation for medical damages for patients on the basis of existing legal acts and the literature.

**Materials and methods.** The analysis of legal acts and literature regarding extrajudicial compensation.

**Conclusions.** The provisions regulating the out-of-court medical compensation for patients are inconsistent and unclear. As a result of the application of the regulations in force by Provincial Commission for Adjudication of Medical Events, there are difficulties for the injured patients to receive compensation or redress. The analysis of legal acts and literature shows that only court proceedings are the most effective way to assert their rights for patients who have suffered so-called medical damage.

**Keywords.** law, patient, responsibility, medical event

## Introduction

Change of the provisions of the Act on Patient Rights and the Patient Rights Ombudsman (hereinafter called the Law on Patients' Rights) was enforced on 1 January 2012.<sup>1</sup> One of the most important goals of amending the provisions of the Act on Patients' Rights was to enable patients to claim compensation for medical errors without using the only legal path. In the justification, the project promoter also pointed out that the purpose

of amending the regulations is to shorten the time of consideration of patients' cases due to medical errors. The justification stresses the fact that consideration of a case for damages for medical malpractice in court lasts on average over 4 years, while the current law introduces a solution that is to allow compensation to a patient in a 3-month period.<sup>2</sup> It should be noted that already at the stage of works over the draft of amendments to the Law on Patients' Rights was criticized by the represen-

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 2.08.2018 | Accepted: 20.10.2018

Publication date: December 2018

tatives of legal and medical circles and by associations representing patients' rights.<sup>3</sup>

On April 28, 2011, the provisions of the Act on Patient Rights, the Ombudsman for Patients' Rights and the Act on Compulsory Insurance, the Insurance Guarantee Fund and the Polish Motor Insurers' Bureau, enforced on January 1, 2012, were amended. The exceptions were the provisions regarding the submission of candidates to provincial commissions for adjudicating on medical events, which came into force within 14 days from the date of the announcement of the above Act, i.e. on June 17, 2011. A new chapter 13A was introduced, in which, i.e. the concept of a medical event and provisions determining damages and compensation in the event of medical events, as well as the legal basis for the functioning of provincial commissions for adjudicating on medical events (hereinafter referred to as a commission) were added. Procedures related to the conduct of proceedings at the Commission for Adjudication of Medical Events have been defined.<sup>4</sup>

The provisions of the Act on Patient Rights should be applied only to medical events that have occurred after 1 January 2012 events that took place before 1 January 2012 remain outside the commission's assessment.<sup>4,5</sup>

## Aim

The aim of the paper is a critical analysis of legal regulations and the functioning of extrajudicial roads in the compensation of medical damages.

The work deals with the structure and functioning of out-of-court redress at the Commission for Adjudication of Medical Events and presenting the consequences of extrajudicial roads.

## Material and methods

The above topic was based on a critical analysis of current legislation from the scope of operation of the commission for adjudication on medical events, as well as analysis of literature in Polish and foreign scientific journals dealing with the subject of medical errors and out-of-court liability without fault. In order to set the time frame for the collected legal acts, the documents were limited to the date of publication between 2011 and 2018 due to the fact of establishing a Provincial Commission for the Adjudication of Medical Events. The thematic review of literature, cross-sectional and original research was also included. The article also takes into account the professional experience of the author, who in the years 2012-2017 was a member of the Commission for Adjudication of Medical Events. The LEX Legal Information System, Legalis 2013 Legal Information System, Google Scholar, PubMed and articles searched for on the websites of publishers of scientific journals were used as the source of the literature.

## Genesis of the creation and definition of a medical event

The out-of-court medical method of compensation in Poland is an alternative for patients and is modelled on the Swedish No Fault Patient Insurance (NFPI), i.e. a guilt-free liability system.<sup>6</sup>

Guilt-free adjudication is also a global trend. In many countries, both in the world and in the European Union, there is a need to introduce a new compensation system in connection with damage to patients during treatment. The dynamic development of medical knowledge means that the traditional civil liability model, based on the principle of guilt, does not lead to full compensation of patients' claims.<sup>7</sup> In some cases, it is difficult to prove medical negligence or even organizational failures in the case of a healthcare provider.

On the other hand, there is an increase in awareness among injured patients and an increase in the number of court cases in the European Union. The waiting time for determining a case or waiting for the first hearing is extended. Problems with evidence are the reason why patients (even after a long period of legal proceedings) may not get adequate compensation.<sup>8</sup>

It is worth emphasizing that there is a serious problem related to reporting the occurrence of medical damage and related barriers reported by healthcare professionals. Research conducted by Jalal P. et al. in 2015 among healthcare workers (doctors, nurses) showed that 50% of the respondents made a medical error in relation to the patient but did not report this fact.<sup>9,10,11,12</sup> Several international reports indicated the occurrence of medical errors and their impact on the health care system. In the United States, medical errors are classified as the eighth main cause of death. In 2008, 6.3 million injuries were reported, and about 1.5 million were associated with a medical error. The estimated average total error cost was about \$13,000. In Australia (2003), approximately 1% of all hospital patients suffered from an adverse health event due to a treatment error. Medical error is an unintentional injury due to treatment or practice that is initially aimed at improving the health of patients. Since the early 90s of the last century, awareness has increased that patients are at risk of injury that can be avoided in the immediate consequences of healthcare. Damage that can be avoided evade the trust of the patient and family to the service provider and institution.<sup>13-15</sup> Revealing the error is an effective technique for restoring lost trust. Medical errors are a serious problem in healthcare, most doctors do not formally report errors, and do not even learn from them. The disclosure of medical errors in healthcare facilities is considered a key element of ongoing activities to improve patient safety and quality of care.<sup>16</sup>

In Poland, the patient or the entitled person has the right to choose between two possibilities of pursuing

claims, i.e.: court and out-of-court, that is, submitting an application to the commission.

An important issue is the fact that the commission does not rule on the extent of damage and guilt, but only the fact of an event and causal relationship between this event and damage, to be able to determine whether it is a medical event or not. A medical event is therefore an objective category, depending on the current state of medical knowledge. Disposition of art. 67a of the Act on Patient's Rights, specifies that a medical event is inconsistent with current medical knowledge regarding: diagnosis if it caused inappropriate treatment or delayed proper treatment, contributing to the development of the disease. It also includes treatment, including the performance of an operation, the use of a medicinal product or a medical device that produces effects in the form of: infection of the patient with a biological pathogen, injury or disorder of health or death of the patient.<sup>17</sup>

It is worth emphasizing that the regulations of Chapter 13a of the Act on Patient Rights regarding principles and the mode of determining compensation and redress in the case of medical events should be applied only to medical events resulting from the provision of health services in a hospital within the meaning of the Act on Medical Activity. Therefore, it should be clearly stated that commissions have no competence to adjudicate for other types of health services than hospital services. Additionally, it should be noted that a medical event refers to an act that may be committed by any medical professional, i.e. a person participating in the process of providing health care during the patient's stay in the medical entity conducting the hospital.<sup>18</sup>

### Structure of the Commission for Adjudication of Medical Events

The provisions of the Act on Patient Rights regulate the status, composition and tasks of the commission. The commissions operate at the relevant provincial offices. The commission consists of 16 members with knowledge of patients' rights and fully public rights. Half of them have at least higher education and a master's degree or other equivalent in the field of medical sciences who have been in the medical profession for at least 5 years or hold a doctorate in medical sciences. The other half must have at least higher education and a master's degree in the field of legal sciences, and should be employed in positions related to the application or creation of law for at least 5 years or have a PhD degree in legal sciences.<sup>18,19</sup>

The voivode appoints 14 members of the commission, while two members of the commission are appointed by the Minister of Health and the Patient's Rights Ombudsman. The voivode appoints 4 members from the candidates nominated by professional self-governments of doctors, dentists, nurses and midwives and laborato-

ry diagnostics, 4 - from the candidates nominated by the bar's professional self-government and self-government of legal advisors and six by social organizations acting for patients' rights. It should also be mentioned that in art. 67 g par. 5 of the Act on Patient's Rights, the legislator specified the obligation of the commission members to warranty confidentiality of information about the patient obtained during the proceedings before the commission, also after the membership in the commission has ceased. The commission's term of office is 6 years. In the event of dismissal or death of a member of the commission, the term of office of the member appointed in his place also expires on the expiry of the term of office of the entire commission.<sup>20-22</sup>

Knowledge in the field of patient rights is an obligatory requirement for all commission members. It should be pointed out that in the provisions of the Act on Patient's Rights, however, there is no requirement to check the knowledge of candidates for commission members from the above-mentioned scope. The candidates for commission members have no obligation to document the above knowledge. No form of verification was foreseen, e.g. in the form of an appropriate course or post-graduate study or even a positive result of the interview. Previous practice has shown that commission members receive training in patient rights only after receiving the nomination and not before obtaining it.<sup>23</sup>

The legislator also pointed out that the members of the commission cannot be persons convicted for intentional crime or intentional fiscal offences, legally punished by disciplinary or professional punishment, against whom a ban on a specific position, performance of a specific profession or conducting a specific economic activity or banned to conduct activities related with care, treatment, education of minors or taking care of them.<sup>24</sup>

The issue of dismissing a member of the Commission is not clearly defined by law. The regulations do not cover the dismissal of a member of the Commission in the event of avoiding the duties of a member of the provincial commission or their improper performance. There is also no appropriate body or institution to supervise and give opinions that would evaluate the work of a Commission member.

The provisions of the Act on Patient's Rights define the situation of exclusion of a member of the commission from participation in the proceedings. The first exclusion concerns the situation when a member of the commission is the applicant or remains in such a legal relationship that the result of the proceedings affects their rights and obligations. The next situation includes the circumstances in which a member of the commission remains with the person submitting the application in a relation that raises doubts as to their impartiality.

Obviously, the exclusion is also indisputable in a situation where the application is submitted by a spouse, relatives or in-laws in a straight line, but also side relatives up to the fourth degree and side affinity to the second grade of the applicant. The exclusion also applies to the relationship of adoption, care or guardianship with the applicant. The legislator does not allow the possibility of participating in commission meeting if the commission member is also a statutory representative or a representative of the applicant.<sup>25,26</sup>

A prerequisite for becoming a commission member to work in the adjudicating commission is to make a declaration on the lack of conflict of interests, which was specified in the Ordinance of the Minister of Health of December 8, 2011 on the model statement on the absence of a conflict of interest filed by a member of Provincial Commission for Adjudication of Medical Events.<sup>27</sup>

The provisions of the Act on Patients' Rights clearly show that the commission is headed by the Chairman, whose tasks include appointing a four-member commission according to the order of receipt of the request for establishing a medical incident from the alphabetical list of members, 2 of them must represent medical professions and 2 of them must represent a legal profession. In practice, the above principle of designating the composition of the commission results in the fact that it may not include a physician. In cases where the subject of the application at the commission meeting is e.g. the assessment of whether a diagnosis that could cause inappropriate treatment or delay the proper treatment of the patient, the doctor's participation in the commission should be obligatory. Another problem is the identification of an even number of members taking part in the meeting. The provisions of the Act state that in the case of an equal number of votes, the chairman's vote is decisive as the commission adopts resolutions by a majority of votes.

The competence of the competent voivode is to determine the remuneration for participation in the commission meeting. It should be noted that the above competence causes that the amount of remuneration for commission members may be different.<sup>28</sup>

### **Application for establishing a medical event**

Sine qua non condition of the entire procedure before the commission is the submission of an application by the patient or his legal representative in case of infection, injury or health disorder. However, in the case of a patient's death, this activity is performed by heirs. Thus, the legislator narrowed the catalogue of persons entitled to submit the application to establish a medical event. It should be pointed out that the above regulation in the Act on Patient Rights is inconsistent with art. 446 §3 and §4 of the Civil Code. It stems from the above

regulation in the Civil Code that if the victim's death resulted from a bodily injury or a bodily disorder, the court may award appropriate compensation to the closest family members of the deceased if his death results in a significant deterioration of their life situation, and the court may also grant to the closest members of the deceased's family an appropriate sum as compensation for the harm suffered. Regulation in the Law on Patient Rights - in comparison with the Civil Code - narrows the circle of persons entitled to compensation in the event of the patient's death. The Act also does not determine which heirs are concerned, so whether only in the first line or also further. It can be assumed, however, that they are both heirs of the will and hereditary on the basis of statute.<sup>29, 30</sup>

It should be pointed out that: "the legislator idealistically assumed, in each case, full capacity on the part of heirs. Experience shows that situations in which a financial issue arises are often extremely conflictogenic. "The legislator also determined that the application for establishing a medical incident is made to the commission responsible for the location of the hospital. It should be pointed out that the above-mentioned regulation results in the fact that proceedings for establishing a medical incident may be conducted outside the applicant's place of residence, which very often causes the costs of the proceedings to establish a medical incident to be increased. In this situation, it is justified - in the author's opinion - to clarify the provisions of the Act on Patients' Rights, which will also enable the submission of an application to the commission responsible for the place of the medical event or the place of residence of the applicant. The provisions of the Act on Patients' Rights show that the application for establishing a medical event can also be submitted by the applicant's attorney.<sup>31,32</sup> It should be added that the submitted application should be accompanied by evidence making the circumstances indicated in the application viable, e.g. medical documentation, payment confirmation, and in the event of the patient's death, the decision on the inheritance. In the light of the provisions of the Act on Patients' Rights, the applicant is required to make the medical event viable i.e. through submission of medical documentation.<sup>33,34</sup>

Another procedural element to which attention should be paid are the time limits for submitting the application. Previous practice indicates that the application is considered formally at meetings convened for this purpose or by the chairman of the commission. In the light of the above, it would be advisable to accept a solution to the examination of the application submitted by the chairman of the commission without convening a commission meeting for this purpose.<sup>35–37</sup>

The provisions of the Act on Patients' Rights also do not specify the possibility of submitting the application for consideration to another commission. It should

be pointed out that such a change would be justified in the case of allegation of reasonable doubts as to the impartiality of commission members or in the absence of an adjudication panel in a given commission in the required number of cases to be considered.<sup>22,38</sup>

The Commission shall forward the application completely and duly at the immediate request to the head of the hospital administering the hospital with which the application is related and to its insurer. The provisions of the Act on Patients' Rights define a 30-day period for the head of the therapeutic entity and its insurer to present his position from the date of receipt of the application along with the evidence to support it. Failure to present a position or presentation by a health care provider after the 30-day period from the date of receipt of the application is tantamount to acceptance of the application in the scope regarding the circumstances indicated therein and the proposed compensation amount and redress.<sup>16,18,39,40</sup>

However, the provisions of the Act on Patients' Rights do not regulate the issue of making the medical documentation available to the parties to proceedings. In practice, the commissions sending the application inform the parties about the possibility of access to medical records at the commission's headquarters. Lack of detailed regulations causes many difficulties for the parties to the proceedings.

### Competences of the Commission for Adjudication of Medical Events

The Article 67i paragraph 1 of the Act on Patients' Rights states that the purpose of the proceedings at the commission is to determine whether the event, which resulted in material or non-material damage, was a medical event. The Commission has no power to determine the extent of the damage suffered by the patient or, in the event of their death – by their heir, or to assess the compensation and redress proposed by the insurer.

The Act on Patients' Rights specifies that the commission notifies the applicant, head of the therapeutic entity running the hospital and its insurer about the date of the meeting at least 7 days before the meeting.

The provisions of the Act on Patients' Rights define directly the competences of the commission in the scope of the proceedings. These are:

- a call for explanations by the applicant, the head of the hospital administering entity with which the application relates, and persons who performed the medical profession in the hospital operating entity and other persons employed or associated with it, during the period in which, according to the application a medical event took place or has been indicated in the application as persons who may have information relevant to the proceedings and the insurer;

- request for documentation maintained by the hospital operator,
- making visits to hospital premises and facilities;
- consultation with a doctor in a given field of medicine from the list of members of the Medical Commission operating at the Patient Rights Ombudsman or a provincial consultant in a given field of medicine, pharmacy or other field applicable in health care.

Regarding the aforementioned powers of the commission, it should be pointed out that the legislator did not specify any sanctions in the event that the summoned witnesses did not appear in order to provide explanations at the commission meeting. In addition, the provisions of the Act on Patients' Rights also do not specify the date of issuing an opinion by an appointed expert. Another issue is the Commission's power to request medical records. However, the provisions of the Act on Patients' Rights do not specify whether it is admissible from all medical entities running hospitals or only from the medical entity running the hospital which is a party to the proceedings.<sup>28</sup>

An important problem related to the issued ruling by the commission is also the specification of the type of this document. If we assume that the legislator appointed commissions as entities performing specific public tasks, i.e. determining whether a medical event occurred, then the documents issued by provincial commissions will be attributable to the value of official documents. Medical errors are one of the major threats for patient safety in all countries. Medication errors are common medical mistakes that can lead to serious consequences and even death of patients. Medical errors are one of the major threats for patient safety. Medication errors are common medical mistakes that can lead to serious consequences. No presentation by the insurer or healthcare entity within 30 days, proposals for compensation and redress result in the obligation to pay the amount specified in the application. In the above situation, the commission deciding on a medical event issues a certificate in which it states the submission of an application to establish a medical event, the amount of compensation or non-contentment and the fact that the above-mentioned proposal has not been presented by the insurer or hospital operator.<sup>18,41,42</sup>

The provisions of the Act on Patients' Rights also define a complaint as a remedy for a declaration of non-compliance with the decision of the commission.<sup>33</sup>

The Commission investigates a complaint in closed session within 30 days of its receipt in a 6-person panel. It is a debatable matter to consider a complaint with a 6-person panel. It is worth recalling that commission members are people with legal or medical education. In the case of a complaint filed against the law, the decision of the commission concerns only the statement or its ab-

sence of violation of the proceedings at the commission. In this situation, the adjudication panel will only deal with the procedural and not the medical issue. The question then arises whether it is necessary for persons with medical training to consider a legal and procedural issue. At the complaint stage, there is no need to expand the composition with another two people. The provisions of the Act on Patients' Rights also do not specify the effects of including a complaint for non-compliance with a law.<sup>43,44</sup>

## Conclusion

Presented issues regards out-of-court resolution of court disputes in Poland, it raises doubts due to imprecise and unclear legal regulations, which instead of facilitating and shortening the patient's claim for damages without using the court path obstruct, among others, the process of the patient receiving compensation. Despite many reservations about the status and competence of the commission, one cannot ignore the fact that the regulation in question is assessed as breakthrough. Based on the current practice, the thesis is that introducing the regulation on out-of-court resolution of court disputes in Poland to the Law on Patients' Rights was right, but the provisions require immediate amendment because these functions are far non-transparent and imprecise. Despite the obligation to issue a decision on a medical incident by the commission, or its absence within 4 months from the date of submitting the application, the applicable provisions make it difficult to obtain redress or monetary compensation for any harm that may result from events recognized by the provincial commission for medical events. Unfortunately, until now, the Legislature has not made significant steps in the matter of amending the regulations. The appointed Provincial Commissions for Adjudication of Medical Events for the new term of 2018-2024 operate on the basis of unchanged regulations.

Currently, court proceedings still remain the most effective alternative for a patient who asserts their claims for generally understood medical damage.

## References



1. Serwach M. Odpowiedzialność za zdarzenia medyczne – nowe regulacje prawne. *Med Prakt.* 2011; 6:106.
2. Śliwka M. *Prawo pacjenta do dokumentacji medycznej a postępowanie przed wojewódzkimi komisjami do spraw orzekania o zdarzeniach medycznych. Kompensacja szkód wynikłych ze zdarzeń medycznych.* Problematyka cywilnoprawna i ubezpieczeniowa, ed. Kowalewski, Toruń: Dom Organizatora; 2011:260.
3. Ziemiak M. *Postępowanie przed wojewódzkimi komisjami do spraw orzekania o zdarzeniach medycznych. Kompensacja szkód wynikłych ze zdarzeń medycznych.* Problematyka cywilnoprawna i ubezpieczeniowa. Ed. Kowalewski, Toruń: Dom Organizatora; 2011:65-84.
4. Przybycień A, Szewczyk P. *Terra incognita, czyli o alternatywnym sposobie kompensacji szkód medycznych.* Edukacja Prawnicza Dodatek Specjalny. 2012; 1(130).
5. Sarnacka E, Jacek A, Porada S. *Odpowiedzialność szpitala z tytułu zdarzeń medycznych.* Etyczne problemy zarządzania w ochronie zdrowia, ed. Hartman J, Zalewski Z, Warszawa: Wolters Kluwer Business, 2013:182.
6. Merry A, McCall A, Smith A. *Errors, Medical Injury, Malpractice Litigation and Compensation.* Medicine and the Law. Cambridge University; 2004.
7. Elgie R, Caulfield T, Christie M. *Medical Injuries and Malpractice.* Health Law Journal; 1993.
8. Caine P. *Atiyah's Accident.* Compensation and the Law. London–Dublin; 1993:401.
9. Poorolajal J, Rezaie S, Aghighi N. Barriers to Medical Error Reporting. *Int J Prev Med.* 2015;6: 97.
10. Ghalandarpourattar S, Kaviani A, Asghari F. Medical error disclosure: The gap between attitude and practice. *Postgrad Med J.* 2012;88:130–133.
11. Bahadori M, Ravangard R, Aghili A, et al. The factors affecting the refusal of reporting on medication errors from the nurses' viewpoints: A case study in a hospital in Iran. *ISRN Nurs.* 2013:876563.
12. Smith M. Thinking ethically about medical mistakes. *J Child Neurol.* 2013;28(6):809-811.
13. O'Connor E, Coates H, Yardley I, et al. Disclosure of patient safety incidents: A comprehensive review. *Int J Qual Health Care.* 2010; 22:371–379.
14. Zaghloul A, Rahman S, Abou El-Enein N. Obligation towards medical errors disclosure at a tertiary care hospital in Dubai. *Int J Risk Saf Med.* 2016;22,28(2):93-99.
15. Kahriman İ, Öztürk H. Evaluating medical errors made by nurses during their diagnosis, treatment and care practices. *J Clin Nurs.* 2016; 25(19-20):2884-2894.
16. Zaghloul A, Elsergany M, Mosallam R. A Measure of Barriers Toward Medical Disclosure Among Health Professionals in the United Arab Emirates. *J Patient Saf.* 2018;14(1):34-40.
17. Rozporządzenie Ministra Zdrowia z dnia 8 grudnia 2011 r. w sprawie wzoru oświadczenia o braku konfliktu interesów składanego przez członka wojewódzkiej komisji do spraw orzekania o zdarzeniach medycznych [Dz. U. Nr 274, poz. 1625].
18. Rozporządzenie Ministra Pracy i Polityki Społecznej w sprawie należności przysługujących pracownikowi zatrudnionemu w państwowej lub samorządowej jednostce sfery budżetowej z tytułu podróży służbowej z dnia 29 stycznia 2013 r. [Dz. U. z 2013r., poz. 167].
19. Nesterowicz M, Wałachowska M. *Odpowiedzialność za szkody wyrządzone przy leczeniu w związku z nowym pozasądowym systemem kompensacji szkód medycznych, Kompensacja szkód wynikłych ze zdarzeń medycznych.* Problematyka cywilnoprawna i ubezpieczeniowa, ed. E. Kowalewski, Toruń: Dom Organizatora. 2011: 28-30.
20. Nesterowicz M, Wałachowska M. Odpowiedzialność za



- szkody wyrządzone przy leczeniu w związku z nowym pozasądowym systemem kompensacji szkód medycznych. *Kompensacja szkód wynikłych ze zdarzeń medycznych. Problematyka cywilnoprawna i ubezpieczeniowa* red. E. Kowalewski, Toruń: Wydawnictwo Dom Organizatora. 2011, s.28 – 29, 30.
21. Piasecki K. *Kodeks postępowania cywilnego. Komentarz do artykułów 1–366*. Tom I, System Informacji Prawnej Legalis 2013 (komentarz do art 243, teza nr 1).
22. Karkowska D. Ustawa o prawach pacjenta i Rzeczniku Praw Pacjenta. Komentarz, Warszawa, 2012:503-505.
23. Uliasz M. *Komentarz do kodeksu postępowania cywilnego*. System Informacji Prawnej Legalis. 2008.
24. Jakubecki A. *Kodeks postępowania cywilnego. Tom I. Komentarz do art. 1-729*, wyd. VII, System Informacji Prawnej Lex Komentarz do art. 424.
25. Świdarska M. *Zgoda uprawnionego a postępowanie przed wojewódzkimi komisjami odszkodowawczymi. Kompensacja szkód wynikłych ze zdarzeń medycznych*. Problematyka cywilnoprawna i ubezpieczeniowa. Tonik Dom Organizatora, Toruń. 2011:219.
26. Kowalewski E, Mogilski W. Istota i charakter ubezpieczenia pacjentów z tytułu zdarzeń medycznych. *Prawo Asekuracyjne*; 2012:13.
27. Przybycień A, Szewczyk P. *Terra incognita, czyli o alternatywnym sposobie kompensacji szkód medycznych*. Edukacja Prawnicza Dodatek Specjalny, 2011:110.
28. Rozporządzenie Ministra Zdrowia z dnia 8 grudnia 2011 r. w sprawie wzoru oświadczenia o braku konfliktu interesów składanego przez członka wojewódzkiej komisji do spraw orzekania o zdarzeniach medycznych [Dz.U.Nr 274, poz. 1625].
29. Rozporządzenie Ministra Pracy i Polityki Społecznej w sprawie należności przysługujących pracownikowi zatrudnionemu w państwowej lub samorządowej jednostce sfery budżetowej z tytułu podróży służbowej z dnia 29 stycznia 2013 r. [Dz.U.z 2013r., poz. 167].
30. Preis J. On the Legal Nature of Medical Events Coverage. *Wiadomości ubezpieczeniowe*. 2015;2:139-151.
31. Piasecki K. *Kodeks postępowania cywilnego. Komentarz do artykułów 1–366*. Tom I. *System Informacji Prawnej Legalis*. 2013 (komentarz do art 243, teza nr 1).
32. Karkowska D. Ustawa o prawach pacjenta i Rzeczniku Praw Pacjenta. Komentarz, Warszawa. 2012: 500-510.
33. Anderson J, Abrahamson K., Your Health Care May Kill You: Medical Errors, *Stud Health Technol Inform*. 2017;234:13-17.
34. Thomson Reuters Accelus, Karberg J. Medical errors and patient safety: reducing medical errors and improving patient safety. *Issue Brief Health Policy Track Serv*. 2014;29:1-18.
35. Pham J, Aswani M, Rosen M. Reducing medical errors and adverse events. *Annu Rev Med*. 2012;63:447-463.
36. Delacroix R. Exploring the experience of nurse practitioners who have committed medical errors: A phenomenological approach. *J Am Assoc Nurse Pract*. 2017;29(7):403-409.
37. Chowaniec C, Chowaniec M, Wilk M. Giving medico-legal opinions in cases with suspicion of medical mistake. part 1. between medicine and justice. *Wiad Lek*. 2017;70(3 pt 2):649-654.
38. Tallentire VR, Smith SE, Skinner J, et al. Exploring patterns of error in acute care using framework analysis. *BMC Med Educ*. 2015;16,15:3.
39. Pazokian M, Zagheri Tafreshi M, Rassouli M. Iranian nurses' perspectives on factors influencing medication errors. *Int Nurs Rev*. 2014;61(2):246-254.
40. Doskin V, Dorinova E, Kartoeva R, et al. Medical errors and conflicts in clinical practice. *Klin Med (Mosk)*. 2014;92(4):57-63.
41. Nazione S, Pace K. An Experimental Study of Medical Error Explanations: Do Apology, Empathy, Corrective Action, and Compensation Alter Intentions and Attitudes? *J Health Commun*. 2015;20(12):1422-1432.
42. Soydemir D, Seren Intepeler S, Mert H. Barriers to Medical Error Reporting for Physicians and Nurses. *West J Nurs Res*. 2017;39(10):1348-1363.
43. Smorti A, Cappelli F, Zarantonello R, et al. Medical error and systems of signaling: conceptual and linguistic definition. *Intern Emerg Med*. 2014;9(6):681-688.
44. Walczak D, Krupa D, Musiałkiewicz R. *Zadośćuczynienie i odszkodowanie za błędy medyczne oraz odpowiedzialność cywilna podmiotów leczniczych w Polsce*. Poznań: Studia Oeconomica Posnaniensia, 2015, vol. 3, no. 12.



## REVIEW PAPER

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# Influence of food-derived advanced glycation end products on health

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## Abstract

**Introduction.** Advanced glycation end products (AGEs) are compounds formed endogenously in the human body. Besides this source of AGEs, they also exist in food and can be generated during cooking. Enhanced endogenous generation and intake of dietary AGEs have physiological impact on human health and are associated with progression of many diseases, including diabetes and its complications.

**Aim.** The purpose of this review is to present the current state of knowledge about the various negative effects of advanced glycation end products on human health.

**Materials and methods.** This study is based on analysis of literature reporting the content of AGEs in food and high or low AGEs dietary interventions in human and animal subjects.

**Results.** Literature data present databases gathering description of AGEs determinations in various types of food.

**Conclusions.** Excessive consumption of AGEs-rich products, especially abundant in protein and fat or cooked for a long time at high temperature, may contribute to the deterioration of human health, including development of hypertension, insulin resistance, and diabetic complications.

**Keywords.** advanced glycation end products, AGEs, CML, diabetes, glycation

## Introduction

Advanced glycation end products (AGEs) are a heterogeneous and complex group of compounds that are generated via a spontaneous reaction called glycation or “Maillard reaction”. Glycation occurs when aldehyde or ketone group of sugar reacts with protein, nucleic acids and lipids. The most important sites which can be glycated including N-terminal amino groups of protein, especially lysine and arginine, guanyl bases of nucleotides, and amino groups of phospholipids. Also, two reactive

dicarbonyl - glyoxal and methylglyoxal are key-precursors of AGEs formed during glycation.<sup>1</sup>

The most common and well characterised AGEs include Nε-carboxymethyllysine (CML) and Nε-carboxyethyllysine (CEL). CML was described for the first time in 1985 by Ahmed. It is formed in oxidative cleavage of fructoselysine or during the reaction between glyoxal and amino group of lysine. Ahmed was also the first to describe CEL in 1997. CEL is an homologue of CML and it is formed during the reaction of methylgly-

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 2.06.2016 | Accepted: 19.07.2018

Publication date: December 2018

oxal with lysine residues of protein.<sup>2</sup> Glycation occurs in physiological conditions, however its severity and extent are associated with aging and several diseases states such as diabetes and its complications, Alzheimer's and Parkinson's diseases, cardiovascular diseases and chronic kidney disease.<sup>3-7</sup>

High levels of AGEs in serum are associated with a reduction of insulin secretion and induction of insulin resistance in human subjects.<sup>8,9</sup> Recent reports indicate that AGEs inhibit the expression of anti-apoptotic proteins and, in this way, regulate the survival of oral cancer cells.<sup>10</sup> Furthermore, AGEs promote proliferation, migration and invasion of breast cancer cells what indicate that AGEs may underlie the pathogenesis of not only diabetic complication but also cancer in diabetes.<sup>11</sup>

Harmful effects of AGEs are dependent of mechanisms of action. Firstly, increased generation of AGEs may be independent of receptors and leads to changes in protein structure, function and stability. Glycation of proteins increases of their molecular weight, alters resistance to proteolysis and ligand binding, decreases hydrophobicity, and induces of protein aggregation.<sup>12</sup> Second mechanism requires interaction between AGEs and receptors for advanced glycation end products (RAGE). This reaction after activation of kinase pathway, leads to the activation of the transcription nuclear factor kappa B which promotes transcription of proinflammatory factors and causes an increase in the formation of reactive oxygen species. Finally, enhanced oxidative stress and inflammation intensify the deleterious effects of AGEs.<sup>13</sup>

### Food-derived AGEs

Advanced glycation end products are generated endogenously, but AGEs also can be formed exogenously and get into the human body with food. One of advanced glycation end products, CML, is one of the most abundant in human body and it was one of the first to be described in food.<sup>14</sup> Both CML and CEL are the most frequent and generally accepted markers for measurement of concentration of glycation products in meals and well-representatives for whole group of AGEs.

The gastrointestinal tract is considered the first barrier against harmful dietary glycation products. Yuan et al observed that, in rats fed with diet high in AGEs, the highest content of CML in the gastrointestinal tract occurs in the ileum, little less in the jejunum, while the lowest level of CML is in the stomach.<sup>15</sup> It is known that approximately 10% of ingested AGEs are transported into bloodstream and only 30% of absorbed AGEs are excreted with urine via kidneys.<sup>16</sup> Rest of ingested AGEs remain in the body. Glycation products may bind to proteins and successively accumulate in organ tissues such as kidneys, liver, bone, heart, brain, muscle, tendons and skin what results in impairment of their functions.<sup>17</sup>

The western style diet, due to high content of in meats and processed foods, is rich in glycation products known as glycotoxins. Literature reports extensively describe the content of various glycation products in various food and methods for their determination such as liquid chromatography which is considered a gold standard for measurement of AGEs in samples. Information about tested products is collected in robust databases that contain more than 1,600 beverages and foods.<sup>18</sup> Generally, the highest content of glycation products is observed in confectioneries, what is connected with heating of products rich in reducing sugars and flour at high temperature for a long time.<sup>18</sup> The highest content of CML, CEL and N $\delta$ -(5-hydro-5-methyl-4-imidazol-2-yl)-ornithine is found in black pudding, different types of cereals, peanut butter, biscuits and rusk.<sup>19</sup> Products high in AGEs also include higher-fat and aged cheeses, butter, cream cheese, margarine, and mayonnaise.<sup>20</sup> Among drink beverages, drinks containing lactic acid bacteria and highly carbonated are the richest in AGEs.<sup>18</sup> Beef is considered a meat with the highest AGEs level among different types of meat, while lower amount of CML is observed in poultry, pork, fish.<sup>20,21</sup> The lowest average content of CML is noted in fruit and vegetables as well as juices.<sup>22</sup> Breads, yogurt, ice cream and milk belong to group of products which are relatively low in CML.<sup>20</sup>

Various types of foods in Western diets are exposed to thermal processing what makes food microbiologically safer as well as improves aroma, taste and appearance. It is known however, the cooking methods have impact on the level of AGEs. Chen and Smith proved that frying and broiling of meat at higher cooking temperature cause an increase in the CML content.<sup>21</sup> Data show that oven cooked pork meat has higher content of AGEs than meat prepared in the autoclave and braised.<sup>23</sup> Among methods which generate low amount of AGEs are steaming, stewing, and boiling. Moreover, preparation of meat dishes with the addition of sauce such as soybean or tomato sauce, markedly increase the generation of glycation products.<sup>24</sup> However, formation of new AGEs is prevented by addition of AGEs inhibitors or acidic solutions of lemon juice and vinegar to the dish.<sup>20</sup> Similarly, it is known that many compounds of natural origin, especially polyphenols, may prevent or inhibit the formation of glycation products.<sup>25</sup>

### Intake of diet high or low in AGEs

The influence of intake of a diet low or high in AGEs on human and animal health is described in many reports. Intake of dietary AGEs is related to enhanced formation of pro-inflammatory mediators, which contribute to tissue injury in patients with diabetes.<sup>26</sup>

The study conducted on group of 450 participants reveals that higher dietary intake of AGEs is correlat-

ed with higher levels of various types of AGEs in plasma and urine. A positive correlation between intake of CML, CEL and N $\delta$ -(5-hydro-5-methyl-4-imidazol-2-yl)-ornithine in meals and their free levels in blood plasma.<sup>27</sup> Similarly, 3 months intake of a diet low in AGEs leads to reduction of serum CML and methylglyoxal concentration in adult obese men. Combination of meals low in glycation products and exercise also causes a decrease in triacylglycerols and an increase in the high-density lipoprotein.<sup>28</sup>

On the other hand, Semba et al. observed that diet abundant in AGEs causes no significant changes in serum and urinary glycation products concentration in healthy adults group. The authors have reported that after 6 weeks of diet containing about 4 times more AGEs did not lead to changes in endothelial functions measured by peripheral arterial tonometry, level of inflammatory mediators as well as endogenous secretory and secretory receptor for AGEs. However, participants who had meals low in AGEs showed a significant decrease in the serum and urinary CML concentration when compared to baseline.<sup>29</sup> Furthermore, the same researchers after investigating diet and physiology of 261 subjects proved that, generally, intake of food-derived AGEs such as fried foods and meat products did not increase of the CML concentration in serum and urine.<sup>30</sup> Surprisingly, Sebekova et al. proved that AGEs level in plasma is higher in vegetarians than omnivores.<sup>31</sup> It might seem that, based on cooking techniques (higher temperature and longer heating time), participants who eat meat and meat-derived products should have higher concentration of glycation products in blood plasma. Overweight children and young people have the same concentration of plasma RAGE and lower level of fructoselysine and CML in plasma due to enhanced removal of modified proteins via kidneys what is manifested by proteinuria as compared to controls.<sup>32</sup>

Intake of food-derived AGEs by human subjects is associated with increased risk of hypertension and arterial stiffness and inflammatory activation what lead to a vascular dysfunction in patients with type 2 diabetes.<sup>33,34</sup> It is known that, consumption of a food low in AGEs decreases insulin resistance in overweight women as well as improves cardiometabolic parameters.<sup>35,36</sup> Likewise, animals representing model of diabetes fed with meals rich in AGEs exhibits deteriorated vascular complications manifested by alternations in structure of endothelial and mesangial cells as well as podocytes in renal cortex.<sup>37</sup> Moreover, analysis of embryos of mice fed with diet containing 3% of advanced glycation end products shows defects in neural tube development in the absence of hyperglycemia.<sup>38</sup> Also, intake of diet abundant in glycation products in experimental mice causes an accumulation of AGEs in Achilles tendon resulting in alternation of its properties and the development of injuries.<sup>39</sup> Induction of

systemic inflammation manifested by elevated secretion of pro-inflammatory cytokines and chemokines and liver inflammation in the absence of steatosis have also been found in case of mice fed a high-AGE diet.<sup>41,42</sup> Nevertheless, in mice with experimental induced diabetes, diet low in AGEs prevented diabetic nephropathy and was considered responsible for low AGEs content in kidneys.<sup>42</sup> Similarly, perinatal exposure to low-AGEs diet decreases AGEs content in serum and immune cell infiltration into the pancreatic islets as well as improves insulin, pro-insulin and glucagon secretion in mice susceptible to type 1 diabetes.<sup>43</sup> Evidence from animal and human studies suggest that dietary AGEs could play a role in development of various disease states. It appears that reduction of the consumption of food-derived AGEs is important to significantly reduces their harmful effects in the human body.

## Conclusions

Glycation leads to formation of advanced glycation end products which exist in food in addition to being endogenously produced. Long-time cooking at high temperatures causes an increase in the AGEs content in meals. Meals abundant in reducing sugars, protein and fat have a higher content of glycation products. Diet high in AGEs, due to their reactivity and harmful potential, is associated with higher content of AGEs in plasma and urine and has deleterious effect on human health resulting in induction of hypertension, insulin resistance, and diabetic complications. On the other hand, animal and human studies indicate that the restriction of dietary intake of AGEs may improve health conditions. Consumers, especially patients with diabetes, should remember about choosing products with low content of glycation products. It is also important to use the cooking methods generating low AGEs content such as steaming, stewing, and boiling instead of broiling and frying.

## References

1. Sadowska-Bartosz I, Galiniak S, Bartosz G. Kinetics of glycoxidation of bovine serum albumin by methylglyoxal and glyoxal and its prevention by various compounds. *Molecules*. 2014;19:4880-4896.
2. Ahmed MU, Brinkmann Frye E, Degenhardt TP, Thorpe SR, Baynes JW. N-epsilon-(carboxyethyl)lysine, a product of the chemical modification of proteins by methylglyoxal, increases with age in human lens proteins. *Biochem J*. 1997;324 (Pt 2):565-570.
3. Kim CS, Park S, Kim J. The role of glycation in the pathogenesis of aging and its prevention through herbal products and physical exercise. *J Exerc Nutrition Biochem*. 2017;21(3):55-61.
4. Vlassara H, Uribarri J. Advanced glycation end products (AGE) and diabetes: cause, effect, or both? *Curr Diab Rep*. 2014;14(1):453.

5. Li J, Liu D, Sun L, Lu Y, Zhang Z. Advanced glycation end products and neurodegenerative diseases: mechanisms and perspective. *J Neurol Sci.* 2012;317(1-2):1-5.
6. Hegab Z, Gibbons S, Neyses L, Mamas MA. Role of advanced glycation end products in cardiovascular disease. *World J Cardiol.* 2012;4(4):90-102.
7. Rabbani N, Thornalley PJ. Advanced glycation end products in the pathogenesis of chronic kidney disease. *Kidney Int.* 2018;93(4):803-813.
8. Okura T, Ueta E, Nakamura R, et al. High serum advanced glycation end products are associated with decreased insulin secretion in patients with type 2 diabetes: A brief report. *J Diabetes Res.* 2017;2017:5139750.
9. Tan KC, Shiu SW, Wong Y, Tam X. Serum advanced glycation end products (AGEs) are associated with insulin resistance. *Diabetes Metab Res Rev.* 2011;27(5):488-492.
10. Ko SY, Ko HA, Shieh TM, et al. Advanced glycation end products influence oral cancer cell survival via Bcl-xl and Nrf-2 regulation in vitro. *Oncol Lett.* 2017;13(5):3328-3334.
11. Sharaf H, Matou-Nasri S, Wang Q, et al. Advanced glycation endproducts increase proliferation, migration and invasion of the breast cancer cell line MDA-MB-231. *Biochim Biophys Acta.* 2015;1852(3):429-441.
12. Szkudlarek A, Sułkowska A, Maciążek-Jurczyk M, Chudzik M, Równicka-Zubik J. Effects of non-enzymatic glycation in human serum albumin. Spectroscopic analysis. *Spectrochim Acta A Mol Biomol Spectrosc.* 2016;152:645-653.
13. Luevano-Contreras C, Chapman-Novakofski K. Dietary advanced glycation end products and aging. *Nutrients.* 2010;2(12):1247-1265.
14. Ames JM1. Determination of N epsilon-(carboxymethyl) lysine in foods and related systems. *Ann N Y Acad Sci.* 2008;1126:20-24.
15. Yuan X, Zhao J, Qu W, et al. Accumulation and effects of dietary advanced glycation end products on the gastrointestinal tract in rats. *Int J Food Sci Technol.* 2018;53:2273-2281.
16. Koschinsky T, He CJ, Mitsuhashi T, et al. Orally absorbed reactive glycation products (glycotoxins): an environmental risk factor in diabetic nephropathy. *Proc Natl Acad Sci USA.* 1997;94(12):6474-6479.
17. Semba RD, Nicklett EJ, Ferrucci L. Does accumulation of advanced glycation end products contribute to the aging phenotype? *J Gerontol A Biol Sci Med Sci.* 2010;65(9):963-975.
18. Takeuchi M, Takino J, Furuno S, et al. Assessment of the concentrations of various advanced glycation end-products in beverages and foods that are commonly consumed in Japan. *PLoS One.* 2015;10(3):e0118652.
19. Scheijen LJ, Clevers E, Engelen L, et al. Analysis of advanced glycation endproducts in selected food items by ultra-performance liquid chromatography tandem mass spectrometry: Presentation of a dietary AGE database. *Food Chem.* 2016;190:1145-1150.
20. Uribarri J, Woodruff S, Goodman S, et al. Advanced glycation end products in foods and a practical guide to their reduction in the diet. *J Am Diet Assoc.* 2010;110(6):911-16.e12.
21. Chen G, Smith JS. Determination of advanced glycation endproducts in cooked meat products. *Food Chem.* 2015;168:190-195.
22. Hulla GLJ, Woodsideb JV, Amesc JM, Cuskelly GJ. Nε-(carboxymethyl)lysine content of foods commonly consumed in a Western style diet. *Food Chem.* 2012;131(1):170-174.
23. Mitra B, Lametsch R, Greco I, Ruiz-Carrascal J. Advanced glycation end products, protein crosslinks and post translational modifications in pork subjected to different heat treatments. *Meat Sci.* 2018;145:415-424.
24. Chao P, Hsu C, Yin M. Analysis of glycativ products in sauces and sauce-treated foods. *Food Chem.* 2009;113(1):262-266.
25. Sadowska-Bartos G, Bartosz G. Prevention of protein glycation by natural compounds. *Molecules.* 2015;20:3309-3334.
26. Uribarri J, Stirban A, Sander D, et al. Single oral challenge by advanced glycation end products acutely impairs endothelial function in diabetic and nondiabetic subjects. *Diabetes Care.* 2007;30:2579-2582.
27. Scheijen LJ, Hanssen NMJ, van Greevenbroek MM, et al. Dietary intake of advanced glycation endproducts is associated with higher levels of advanced glycation endproducts in plasma and urine: The CODAM study. *Clin Nutr.* 2018;37(3):919-925.
28. Macías-Cervantes MH, Rodríguez-Soto JM, Uribarri J, Díaz-Cisneros FJ, Cai W, Garay-Sevilla ME. Effect of an advanced glycation end product-restricted diet and exercise on metabolic parameters in adult overweight men. *Nutrition.* 2015;31(3):446-451.
29. Semba RD, Gebauer SK, Baer DJ, et al. Dietary intake of advanced glycation end products did not affect endothelial function and inflammation in healthy adults in a randomized controlled trial. *J Nutr.* 2014;144(7):1037-1042.
30. Semba RD, Ang A, Talegawkar S, et al. Dietary intake associated with serum versus urinary carboxymethyl-lysine, a major advanced glycation end product, in adults: the Energetics Study. *Eur J Clin Nutr.* 2012;66(1):3-9.
31. Sebeková K, Krajciová-Kudláčková M, Schinzel R, Faist V, Klvanová J, Heidland A. Plasma levels of advanced glycation end products in healthy, long-term vegetarians and subjects on a western mixed diet. *Eur J Nutr.* 2001;40(6):275-281.
32. Sebeková K, Somoza V, Jarcusková M, Heidland A, Podracká L. Plasma advanced glycation end products are decreased in obese children compared with lean controls. *Int J Pediatr Obes.* 2009;4(2):112-118.
33. Mirmiran P, Yousefi R, Mottaghi A, Azizi F. Advanced glycation end products and risk of hypertension in Iranian adults: Tehran lipid and glucose study. *J Res Med Sci.* 2018;23:43.

34. Di Pino A, Currenti W, Urbano F, et al. High intake of dietary advanced glycation end-products is associated with increased arterial stiffness and inflammation in subjects with type 2 diabetes. *Nutr Metab Cardiovasc Dis*. 2017;27(11):978-984.
35. Mark AB, Poulsen MW, Andersen S, et al. Consumption of a diet low in advanced glycation end products for 4 weeks improves insulin sensitivity in overweight women. *Diabetes Care*. 2014;37(1):88-95.
36. Baye E, Kiriakova V, Uribarri J, Moran LJ, de Courten B. Consumption of diets with low advanced glycation end products improves cardiometabolic parameters: meta-analysis of randomised controlled trials. *Sci Rep*. 2017;7(1):2266.
37. Lv X, Lv GH, Dai GY, Sun HM, Xu HQ. Food-advanced glycation end products aggravate the diabetic vascular complications via modulating the AGEs/RAGE pathway. *Chin J Nat Med*. 2016;14(11):844-855.
38. Li RL, Zhao WW, Gao BY. Advanced glycation end products induce neural tube defects through elevating oxidative stress in mice. *Neural Regen Res*. 2018;13(8):1368-1374.
39. Skovgaard D, Svensson RB, Scheijen J, et al. An advanced glycation endproduct (AGE)-rich diet promotes accumulation of AGEs in Achilles tendon. *Physiol Rep*. 2017;5(6). pii:e13215.
40. Sowndhar Rajan B, Manivasagam S, Dhanusu S, et al. Diet with high content of advanced glycation end products induces systemic inflammation and weight gain in experimental mice: Protective role of curcumin and gallic acid. *Food Chem Toxicol*. 2018;114:237-245.
41. Patel R, Baker SS, Liu W, et al. Effect of dietary advanced glycation end products on mouse liver. *PLoS One*. 2012;7(4):e35143.
42. Zheng F, He C, Cai W, Hattori M, Steffes M, Vlassara H. Prevention of diabetic nephropathy in mice by a diet low in glycoxidation products. *Diabetes Metab Res Rev*. 2002;18(3):224-237.
43. Borg DJ, Yap FYT, Keshvari S, et al. Perinatal exposure to high dietary advanced glycation end products in transgenic NOD8.3 mice leads to pancreatic beta cell dysfunction. *Islets*. 2018;10(1):10-24.



## REVIEW PAPER

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# The effect of alcohol on neuroglia in the developing brain and in adults

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### Abstract

**Introduction.** During puberty, the young body undergoes transformation not only within the reproductive and hormonal systems, but also significant changes in the central nervous system (CNS). Matured neural connections improve the integration of distant brain regions, the plasticity of neurons increases, and thus specialization of the brain occurs in the performance of specific tasks. During these transformations, both neurons and the accompanying neuroglia are sensitive to all toxic factors, among which ethanol occupies a special place. It causes an increase in the activity of glial cells, which by directing pro-inflammatory cytokines directly contribute to the death of apoptotic neurons. A long-lasting and irreversible impairment of brain function, especially in the hippocampus occurs as a result of alcohol abuse during the period of development.

**Aim.** This paper presents an overview of current knowledge about the effects of alcohol on neuroglia in the developing brain and in adults.

**Materials and methods.** The literature review of the following databases has been conducted: EBSCO, PubMed, Science Direct, Springer Link.

**Conclusions.** The results of alcohol research have shown that it affects the neurotransmission and fluidity of cell membranes, changing the activity of neurons. By binding to GABA receptor (GABA) and N-methyl-D-aspartate receptors (NMDA receptor for glutamate), ethanol suppresses brain function. In addition to increased sensitivity and susceptibility to the addictive effects of ethanol, the neurogeneration activity is intensified followed by the induction and release of pro-inflammatory cytokines, which in the first stage disrupt the cortical function hindering logical thinking and disrupting the limbic system, directly affecting the memory and learning processes. Next, the cerebellum is attacked, which results in the impairment of balance and motor coordination, and consequently acts on the brain stem, directly affecting the respiratory and circulatory control centers.

**Keywords.** brain, alcohol, neuroglia

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 10.09.2018 | Accepted: 23.10.2018

Publication date: December 2018

Krawczyk-Marć I, Galiniak S, Sęk-Mastej A, Marć M, Orkisz S, Wawrzyniak A. *The effect of alcohol on neuroglia in the developing brain and in adults.* Eur J Clin Exp Med. 2018;16(4):335–340. doi: 10.15584/ejcem.2018.4.11

## Introduction

For a long time it was believed that glial cells are mainly supportive, nutritious and adjuvant to neurons. In the era of the science progress and the development of histological techniques, the knowledge about neurocognitive cells has been extended to include their active participation in the neuronal functions of information transfer and neuronal plasticity, which forms the basis in the processes of learning and memory. Glial cells alone do not conduct nerve impulses, but supports neurons in this function. Neuroglia has important functions in forming synaptic structures, and thus in synaptic transmission, and participates in developmental myelination of nerve fibers.<sup>1</sup> The results of alcohol research showed not only increased susceptibility of the brain to the addictive effects of ethanol, but also increased activity of glial cells that contribute to the release of factors associated with inflammation. The consequence of this process are morphological changes in myelin sheaths leading to the death of apoptotic neurons. In addition, these processes are accompanied by impairment of cognitive abilities and disturbances in behavioral responses. Interactions between glial cells suggest that therapies of alcoholism based on the pathology of specific types of neuroglia may contribute to the understanding of interactions between different brain cells.<sup>2</sup>

## Alcoholism

According to the definition of the National Institute of Alcohol Abuse, alcoholism is a chronic, recurrent cerebral disease, consisting of compulsive use of alcohol, loss of control over its consumption and a negative emotional state in the absence of it. The consequences of alcohol abuse are various pathologies e.g. behavioral or neurological ones, which are dependent on metabolic disorders at the cellular level. Such disorders in the nervous system contribute to the incorrect exchange of information between brain centers that control alcohol consumption and regions involved in emotional and cognitive regulation. This leads to significant changes in the structure and functioning of the brain, and neuropathological consequences lead to dementia. Alcohol-induced brain changes are also reflected in structural damage in the gray and white matter.<sup>3</sup>

## Glial cells

CNS disorders are more and more often considered not only related to neuronal dysfunction, but to a large extent controlled by inflammatory processes controlled by glial cells. In many neurodegenerative diseases, e.g. in multiple sclerosis (MS), Alzheimer's disease (AD), stroke or Parkinson's disease (PD), glial cells are involved in the disease process.<sup>4,5</sup> The normal activity of neurons and their survival are fully dependent on interaction with glial cells that support them in neurotrans-

mission, strengthen functional potentials, participate in the repair of brain damage, act neuroprotective and are involved in providing substrates necessary for the production of many neurotransmitters, as well as in their decomposition. Ependymal glia, astrocytes, oligodendrocytes are the basic cells present in CNS apart from the neurons.<sup>1</sup> Microglia and astrocytes are responsible for the immunological functions and play a key role in the inflammatory response. It is presumed that astrocytes can be formed indirectly from radial glia, one of which is the formation of scaffolding for newly formed neurons.<sup>5</sup>

One of the astrocyte divisions relates to their ability to respond to CNS damage. Inactive, resting and reactive astrocytes were distinguished. The resting type exists in normal, unchanged glial tissue in the CNS, while reactive astrocytes locate closer to the site of injury and together with microglia participate in the formation of glial scars.<sup>6</sup> Astrocytes support a number of activities necessary for the functioning of neurons, including participation in the formation and maintenance of selective, necessary for the proper functioning of the CNS blood-brain barrier (BBB) thus protecting the brain from the influx of toxic substances and ions, regulate extracellular concentrations of ions and neurotransmitters, synthesize metabolic substrates for neurons (glycogen, sterols and lipoproteins), remove excess neurotransmitters (glutamate) released by active neurons.<sup>7</sup> In addition, they secrete growth substances such as nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) or fibroblast growth factor (FGF) playing important roles in the repair and growth processes of neurons. Like most glial cells, astrocytes may play a primary role in CNS diseases<sup>8</sup>. Microglia ensures maintenance of homeostasis in the CNS, monitors the survival of neurons and acts as immunologically competent cells. The microglial cells originate from macrophages located outside the nervous system and are dispersed throughout the CNS. They migrate to the nervous system during fetal life. In the normal brain and spinal cord, microglia cells are inactive, which is why they are called rest microglia. When damage occurs in the CNS, the number of these cells increases rapidly and become effector cells of the immune system. Activation of microglia results in a change in their morphological characteristics. Their proliferation, changes in receptor expression and change in function are induced, and the stimulus that contributes to such changes is most likely the depolarization of the neuronal membrane that arises as a result of damage. A significant part of activation of microglia also play pro-inflammatory cytokines, growth factors, complement proteins, free radicals, neurotoxins, nitric oxide, prostaglandins, ATP and stimulating amino acids. Activated microglial cells are able to produce many growth and inflammatory factors.<sup>9-13</sup>



Ependymal glia plays key roles in the processes of CNS development and physiology. Under normal conditions, specialized ciliated ependymal cells create a cerebrospinal fluid barrier - the brain, participating actively in cellular filtration in CNS.<sup>14</sup>

The speed and efficiency of nerve impulses transmission within the nervous system is based on the presence of myelin sheaths - structures produced by oligodendrocytes, which protrusions form a spiral membrane around the axons of many neurons. Oligodendrocytes appear and differentiate last in the developing brain. They actively participate in the metabolic transformation of neurons due to the possibility of supplying them with iron.<sup>15</sup> Oligodendrocytes are mainly associated with the white matter of the brain, and their main functions include the formation of myelin sheaths around neuronal scars. Damage to white matter and loss of oligodendrocytes are features of many neurodegenerative diseases. In response to oligodendrocyte damage, oligodendrocyte precursor cells (OPCs) initiate their proliferation and differentiation for remyelination. During the destruction of oligodendrocytes, their cytoplasm vacuoles and their nucleus becomes pycnotic. Although the mechanisms of oligodendrogenesis and remyelination in CNS diseases are still largely unknown and under-researched, support for other glial cells and neurons is necessary for the proliferation and differentiation of OPC.<sup>16-18</sup> Understanding these complex glial-neuronal interactions may contribute to the treatment of brain injuries and neurodegenerative diseases.<sup>1,19</sup>

### Effect of alcohol on glia and central nervous system (CNS) structures

Post-mortem examinations in humans have shown that long-term alcohol intake leads to myelin damage to various degrees, causing its damage at the macroscopic level. Disorders of myelin sheaths have been observed in diseases such as Marchiafavy-Bignami's disease, Wernicke-Korsakoff syndrome, hepatic encephalopathy, central pontine myelinolysis, alcoholic cerebellar degeneration, and these mainly affect the areas of the white matter of the brain. In these disorders, BBB damage occurs or nutritional deficiencies associated with lack of thiamine occur.<sup>20</sup>

One of the areas most exposed to ethanol is the corpus callosum (CC), which is the place where information is transmitted between the right and left hemispheres of the brain. Human CC begins to develop around the fifth week after fertilization, at the time of formation of brain follicles and continues throughout the second trimester. During this period of life, the developing brain is the most sensitive to alcohol. This area of the white matter consists mainly of about 200 million myelinated axons, which carry nerve impulses to the receptors, glial cells - mainly oligodendrocytes and blood vessels.<sup>21</sup> CC is an in-

tegral part of motor function and is involved in higher cognitive processes such as verbal learning, memory, processing of abstract or complex concepts.<sup>22</sup>

In studies relating to the CC area in alcoholism, it has been shown that there is a significant reduction of oligodendrocytes and a decrease in the expression of genes associated with specific myelin proteins such as: myelin basic protein (MBP), myelin proteolipid protein (PLP), myelin-associated glycoprotein (MAG) or 2'3'-cyclic nucleotide 3' phosphodiesterase (CNP) that are necessary for its production.<sup>23</sup> In the case of CC the strongest atrophy is observed in its parts: trunk (body), genu and splenium. This applies mainly to damage to sheaths and blood vessels.<sup>24</sup> Alcohol disturbs the expression of major oligodendrocyte and myelin proteins, and during prenatal development it can induce oligodendrocyte apoptosis, leading to drastic reduction of already differentiated oligodendrocytes and their progenitor cells in the CC area. After discontinuation of exposure to alcohol, the populations of these cells return to the original number. However, it has been shown that in young adult mice there are shortages in the level of MBP or in the structure of nerve fibers in the CC area.<sup>25,26</sup>

The CC atrophy in alcoholics is correlated with the consumption of alcohol throughout all life. It is particularly evident in the prefrontal area of CC in patients with Wernicke's alcohol encephalopathy, and the extreme manifestation of alcohol toxicity in CC is Marchiafava-Bignami disease, which mainly affects older alcoholics. It is characterized by demyelination, necrosis and cystic degeneration of the middle layer of CC.<sup>24</sup>

Other areas of the brain exposed to the harmful effects of alcohol are the forebrain and the cerebral cortex, which are the first to manifest disorders related to motor coordination and disturbances in the thinking process. The effect of these changes is the loss of control over emotions, increased memory loss for which the midbrain is responsible, and as a consequence, the most important vital activity centers located in the brain stem are damaged.<sup>27-29</sup>

Animal studies show that high doses of alcohol inhibit the growth of new neurons, and this deficiency causes long-term deficits in key areas of the brain such as the hippocampus.<sup>30,31</sup> Even a small dose of alcohol, especially during adolescence, contributes directly to the reduction of its volume and difficulties in acquiring knowledge. Until recently, it was assumed that the number of neurons in the adult brain was established early in life, but it turned out that new cells are generated in adults by neurogenesis. They originate from stem cells that can divide without limitations, renew and initiate the growth of different cell types. Discovery of brain-stem cells and neurogenesis in adults allowed a new way to look at the problem of alcoholic changes in the brain.<sup>32</sup>

Drinking alcohol during pregnancy can cause many changes in the brain of the developing fetus, which are associated with both physical and mental development. The most known and the most serious syndrome of congenital malformations in children is a group of conditions, called fetal alcohol syndrome (FAS). Children with FAS have different facial features and are significantly smaller than average. Their brains contain fewer nerve ganglia and fewer neurons able to function properly.<sup>33,34</sup> Incorrect activation of the developing immune system can have long-term negative consequences. There is an increase in the level of such pro-inflammatory cytokines as: IL-1 $\beta$ , TNF- $\alpha$ , CD11b, CCL4 and TGF- $\beta$ , which activates microglial cells especially in the hippocampus. Activation of microglia contributes to deficits in learning and memory, especially in children diagnosed with FAS. The effect of these activities is the induction of neuroimmune responses, resulting in long-term changes in cognitive functions and behavior.<sup>35</sup>

Particular sensitivity to harmful effects of alcohol during adolescence was observed in the olfactory and peri-nasal cerebral cortex areas of rats. In these areas there are time intervals known as “windows” with a decidedly high and selective susceptibility to the harmful effects of alcohol. Ethanol induces sensitization and potentiation of neuronal conduction along with intense prefrontal cortex activation, predisposing to increased alcohol intake and addiction in adult life.<sup>36</sup>

Glial cells are actively involved in the immune response in the CNS, and their dysregulation has a significant impact on brain damage leading to neurodegeneration. Glial cells play a significant role in the CNS immune response. Ethanol has immunomodulatory activity and induces specific changes in tissues and organs. These effects depend mainly on the type of cells and the dose of ethanol. Even low ethanol concentrations stimulate inflammatory processes in the brain and glial cells by increasing the expression of cytokines and inflammatory mediators and by activating signaling pathways involving kinases and inflammatory transcription factors. Receptors that recognize the so-called Molecular patterns associated with pathogens that include Toll-like receptors (TLRs) such as TLR4 / IL-1RI can be involved in ethanol-mediated inflammation because they activate specific signaling pathways inside the cells and by blocking them eliminate the production of alcohol-induced status mediators inflammatory and cell death.<sup>2</sup> Chronic alcohol exposure induces atrophic features in astrocytes, mainly in the hippocampus, causing a reduction in their number in the general glial cell population. The reaction of astrocytes to pathogenic alcohol exposure is not limited only to changes in their number, morphology or development, but disrupts the regulation of neuro-inflammatory processes, calcium signaling and inhibits the neurotransmission and water-electrolyte balance.

As a result of the action of alcohol, there is a simultaneous change in the number of astrocytes and a decrease in the number of their markers, mainly glial fibrillary acid protein (GFAP), which may be the direct cause of degeneration of neurons.<sup>3</sup>

The harmful effect of alcohol contributes to the damage of glial cells, disrupting the activity of neurons. Neuronal signals, which directly translate into the physiology of glial cells under the influence of alcohol, significantly interfere with the development, morphology, physiology and gene expression of astrocytes, oligodendrocytes, and microglia. The effects of alcohol on oligodendrocytes were among the first to draw the attention of clinicians because they caused serious neurological and cognitive disorders in connection with myelin pathology.<sup>3,37</sup>

Long-term alcohol abuse usually leads to loss of the white matter of the brain and impairment of the executive function. In addition to chronic degenerative neuropathology, alcoholics are predisposed to the development of potentially life-threatening brain stem damage due to a deficiency of thiamine, which has no toxic effect on neuroglia, myelin sheaths and microcirculation.<sup>38</sup>

The process of myelination of cortical neurons increases during puberty, increasing the speed and efficiency of nerve conductivity, improving communication between different areas of the brain, leading to rapid neurological and neurochemical changes. New connections between neurons which is closely correlated with pulse control, memory, speech and movement are created. During embryonic development, mainly glial cells are exposed to teratogenic effects of ethanol.<sup>39,40</sup>

Destructive, apoptotic effects of alcohol on oligodendrocytes, especially in the areas of CNS white matter and neurons in the developing brain, may explain the wide range of neuropsychiatric disorders as a consequence of even short-term exposure to alcohol during fetal life. Destroying oligodendrocytes that begin to myelinate axons can lead to long-term and irreversible neurobehavioral disorders. Sensitivity of neurons to apoptosis is associated with the period of rapid synaptogenesis, while oligodendrocytes coincide during the most intense myelination.<sup>32</sup> Oligodendrocytes have been shown to undergo maturation changes in the third trimester of pregnancy in the macaque. The emerging oligodendrocyte precursor cells first differentiate into promyelinating cells and then into the myelinating oligodendrocyte.<sup>39</sup>

It is not known whether the alcohol inducing oligodendrocyte apoptosis is dependent on the same mechanism (blockade of NMDA glutamate receptors and hyperactivation of GABA receptors), which causes neuroapoptosis. Existing signaling between neurons and oligodendrocytes via synapses, suggests similar mechanisms of cell surface receptors triggering these two toxic phenomena. The specificity of alcohol-induced apopto-

sis lies in the fact that the cell death of both neurons and oligodendrocytes is mutually symmetrical. The death of brain cells exposed to alcohol is accurately reflected by the same number and distribution of dying cells among homologous populations of cells in the opposite hemisphere. This feature of alcohol neurotoxicity can significantly reduce the ability to recover function, because the extent of recovery can depend on the availability of intact opposite populations of cells with similar functional properties.<sup>39</sup>

In addition to the impairment of myelination, even short-term exposure to alcohol disturbs the processes of gliogenesis, weakens immune function and the time of inflammatory reactions, leading to increased susceptibility to infection. The consequence of these changes is the atrophy of the brain in adults and the reduction of glial cells mainly in the hippocampus.<sup>3</sup> Through the direct influence of alcohol on neuroglia, specific neurocognitive proteins are damaged, which contributes to the formation of oxidative stress and loss of metabolic support for neurons, which also interferes with neurogenesis.<sup>41,42</sup>

Due to the key roles of astrocytes and oligodendrocytes in neurotransmission and signal transduction, these cells most likely play a central role in the molecular mechanisms underlying communication disorders associated with alcoholism between different areas of the brain. It has been shown that there are markers of astrocytes that change in response to ethanol exposure or during its discontinuation. These include intercellular protein, glutamate transporters, and enzymes associated with glutamate and GABA metabolism. Both changes in proteins and their regulatory pathways cause dysfunction of gray and white neurons in the CNS. In addition, alcohol alters the expression of astrocytes and myelin proteins as well as oligodendrocyte transcription factors relevant to the maintenance and plasticity of myelin sheaths. These changes accompany DNA and histone modifications resulting in abnormal gene expression and protein translation.<sup>3</sup>

It has also been shown that alcohol may cause permanent changes in the regulation of cytokines and the sensitivity of the hypothalamic-pituitary-adrenal axis, resulting in an immunosuppressive effect, which may increase susceptibility to infection.<sup>43-45</sup>

In conclusion, alcohol is a well-known cytotoxic agent that causes various types of damage in the brain. Even short-term brain exposure to alcohol during puberty shows a long-term impairment of the brain function that does not disappear with age. Changes in the adolescent brain are difficult to detect because they have a significant impact on long-term thinking and memory processes. Understanding the mechanisms of alcohol influence on long-term memory and the ability to learn people who abuse alcohol, will allow the appropriate prevention of alcohol addiction treatment.

## Conclusions

- Alcohol consumption causes structural and functional changes in the brain cells.
- Changes in the brain caused by alcohol are irreversible.
- Exposure to ethanol during puberty has a significant impact on the limbic system responsible for memory and learning processes, causing cognitive deficits and behavioral disorders during adulthood.
- During the development and puberty period, alcohol can cause irreversible changes that affect a person's life.

## References

1. Jäkel S, Dimou L. Glial cells and their function in the adult brain: a journey through the history of their ablation. *Front Cell Neurosci.* 2017;11:24. doi: 10.3389/fncel.2017.00024
2. Blanco AM, Guerri C. Ethanol intake enhances inflammatory mediators in brain: role of glial cells and TLR4/IL-1RI receptors. *Front in Biosci.* 2007;12: 2616-2630.
3. Miguel-Hidalgo JJ. Molecular neuropathology of astrocytes and oligodendrocytes in alcohol use disorders. *Front MolNeurosci.* 2018; 20:11:78. doi: 10.3389/fnmol.2018.00078
4. Sofroniew MV. Astrocyte barriers to neurotoxic inflammation. *Nat Rev Neurosci.* 2015;16(5):249-63.
5. Domingues HS, Portugal CC, Socodato R, Relvas JB. Oligodendrocyte, astrocyte, and microglia crosstalk in myelin development, damage, and repair. *Front Cell Dev Biol.* 2016;4:71. doi: 10.3389/fcell.2016.00071
6. Nash B, Ioannidou K, Barnett S.C. Astrocyte phenotypes and their relationship to myelination. *J Anat.* 2011;219:44-52.
7. Correale J, Farez MF. The role of astrocytes in multiple sclerosis progression. *Front Neurol.* 2015;6:180. doi: 10.3389/fneur.2015.00180.
8. Sofroniew M.V. Astroglisis. *Cold Spring HarbPerspect Biol.* 2015;7(2): a020420. doi: 10.1101/cshperspect.a020420.
9. Arcuri C, Mecca C, Bianchi R, Giambanco I, Donato R. The pathophysiological role of microglia in dynamic surveillance, phagocytosis and structural remodeling of the developing CNS. *Front MolNeurosci.* 2017;10:191. doi: 10.3389/fnmol.2017.00191
10. Ginhoux F, Prinz M. Origin of microglia: current concepts and past controversies. *Cold Spring HarbPerspect Biol.* 2015;7(8): a020537. doi: 10.1101/cshperspect.a020537.
11. Achur RN, Freeman WM, Vrana KE. Circulating cytokines as biomarkers of alcohol abuse and alcoholism. *J NeuroimmunePharmacol.* 2010;5(1):83-91.
12. Doremus-Fitzwater TL, Gano A, Panaccia JE, Deak T. Male adolescent rats display blunted cytokine responses in the CNS after acute ethanol or lipopolysaccharide exposure. *PhysiolBehav.* 2015;148:131-44.
13. Walter TJ, Vetreno RP, Crews FT. Alcohol and stress activation of microglia and neurons: brain regional effects. *Alcohol ClinExp Res.* 2017; 41(12), 2066-2081

14. Jiménez AJ, Domínguez-Pinos MD, Guerra MM, Fernández-Llebrez P, Pérez-Figares JM. Structure and function of the ependymal barrier and diseases associated with ependyma disruption. *Tissue Barriers*. 2014;2.doi: 10.4161/tisb.28426
15. Wawrzyniak-Gacek A. Distribution of various types of oligodendrocytes and cellular localisation of iron in the frontal cortex of the adult rat. *Folia Morphol*. 2002;61(2):115–121.
16. Edgar N, Sibille E. A putative functional role for oligodendrocytes in mood regulation. *Transl Psychiatry*. 2012;2.doi: 10.1038/tp.2012.34.
17. Dulamea AO. Role of oligodendrocyte dysfunction in demyelination, remyelination and neurodegeneration in multiple sclerosis. *AdvExp Med Biol*. 2017; 958: 91-127.
18. Tauheed AM, Ayo JO, Kawu MU. Regulation of oligodendrocyte differentiation: Insights and approaches for the management of neurodegenerative disease. *Pathophysiology*. 2016;23(3):203-210.
19. Bugiani M, Postma N, Polder E, et al. Hyaluronan accumulation and arrested oligodendrocyte progenitor maturation in vanishing white matter disease. *Brain*. 2013;136(Pt 1):209-222.
20. Zahr NM, Pfefferbaum A. Alcohol's effects on the brain: neuroimaging results in humans and animal models. *Alcohol Res*. 2017;38(2):183-206.
21. Gao Y, Yan K, Yang L, Cheng G, Zhou W. Biometry reference range of the corpus callosum in neonates: An observational study. *Medicine (Baltimore)*. 2018;97(24). doi: 10.1097/MD.00000000000011071
22. Boiagina O. General principle of the corpus callosum internal structure in adult human. *Georgian Med News*. 2017; 262: 82-87.
23. Lewohl JM, Wixey J, Harper CG, Dodd PR. Expression of MBP, PLP, MAG, CNP, and GFAP in the Human Alcoholic Brain. *Alcohol ClinExp Res*. 2005;29(9):1698–705.
24. Kapogiannis D, Kisser J, Davatzikos C, Ferrucci L, Metter J, Resnick SM. Alcohol consumption and premotor corpus callosum in older adults. *Eur Neuropsychopharmacol*. 2012;22(10):704-710.
25. Saito M, Chakraborty G, Hui M, Masiello K, Saito M. Ethanol-induced neurodegeneration and glial activation in the developing brain. *Brain Sci*. 2016;6(3),31. doi.org/10.3390/brainsci6030031.
26. Newville J, Valenzuela CF, Li L, Jantzie LL, Cunningham LA. Acute oligodendrocyte loss with persistent white matter injury in a third trimester equivalent mouse model of fetal alcohol spectrum disorder. *Glia*. 2017;65(8):1317–1332.
27. Oscar-Berman M, Marinkovic K. Alcoholism and the brain: an overview. *Alcohol Res Health*. 2003;27(2):125-33.
28. Squeglia LM, Jacobus J, Tapert SF. The effect of alcohol use on human adolescent brain structures and systems. *Handb Clin Neurol*. 2014;125:501–510.
29. McClintick JN, McBride WJ, Bell RL, et al. Gene expression changes in the ventral hippocampus and medial prefrontal cortex of adolescent alcohol-preferring (P) rats following binge-like alcohol drinking. *Alcohol*. 2018;68:37-47.
30. Nixon K., Crews FT. Binge ethanol exposure decreases neurogenesis in adult rat hippocampus. *J Neurochemistry*. 2002;83(5):1087-1093.
31. Herrera DG, Yague, AG, Johnsen-Soriano S, et al. Selective impairment of hippocampal neurogenesis by chronic alcoholism: protective effects of an antioxidant. *Proc Natl AcadSci U S A*. 2003;100(13):7919-7924.
32. Crews FT, Nixon K. Alcohol, neural stem cells, and adult neurogenesis. *Alcohol Res Health*. 2003;27(2):197-204.
33. Woods KJ, Thomas KGF, Molteno CD, Jacobson JL, Jacobson SW, Meintjes EM. Prenatal alcohol exposure affects brain function during place learning in a virtual environment differently in boys and girls. *Brain Behav*. 2018. doi: 10.1002/brb3.1103.
34. Miller MW. Effect of prenatal exposure to ethanol on the pyramidal tract in developing rats. *Brain Res*. 2017;1672:122-128.
35. Boschen KE, Ruggiero MJ, Klintsova AY. Neonatal binge alcohol exposure increases microglial activation in the developing rat hippocampus. *Neuroscience*. 2016;324:355–366.
36. Söderpalm B, Ericson M. Neurocircuitry involved in the development of alcohol addiction: the dopamine system and its access points. *Curr Top BehavNeurosci*. 2013;13:127-61.
37. Abrahao KP, Salinas AG, Lovinger DM. Alcohol and the brain: neuronal molecular targets, synapses, and circuits. *Neuron*. 2017;96(6):1223–1238.
38. de la Monte SM, Kril JJ. Human alcohol-related neuropathology. *ActaNeuropathol*. 2014;127(1):71-90.
39. Creeley CE, Dikranian KT, Johnson SA, Farber NB, Olney JW. Alcohol-induced apoptosis of oligodendrocytes in the fetal macaque brain. *ActaNeuropatholCommun*. 2013;1:23. doi: 10.1186/2051-5960-1-23.
40. Kane CJ, Phelan KD, Douglas JC, et al. Effects of ethanol on immune response in the brain: region-specific changes in adolescent versus adult mice. *Alcohol Clin Exp Res*. 2014;38(2):384-391.
41. Crews FT, Nixon K. Mechanisms of neurodegeneration and regeneration in alcoholism. *Alcohol Alcohol*. 2009;44(2):115-127.
42. Oswald BB, Corner AC. Rodent models of adolescent alcohol and drug self- administration: Implications for understanding adult substance abuse. *J Addiction Prevention*. 2013;1(1):14.
43. Vore AS, Doremus-Fitzwater T, Gano A, Deak T. Adolescent ethanol exposure leads to stimulus-specific changes in cytokine reactivity and hypothalamic-pituitary-adrenal axis sensitivity in adulthood. *Front BehavNeurosci*. 2017; 11: 78. doi: 10.3389/fnbeh.2017.00078.
44. Szabo G, Saha B. Alcohol's effect on host defense. *Alcohol Res*. 2015;37(2):159–170.
45. Gauthier TW. Prenatal alcohol exposure and the developing immune system. *Alcohol Res*. 2015;37(2):279–285.



## REVIEW PAPER

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# Inflammatory bowel disease: clinical aspects

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## Abstract

**Introduction.** Inflammatory bowel disease is a complex disease which arises as a result of an interaction between environmental and genetic factors leading to immunological responses and inflammation in the intestine.

**Aim.** To review medical approaches used in inflammatory bowel disorders.

**Materials and methods.** An analysis of literature regarding inflammatory bowel diseases, Leśniowski-Crohn's disease, ulcerative colitis and mataloproteinases.

**Results.** Current evidence suggests that patients with inflammatory bowel disease may have an elevated risk of endothelial dysfunction and coronary artery disease. Over the past two decades, great advances have been made in our understanding of the interplay between the inflammatory bowel disease.

**Conclusions.** Inflammatory bowel diseases are increasing in Europe. The diagnosis is usually confirmed by biopsies on colonoscopy.

**Keywords.** inflammatory bowel diseases, Leśniowski-Crohn's disease, ulcerative colitis, mataloproteinases

## Introduction

Chronic inflammatory bowel diseases are divided into Leśniowski-Crohn's disease, ulcerative colitis and undetected colitis.<sup>1-5</sup> Inflammatory changes in ulcerative colitis include mucosa and occur continuously from the rectum to the more proximal parts of the colon. In Leśniowski-Crohn's disease, the changes may include the entire digestive tract.<sup>6</sup> The symptoms include diarrhea, frequent bloody stools, and abdominal pain.

Most patients with non-specific inflammatory bowel diseases from the moment of diagnosis are treated conservatively. However, a significant group of patients do not undergo such therapy during the course of the disease and require surgical procedures. Indications for surgical treatment depend on the efficacy and success of conservative treatment, the severity of the disease, and associated complications. Due to clinical differences, Leśniowski-Crohn's disease is character-

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 11.06.2018 | Accepted: 27.08.2018

Publication date: December 2018

ized by a different specialty of surgical treatment than ulcerative colitis.<sup>7</sup>

Material and methods

We reviewed the literature regarding the chronic inflammatory bowel diseases published between 1945 and 2018 (Figure 1). We found more than 500 articles studying this type of chronic inflammatory bowel diseases such as Leśniowski-Crohn’s disease, ulcerative colitis and undetected colitis. Our review includes recent studies regarding Leśniowski-Crohn’s disease, ulcerative colitis and undetected colitis.

Results

In Leśniowski-Crohn’s disease, about 50-80% of patients require surgical treatment during the course of the disease.<sup>1-5</sup> The correct diagnosis of nonspecific inflammatory bowel diseases relies on a multidisciplinary approach based on clinical, laboratory, endoscopic, and histologic examination.

Indications for planned surgery are:<sup>8-10</sup>

- ineffective conservative treatment,
- incomplete occlusion,
- accessing cachexia, intraabdominal abscesses and internal or external fistulas, which cause malabsorption syndrome,
- severe parenteral symptoms,
- perianal lesions (fistulas, perianal abscesses, anal stenosis, anal fissures),
- intestinal epithelium or dysplasia,
- children’s developmental delay,

Urgent indications:<sup>11-12</sup>

- hemorrhage,
- occlusion,
- perforation,
- abdominal or perirectal dissemination causing sepsis, fulminant disease or acute phase of disease that does not undergo pharmacological treatment.

In the surgical treatment of Leśniowski-Crohn’s disease concerning the small intestine, the rule of economical resections applies, and the resection limits are determined by macroscopic changes and the mesenteric Fazio symptom (assessment of the mesentery infiltration thickness).

In the treatment of colorectal cholangitis, the extent and type of surgery depends on the severity and extent of the disease, the status of the colon and rectal susceptibility, functional sphincter efficiency and the extent of previous resections. It is recommended to perform a colectomy with ileo-rectum anastomosis (in the absence of changes in the rectum) or proctocolectomy with definitive ileostomy (if the rectum is altered diseased).

Surgical treatment of ulcerative colitis is fundamentally different from the surgical treatment of Crohn’s disease. In ulcerative colitis, the aim of the operation is to

remove the entire large intestine and rectal mucosa. After the procedure, the quality of life of the vast majority of patients improves. The necessity of surgical treatment is in the group of 20-25% of Colitis Ulcerosa patients.

Indications for planned surgery are:

- solid symptoms of exacerbation of the disease, despite the optimal conservative treatment
- a large intestine or a pre-cancerous lesion in the large intestine (dysplasia associated lesion or mass-DALM or flat-dysplasia)
- some local complications (occurring rarely in ulcerative colitis) such as narrowing of the colon, or internal fistulas (e.g., recto-stitch) or external
- growth and maturation delay in children

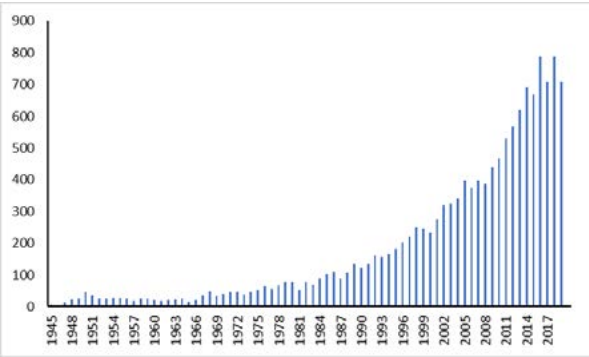
Urgent indications are:

- a severe disease that does not undergo intensive 7-10 days of conservative treatment followed by emergency treatment with cyclosporin or infliximab,
- toxic distension of the colon (megacolon toxicum, when intensive conservative treatment lasting from 24 to 48 hours did not bring any improvement

Emergency indications:

- production of the large intestine with diffuse fecal peritonitis,
- massive bleeding,
- elastic bowel disease,

The surgery of choice for urgent or urgent indications is a colectomy with ileostomy with an occluded stump of the rectum (Hartmann’s operation) or sewn into the skin over the pubic symphysis.



**Fig. 1.** Number of publications on chronic inflammatory bowel diseases (Leśniowski-Crohn’s disease, ulcerative colitis and undetected colitis) from the Library of National Center for Biotechnology Information (NCBI) PubMed Data Base over the years starting from 1945

Currently, is possible to achieve the expected therapeutic results and elimination/reduction of the risk of physical development. The planned indications are: complete proctocolectomy with the final ileostomy using the Brooke method; complete reconstructive proctocolectomy with intestinal ileum (pouch) and anastomosis

of the anal canal (ileo-pouch anal anastomosis - IPAA). The technique of treatment in the case of inflammatory bowel diseases differs from that used in oncology, the wide excision of mesorectum tissues is not justified and the preparation should be conducted close to the rectum wall in order to minimize the risk of postoperative disorders of sexual function, micturition or defecation. However, surgical treatment is not a perfect and final therapeutic solution in non-specific inflammatory bowel diseases. Operations in Crohn's disease are characterized by a large number of adverse effects (e.g. metabolic consequences of short bowel syndrome), complications and relapses, both early and late. Specification of those patients in whom surgical treatment could be characterized by a more severe postoperative course, higher risk of complications and recurrences of the disease would allow more precise selection of qualification criteria, adjust the time of surgical intervention or special surveillance to improve treatment outcomes.

**Table 1.** Markers for nonspecific inflammatory bowel diseases

Marker	Name	References
TF(+) MPs	<i>Procoagulant microparticles</i>	(Palkovits et al. 2013) <sup>13</sup>
PAF	<i>Platelet activation factor</i>	(Saluk et al. 2014) <sup>14</sup>
Anti-I2	<i>Antibodies to Pseudomonas fluorescens-associated sequence I2</i>	(Zatorski et al. 2015) <sup>15</sup>
PAB	<i>Pancreatic antibody (an antibody to a trypsin-sensitive protein in pancreatic secretions)</i>	(Fakhoury et al. 2014) <sup>16</sup>
HLE	<i>Human leucocytic elastase</i>	(Fakhoury et al. 2014) <sup>16</sup>
HLE	<i>Human leucocytic elastase</i>	(Fakhoury et al. 2014) <sup>16</sup>
Anti-CBir1 flagellin	<i>Antibodies to bacterial flagellin</i>	(Cioffi et al. 2015) <sup>17</sup>
ENA-78	<i>Epithelial neutrophil activating peptide</i>	(Cioffi et al. 2015) <sup>17</sup>
N	<i>Neopterine</i>	(Cioffi et al. 2015) <sup>17</sup>
ASCAs	<i>Anti-Saccharomyces cerevisiae antibodies</i>	(Thorsvik et al. 2017) <sup>18</sup>
MRP-8/MRP-14 or S100A8/A9	<i>Calprotectin</i>	(Vatn et al. 2015) <sup>19</sup>
L	<i>Lactoferrin</i>	(Acevedo et al. 2018) <sup>20</sup>

In the current arsenal of laboratory, imaging and endoscopic examinations there is no marker that would allow such selection of patients. Based on the analysis of over 500 papers described nonspecific inflammatory

bowel diseases, endoscopic evaluation is the main diagnostic process. Laboratory tests in the diagnosis of inflammatory bowel diseases play an auxiliary role. The most important currently known markers for nonspecific inflammatory bowel diseases are presented in Table 1.

Although considerable progress in the research has been achieved, there is still a long way to go toward the ultimate goal of an ideal biomarker in nonspecific inflammatory bowel diseases.<sup>21-31</sup>

**Inflammatory Markers Belonging to Extracellular Matrix**

Inflammatory bowel diseases have biomarkers which can be used to predict disease and treatment outcomes.<sup>32</sup> The Extracellular Matrix components are depolymerized into the small fragments, which are released into circulation.<sup>33</sup> ECM is composed of fibrous proteins and glycosaminoglycans (GAGs) and is involved in proliferation, migration, and adhesion.<sup>34-36</sup> Sulfated GAG types are connected with the intestinal epithelium and regulate its permeability.<sup>37-38</sup>

Marker	Names	References
HA	Hyaluronan	(Petrey et al. 2018) <sup>39</sup>
LN	Laminin	(Koutroubakis et al. 2003) <sup>40</sup>
SDC-1	Syndecan-1	(Koutroubakis et al. 2003) <sup>40</sup>
FN	Fibronectin	(Hundorfean et al. 2010) <sup>41</sup>

**Conclusions**

Inflammatory bowel diseases are increasing in Europe. The diagnosis is usually confirmed by biopsies on colonoscopy.

**Acknowledgments**

Dorota Bartusik-Aebisher acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).

**References**

1. Skok P, Skok K. Acute febrile neutrophilic dermatosis in a patient with Crohn's disease: case report and review of the literature. *Acta Dermatovenerol Alp Pannonica Adriat.* 2018;27(3):161-163.
2. Harris KG, Chang EB. The intestinal microbiota in the pathogenesis of inflammatory bowel diseases: new insights into complex disease. *Clin Sci (Lond).* 2018;132(18):2013-2028.
3. Florin THJ, Wright JD, Jambhrunkar SD, Henman MG, Popat A. A well-tolerated and rapidly acting thiopurine for IBD? *Drug Discov Today.* 2018; pii: S1359-6446(18)30290-3.
4. Kaida-Yip F, Deshpande K, Saran T, Vyas D. Biosimilars: Review of current applications, obstacles, and their future in medicine. *World J Clin Cases.* 2018;6(8):161-166

5. Szántó K, Nyári T, Bálint A, et al. Biological therapy and surgery rates in inflammatory bowel diseases - Data analysis of almost 1000 patients from a Hungarian tertiary IBD center. *PLoS One*. 2018;13(7):e0200824.
6. Stawiski K, Strzałka A, Puła A, Bijakowski K. PancreApp: An Innovative Approach to Computational Individualization of Nutritional Therapy in Chronic Gastrointestinal Disorders. *Stud Health Technol Inform*. 2015; 216:325-328.
7. Lu B, Niu LL, Xu XG, Yao SL, Tan XY. Ulcerative colitis in an adult patient mimicking Henoch-Schönlein purpura: A case report. *Medicine (Baltimore)*. 2018;97(35):e12036.
8. Aytac E, Ozuner G, Isik O, Gorgun E, Remzi FH. Surgical management of patients with ulcerative colitis during pregnancy: maternal and fetal outcomes. *J Crohns Colitis*. 2015 ;9(1):82-85.
9. Mattioli G, Barabino A, Aloï M, et al. Paediatric ulcerative colitis surgery: Italian survey. *J Crohns Colitis*. 2015;9(7):558-566.
10. Burke KE, Haviland MJ, Hacker MR, Shainker SA, Cheifetz AS. Indications for Mode of Delivery in Pregnant Women with Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2017;23(5):721-726.
11. Ashton JJ, Ennis S, Beattie RM. Early-onset paediatric inflammatory bowel disease. *Lancet Child Adolesc Health*. 2017;1(2):147-158.
12. Singeap AM, Stanciu C, Cojocariu C, Sfarti C, Trifan A. Capsule Endoscopy in Inflammatory Bowel Disease: Current Applications. *Arch Iran Med*. 2015;18(6):379-383.
13. Palkovits J, Novacek G, Kollars M, et al. Tissue factor exposing microparticles in inflammatory bowel disease. *Journal of Crohn's & Colitis*. 2013;7(3): 222–229.
14. Saluk J, Bijak M, Ponczek MB, Wachowicz B. The formation, metabolism and the evolution of blood platelets. *Postępy Higieny i Medycyny Doświadczalnej*. 2014;68: 384–392.
15. Zatorski H, Sałaga M, Zielińska M, Fichna J. Genetic factors in pathogenesis, course and treatment of inflammatory bowel diseases. *Postępy Higieny i Medycyny Doświadczalnej*. 2015; 69:335–344.
16. Fakhoury M, Negrulj R, Mooranian A, al-Salami H. Inflammatory bowel disease: clinical aspects and treatments. *J Inflamm Res*. 2014; 7:113–120.
17. Cioffi M, Rosa AD, Serao R, Picone I, Vietri MT. Laboratory markers in ulcerative colitis: current insights and future advances. *World J Gastrointestinal Pathophysiol*. 2015; 6(1):13–22.
18. Thorsvik S, Damås JK, Granlund AB. Fecal neutrophil gelatinase-associated lipocalin as a biomarker for inflammatory bowel disease. *J Gastroenterol Hepatol*. 2017; 32(1): 128–135.
19. Vatn MH, Sandvik AK. Inflammatory bowel disease. *Scandinavian J of Gastroenterol*. 2015;50(6) 748–762.
20. Acevedo D, Salvador MP, Girbes J, Estan N. Fecal calprotectin: a comparison of two commercial enzymeimmunoassays and study of fecal extract stability at room temperature. *J Clin Med Res*. 2018; 10(5), 396–404.
21. Lallemand C, Liang F, Staub F, Simansour M, Vallette B, Huang L, Ferrando-Miguel R, Tovey MG. A Novel System for the Quantification of the ADCC Activity of Therapeutic Antibodies. *J Immunol Res*. 2017;2017:3908289.
22. Abraham BP, Thirumurthi S. Clinical significance of inflammatory markers. *Curr Gastroenterol Rep*. 2009;11(5):360-367.
23. Malicková K, Janatková I, Fucíková T, Adamec S, Lukás M. Initial experience with detection of *Saccharomyces cerevisiae* antibodies in patients with primary nonspecific inflammatory bowel disease. *Epidemiol Mikrobiol Immunol*. 2001;50(3):131-135.
24. Eda K, Mizuochi T, Takaki Y, Ushijima K, Umeno J, Yamashita Y. Successful azathioprine treatment in an adolescent with chronic enteropathy associated with *SLCO2A1* gene: A case report. *Medicine (Baltimore)*. 2018;97(41):e12811.
25. Umeno J, Matsumoto T, Hirano A, Fuyuno Y, Esaki M. Genetic analysis is helpful for the diagnosis of small bowel ulceration. *World J Gastroenterol*. 2018;24(28):3198-3200.
26. Derkacz A, Olczyk P, Komosinska-Vassev K. Diagnostic Markers for Nonspecific Inflammatory Bowel Diseases. *Dis Markers*. 2018;2018:7451946.
27. Shivashankar R, Lichtenstein GR. Mimics of Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2018;24(11):2315-2321.
28. You JY. Features and management of very early onset inflammatory bowel disease. *Zhongguo Dang Dai Er Ke Za Zhi*. 2018;20(5):341-345.
29. Mang T, Scharitzer M. Imaging of gastrointestinal inflammation: Characteristic patterns and signs. *Radiologe*. 2018;58(4):281-291.
30. Gupta AS, Nunley JR, Feldman MJ, Ortega-Loayza AG. Pyoderma Gangrenosum of the Scalp: A Rare Clinical Variant. *Wounds*. 2018;30(2):16-20.
31. Yamada Y, Sugimoto K, Yoshizawa Y, et al. Mesenteric inflammatory veno-occlusive disease occurring during the course of ulcerative colitis: a case report. *BMC Gastroenterol*. 2018; 11;18(1):9.
32. Klimczak K, Lykowska-Szuber L, Eder P, et al. The diagnostic usefulness of fecal lactoferrin in the assessment of Crohn's disease activity. *Eur J Intern Med*. 2015;26(8):623-627.
33. Truffi M, Sorrentino L, Monieri M, et al. Inhibition of Fibroblast Activation Protein Restores a Balanced Extracellular Matrix and Reduces Fibrosis in Crohn's Disease Strictures Ex Vivo. *Inflamm Bowel Dis*. 2018;24(2):332-345.
34. van der Smitten A, Hintze V, Scharnweber D, et al. Growth promoting substrates for human dermal fibroblasts provided by artificial extracellular matrices composed of collagen I and sulfated glycosaminoglycans. *Biomaterials*. 2011;32(34):8938-8946.
35. Nakahara Y, Matsusaki M, Akashi M. Fabrication and enzymatic degradation of fibronectin-based ultrathin films. Fabrication and enzymatic degradation of fibronectin-based ultrathin films. *J Biomater Sci Polym Ed*. 2007;18(12):1565-1573.



36. Matsushima H, Bogenmann E. Modulation of neuroblastoma cell differentiation by the extracellular matrix. *Int J Cancer*. 1992;51(5):727-732.
37. Kliemt S, Lange C, Otto W, et al. Sulfated hyaluronan containing collagen matrices enhance cell-matrix-interaction, endocytosis, and osteogenic differentiation of human mesenchymal stromal cells. *J Proteome Res*. 2013;12(1):378-389.
38. Klimczak K, Lykowska-Szuber L, Eder P, et al. The diagnostic usefulness of fecal lactoferrin in the assessment of Crohn's disease activity. *Eur J Intern Med*. 2015;26(8):623-627.
39. Petrey AC, de la Motte CA. Hyaluronan in inflammatory bowel disease: cross-linking inflammation and coagulation. *Matrix Biology*. 2018; 1461: 4C.
40. Koutroubakis IE, Petinaki E, Dimoulis P. Serum laminin and collagen IV in inflammatory bowel disease. *J Clin Pathol*. 2003; 56(11):817-820.
41. Hundorfean G, Neurath MF, Sitaru C. Autoimmunity against type VII collagen in inflammatory bowel disease. *J Cell Mol Med*. 2010;14(10):2393-2403.



## REVIEW PAPER

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# Inflammatory bowel disease: the function of metalloproteinases

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## Abstract

**Introduction.** Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the colon and small intestine.

**Aim.** The aim of this work was to review the current literature regarding matrix metalloproteinases. The databases such as PubMed, ScienceDirect and Springer were utilized to search the literature for relevant articles.

**Materials and methods.** An analysis of literature. We collected information, data, and examples of the function of metalloproteinases.

**Results.** Herein we show that metalloproteinases play a role in such processes as the immune response, angiogenesis, the epithelial barrier function, fibrosis induced by the inflammatory process, and in the process of carcinogenesis.

**Conclusions.** Further studies on the role of metalloproteinases in the process of carcinogenesis associated with inflammatory bowel diseases are required.

**Keywords.** inflammatory bowel disease, matrix metalloproteinases, extracellular matrix

## Introduction

Matrix metalloproteinases (MMPs) are the main group of enzymes responsible for collagen and other protein degradation in the extracellular matrix (ECM).<sup>1-5</sup> Matrix metalloproteinases are also responsible for the activation or inhibition of the function of numerous cytokines, chemokines, receptors, adhesion molecules or signaling substances affecting inflammatory processes in the intestine.<sup>6-10</sup> A typical structure of MMPs consists of several distinct domains. The MMP family can be di-

vided into six groups: collagenases, gelatinases, stromelysins, matrilysins, membrane-type MMPs, and other non-classified MMPs.<sup>10-14</sup> The MMP functions are listed in the Table 1.

Invading neutrophils produce large amounts of matrix metalloproteinase MMP8 and MMP9, which proteolytically cleave collagen into small fragments.<sup>25</sup> These collagen fragments are further cleaved to the tripeptide, PGP, by epithelial- and neutrophil-derived prolyl endopeptidase (PE).<sup>26</sup>

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 5.09.2018 | Accepted: 20.10.2018

Publication date: December 2018

**Table 1.** MMP functions<sup>1-42</sup>

MMPs name	Function
MMP 1	inhibition of fibrosis <sup>17,18</sup>
MMP 2	inhibition of angiogenesis, influence on the epithelial barrier function, inhibition of fibrosis <sup>17,18</sup>
MMP 3	outflow to the production of Endostatin <sup>19</sup>
MMP 7	alpha-defensin activation, chemokine expression, ulcer healing, Endostatin production <sup>20</sup>
MMP 8	neutrophil infiltration <sup>21</sup>
MMP 9	Chemokine expression, neutrophil infiltration, production of anti-angiogenic factors, processing, VEGF-A activation, inhibition of goblet cell differentiation, inhibition of fibrosis <sup>21</sup>
MMP 10	healing of ulcers <sup>22,23</sup>
MMP 13	TNF-alpha activation and Endostatin production <sup>24</sup>
MMP 20	Endostatin production <sup>24</sup>

**The role of metalloproteinases in fibrosis in non-specific inflammatory bowel diseases**

Fibrosis is the process of pathological collection of the substance in the intracellular space in the intestinal wall, which accompanies chronic inflammatory processes. Expression of MMP and the balance between their level and the level of metalloproteinase inhibitors (TIMPs and others) play an essential role in ECM homeostasis. Disruption of this balance leads to the deposition of collagen and fibrosis. Despite advances in the treatment of inflammatory bowel disease (IBD), there are no medications to prevent or reverse the process of fibrosis. In ulcerative colitis, fibrosis affects the mucosa and submucosa. Crohn's disease affects the entire thickness of the intestinal wall and can lead to intestinal stenosis. Treatment of stenosis is a surgical procedure. The increase in ALK5, TIMP, Smad-2, Smad-3 phosphorylation leads to collagen accumulation in the intestinal wall.<sup>27-29</sup> Glutamine has an effect that lowers fibrosis in induced TNBC enteritis by reducing overexpression of TGF-beta, Smad and TIMP phosphorylation.<sup>30-31</sup> Interleukin-13 also participates in fibrosis processes by affecting the concentration of MMP-1 and TIMP-1.<sup>28-32</sup> The cytokine may inhibit the expression of MMP-1, MMP-2, MMP-9. MMP-2 is reduced in the form of a narrowing Crohn's disease.<sup>29-33</sup> In studies on DSL-induced dextran sulfate, an increase in gelatinase expression (MMP-2 and MMP-9) may prevent fibrosis by collagen degradation.<sup>28-33</sup>

**The role of metalloproteinases in the process of carcinogenesis, colitis associated cancer (CAC)**

Patients with IBD have an increased risk of colorectal cancer compared to the entire population.<sup>39</sup> The risk of cancer in ulcerative colitis increases significantly 8-10

years from the beginning of the disease and increases as the disease progresses. It also depends on the extent of changes in the intestine, the higher risk occurs in the extensive form (E3-classification of ulcerative colitis depending on the extent of the disease) compared to left-sided (E 2), in disease located only in the rectum (E 1) does not increase. Colon cancer is the cause of death of 1 in 6 patients with colitis ulcerosa.<sup>40</sup>

An increase in MMP-9 expression is observed during the carcinogenesis process and the adenocarcinoma sequence. MMP-9 may be a marker of early stages of carcinogenesis.<sup>41</sup> However, cancer associated with chronic inflammation does not arise as a sporadic or genetically determined adenoma-dysplasia carcinoma, but as an inflammation-dysplasia-carcinoma (where the p53 mutation plays a key role in the early stage of carcinogenesis).<sup>40</sup>

Metalloproteinase 9, which is a mediator of inflammatory bowel process, may also play a protective role in the process of carcinogenesis (Colitis Associated Cancer - CAC). MMP-9 may have a double meaning in CAC. In experiments in mice, MMP-9 -/- individuals have been shown to be more susceptible (in comparison to individuals able to produce MMP-9) to develop CAC. It is emphasized that it protects the development of CAC by activating the Notch-1 molecule with subsequent inhibition of beta-catenin expression. Notch-1 activation by MMP-9 also leads to increased expression of p53 protein, increase in p21 Waf / Cip1 protein (regulator), a cell cycle inhibitor, as well as an increase in Bax family proteins (Bcl-2 family proteins that accelerate apoptosis).<sup>41</sup>

In contrast to the protective role of MMP-9 in the development of CAC, in experiments on mice, it was found that the activation of neutrophilia by CXCL2 chemokines increases the production of MMP-9, which in turn through the activation of VEGF (vascular epithelial growth factor) accelerates neoangiogenesis. This process has essential in the development of cancer.

There was also an effect on the expression of MMP-9, integrin linked kinase (ILK) - a protein responsible for such cellular processes as migration, proliferation and adhesion. ILK through MMP-9, MMP-2 and MMP3 promotes neoplasia (carcinogenesis, tumorigenesis).<sup>29</sup>

Infliximab (anti-TNF-alpha antibody) as well as celecoxib (gelatinase inhibitor) may have been shown to be preventive in the case of CAC by decreasing the concentration of metalloproteinase.<sup>32</sup>

Metalloproteinase -10 may have an inhibitory effect on the carcinogenesis process, it may also act to inhibit the development of dysplastic changes in IBD.<sup>42</sup>

**Conclusions**

Further studies on the role of metalloproteinases in the process of carcinogenesis associated with inflammatory bowel diseases are required.

## Acknowledgments

Dorota Bartusik-Aebischer acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).

## References

1. Jabłońska-Trypuć A, Matejczyk M, Rosochacki S. Matrix metalloproteinases (MMPs), the main extracellular matrix (ECM) enzymes in collagen degradation, as a target for anticancer drugs. *J Enzyme Inhib Med Chem*. 2016;31(1):177-183.
2. Fink K1, Boratyński J. The role of metalloproteinases in modification of extracellular matrix in invasive tumor growth, metastasis and angiogenesis. *Postepy Hig Med Dosw (Online)*. 2012; 66:609-628.
3. Malemud CJ. Matrix metalloproteinases (MMPs) in health and disease: an overview. *Front Biosci*. 2006;11:1696-1701.
4. Candelario-Jalil E, Yang Y, Rosenberg GA. Diverse roles of matrix metalloproteinases and tissue inhibitors of metalloproteinases in neuroinflammation and cerebral ischemia. *Neuroscience*. 2009;158(3):983-994.
5. Velinov N, Poptodorov G, Gabrovski N, Gabrovski S. The role of matrix metalloproteinases in the tumor growth and metastasis. *Khirurgiia (Sofia)*. 2010;(1):44-49.
6. Bonnans C, Chou J, Werb Z. Remodelling the extracellular matrix in development and disease. *Nat Rev Mol Cell Biol*. 2014;15(12):786-801.
7. Jarvelainen H, Sainio A, Koulu M, Wight TN, Penttinen R. Extracellular matrix molecules: potential targets in pharmacotherapy. *Pharmacol Rev*. 2009;61:198-223.
8. Hynes RO, Naba A. Overview of the matrisome—an inventory of extracellular matrix constituents and functions. *Cold Spring Harb Perspect Biol*. 2012;4:a004903.
9. Rozario T, DeSimone DW. The extracellular matrix in development and morphogenesis: a dynamic view. *Dev Biol*. 2010;341:126-140.
10. Frantz C, Stewart KM, Weaver VM. The extracellular matrix at a glance. *J Cell Sci*. 2010;123:4195-4200.
11. Gross J, Lapiere CM. Collagenolytic activity in amphibian tissues: a tissue culture assay. *Proc Natl Acad Sci USA*. 1962;48:1014-1022.
12. Herzog C, Haun RS, Ludwig A, Shah SV, Kaushal GP. ADAM10 is the major sheddase responsible for the release of membrane-associated meprin A. *J Biol Chem*. 2014;289:13308-13322.
13. Khokha R, Murthy A, Weiss A. Metalloproteinases and their natural inhibitors in inflammation and immunity. *Nature Rev Immunol*. 2013;13:649-665.
14. Simon-Assmann P, Keding M, De Arcangelis A, Rousseau V, Simo P. Extracellular matrix components in intestinal development. *Experientia*. 1995;51:883-900.
15. Biancheri P, Giuffrida P, Docena GH. The role of transforming growth factor (TGF)- $\beta$  in modulating the immune response and fibrogenesis in the gut. *Cytokine Growth Factor Rev*. 2013;25:45-55.
16. Mott JD, Werb Z. Regulation of matrix biology by matrix metalloproteinases. *Curr Opin Cell Biol*. 2004;16:558-564.
17. Hrabec E, Naduk J, Stręk M, Hrabec Z. Kolagenazy typu IV (MMP-2 i MMP-9) i ich substraty — białka macierzy pozakomórkowej, hormony, cytokiny i ich receptory. *Post Biochem*. 2007;53:37-45.
18. Meng L, Uzui H, Guo H, Tada H. Role of SGLT1 in high glucose level-induced MMP-2 expression in human cardiac fibroblasts. *Mol Med Rep*. 2018;17(5):6887-6892.
19. Tokai N, Yoshida S, Kotani T, et al. Serum matrix metalloproteinase 3 levels are associated with an effect of iguratimod as add-on therapy to biological DMARDs in patients with rheumatoid arthritis. *PLoS One*. 2018;13(8):e0202601.
20. Sohail A, Marco M, Zhao H, et al. Characterization of the dimerization interface of membrane type 4 (MT4)-matrix metalloproteinase. *J Biol Chem*. 286: 33178-33189.
21. Sorsa T, Tervahartiala T, Leppilähti J, et al. Collagenase-2 (MMP-8) as a point-of-care biomarker in periodontitis and cardiovascular diseases. Therapeutic response to non-antimicrobial properties of tetracyclines. *Pharmacol Res*. 2011;63:108-113.
22. Derosa G, D'Angelo A, Ciccarelli L, et al. Matrix metalloproteinase-2, -9, and tissue inhibitor of metalloproteinase-1 in patients with hypertension. *Endothelium*. 2006;13:227-231.
23. Rodriguez JA, Orbe J, Martinez de Lizarrondo S, et al. Metalloproteinases and atherothrombosis: MMP-10 mediates vascular remodeling promoted by inflammatory stimuli. *Front Biosci*. 2008;13:2916-2921.
24. Suomela S, Koljonen V, Skoog T, Kukko H, Böhring T, Sarialho-Kere U. Expression of MMP-10, MMP-21, MMP-26, and MMP-28 in Merkel cell carcinoma. *Virchows Arch*. 2009; 455: 495-503.
25. Koelink PJ, Overbeek SA, Braber S, et al. Collagen degradation and neutrophilic infiltration: a vicious circle in inflammatory bowel disease. *Gut*. 2014;63(4):578-587.
26. Schaefer L, Reinhardt DP. Special issue: Extracellular matrix: Therapeutic tools and targets in cancer treatment. *Adv Drug Deliv Rev*. 2016;97:1-3.
27. Fujimoto K, Nakajima K, Yaoita Y. Expression of matrix metalloproteinase genes in regressing or remodeling organs during amphibian metamorphosis. *Dev Growth Differ*. 2007;49:131-143.
28. Kim HY, Nelson CM. Extracellular matrix and cytoskeletal dynamics during branching morphogenesis. *Organogenesis* 2012;8:56-64.
29. Suomela S, Koljonen V, Skoog T, Kukko H, Böhring T, Sarialho-Kere U. Expression of MMP-10, MMP-21, MMP-26, and MMP-28 in Merkel cell carcinoma. *Virchows Arch*. 2009; 455: 495-503.
30. Ferrara N. Binding to the extracellular matrix and proteolytic processing: two key mechanisms regulating va-

- scular endothelial growth factor action. *Mol Biol Cell*. 2010;21:687–689.
31. Giannandrea M, Parks WC. Diverse functions of matrix metalloproteinases during fibrosis. *Dis Model Mech*. 2014;7:193–203.
32. Yamashita CM, Dolgonos L, Zemans RL, et al. Matrix metalloproteinase 3 is a mediator of pulmonary fibrosis. *Am J Pathol*. 2011;179:1733–1745.
33. Troeberg L, Nagase H. Proteases involved in cartilage matrix degradation in osteoarthritis. *Biochim Biophys Acta*. 2012;1824:133–145.
34. Bissell MJ, Hines WC. Why don't we get more cancer? A proposed role of the microenvironment in restraining cancer progression. *Nature Med*. 2011;17:320–329.
35. Ferrara N. Binding to the extracellular matrix and proteolytic processing: two key mechanisms regulating vascular endothelial growth factor action. *Mol Biol Cell*. 2010;21:687–689.
36. Lee S, Park HI, Sang QX. Calcium regulates tertiary structure and enzymatic activity of human endometase/matri-lysin-2 and its role in promoting human breast cancer cell invasion. *Biochem J*. 2007;403:31–42.
37. Ito E, Yana I, Fujita C, et al. The role of MT2-MMP in cancer progression. *Biochem Biophys Res Commun*. 2010;393:222–227.
38. Sohail A, Sun Q, Zhao H, Bernardo MM, Cho JA, Fridman R. MT4-(MMP17) and MT6-MMP (MMP25), a unique set of membrane- anchored matrix metalloproteinases: properties and expression in cancer. *Cancer Metastasis Rev*. 2008;27:289–302.
39. Taman H, Fenton CG, Hensel IV, Anderssen E, Florholmen J, Paulssen RH. Transcriptomic Landscape of Treatment-Naïve Ulcerative Colitis. *J Crohns Colitis*. 2018;12(3):327–336.
40. Krawczak K, Karczmarek-Borowska B, Maciąg M, Guz W. Rare case of slowly progressing lung cancer with colon metastases. *Wiad Lek*. 2017;70(1):148–151.
41. Volkov AM, Murashov IS, Polonskaya YV, et al. Changes of Content of Matrix Metalloproteinases and Their Tissue Expression in Various Types of Atherosclerotic Plaques. *Kardiologiia*. 2018;(10):12–18.
42. Zhai Y, Kuick R, Tipton C, et al. Arid1a inactivation in an Apc- and Pten-defective mouse ovarian cancer model enhances epithelial differentiation and prolongs survival. *J Pathol*. 2016;238(1):21–30.



## REVIEW PAPER

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# Medicinal & Aromatic Plants

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## Abstract

**Introduction.** The objective of this study is to discuss the potential of plants species in *medical applications*.

**Aim.** The main purpose of this study is to discuss ethnobotanically selected plants used in medicine.

**Materials and methods.** We analysed literature and collected information, data, and examples of selected plants used in medicine.

**Results.** The literature shows that for several decades, the properties of medicinal plants have been investigated and reported in the biomedical and pharmaceutical literature.

**Conclusions.** This review includes studies on plants material. The properties of various plants physiology were discussed with the option for the use in phytotherapy.

**Keywords.** phytotherapy, medicinal plants, otorhinolaryngology

## Introduction to plants and they properties

The use of Herbal medicines may influence many therapies by inducing interacting with other medications.<sup>1</sup> Despite concerns over its safety or efficacy, and cost-effectiveness, the use of Herbal medicines is common among patients undergoing otolaryngologic and head and neck surgery.<sup>1</sup> *Echinacea* and osteopathic manipulative treatment have been proposed as preventive measures.<sup>2</sup> In otitis-prone young children, treating colds with this form of *echinacea* does not decrease the risk of acute otitis media, and may in fact

increase risk. A regimen of up to five osteopathic manipulative treatments does not significantly decrease the risk of acute otitis media.<sup>2</sup> The aim of Schapowal *et al.* study was to assess the relative efficacy of a sage/*echinacea* spray and a chlorhexidine/lidocaine spray in the treatment of acute sore throats.<sup>3</sup> An *echinacea* preparation is as efficacious and well tolerated as a chlorhexidine/lidocaine spray in the treatment of acute sore throats.<sup>3</sup>

Little data is available on complementary and alternative medicine use in children attending otolar-

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 8.08.2018 | Accepted: 12.10.2018

Publication date: December 2018

ngology services.<sup>4</sup> Despite concerns regarding the efficacy, safety and cost effectiveness of complementary and alternative medicine, its use among the pediatric otolaryngology population is more common than many providers may realize.<sup>1</sup> To evaluate the effectiveness and safety of a preparation containing *echinacea*, propolis, and vitamin C in the prevention of respiratory tract infections in children during a 12-week winter period.<sup>4</sup> The total number of illness days and duration of individual episodes were also significantly lower in the Chizukit group. Adverse drug reactions were rare, mild, and transient. A preventive effect of a product containing *echinacea*, propolis, and vitamin C on the incidence of respiratory tract infections was observed.<sup>4</sup>

Pigments of plants

One of the most common pigments is called chlorophyll, and it is responsible for the green color of plants which means that most other colors are absorbed. When thinking of plants, there is a spectrum of colors. Although plants do tend to be green in color due to the chlorophyll, plants have pink, red, white, yellow, or even highly patterned leaves and flowers. Leaves change color in autumn because chlorophyll is the first pigment to degenerate when trees overwinter.

Non-green plants do not need sunlight to create chlorophyll and can display an array of different rainbow colors. Sunlight is made up of all wavelengths such as ultraviolet (UV-A, UV-B, UV-C) and infrared.<sup>5</sup> Each non-green plant can selectively absorb certain wavelengths for photosynthesis and reflect others that are deemed less useful. For example, chlorophyll absorbs mainly reds and blues, while reflecting green. Non-green plants have many other pigments that absorb green wavelengths and reflect red or yellow. In art but not in nature all colors are considered to be “trans-seasonal.” That is, they can span the season and are no longer limited to specific times of year. However, we live in a multi-hued world where nature provides the colors. The seasons such as spring bring nautical shades and pastels, while winter is about jewel tones and more cold textures. A living kaleidoscope of seasonal color begins from pistachio green; porcelain blue through mandarin orange, copper brown, and buckskin ending with ultra violet and black coffee.

For each garden, it is worthwhile to consider a few rules for combining individual colors in the plant composition. Plants in gray shades usually are inconspicuous but they are the perfect backdrop for other plants. In plants, gray or silvery-gray color is most common on leaves.

Throughout the past and current century, the techniques of natural dyeing in many ancient cultures have been discovered. Textile fragments were dyed using flowers leafs and roots. Native plants that continue to be

used for black color dyes in textile are: *Northern Catalpa*, *Sumac*, *May Apple* and *Sand Evening Primrose*. Black plants are in fact very dark shades of red, blue, purple and brown. Some examples of black plants by botanical name and common name are *Zantedeschia* (known as *Calla Lily*) and *Tacca Chantrieri* called *Cats Whiskers*. These plants start out with a green bloom and as it ages, the bloom turns purple, black, maroon, brown, or bronze.

*Hairy Coneflower*, *Red Mulberry*, *Mountain alder*, *Summer Grape* and *Black Locust* can be used to create blue and purple dyes. Blue plant colors range from cool-icy to deep royal blues. *Adenophora* is a genus of flowering plants in the family *Campanulaceae*, the *Bellflowers*. Plants of this genus are native to eastern Asia, with a few species occurring in Europe. Many are endemic to either China or Siberia. The blue color has a calming effect and gives the impression of cool freshness. A list of blue plants by botanical name and common name is presented in Table 1.

Table 1. Botanical and common names of representative blue plants

Common name	Botanical name
<i>Aechmea</i>	<i>Blue rain</i>
<i>Agapanthus</i>	<i>African lily</i>
<i>Cineraria</i>	<i>Airplant</i>
<i>Hyacinthus</i>	<i>Hyacinth</i>
<i>Muscari</i>	<i>Grape hyacinth</i>
<i>Primula veris</i>	<i>Primrose</i>

To produce brown dye the following plants were often used: *Rickly poppy*, *Texas Paintbrush*, *Elderberry* and *Downy Phlox*. Brown seems like an obvious color for plants, especially trees. Each year in the fall you can see all the beauty in brown plants, with shades of auburn, mahogany and chestnut (Table 2).

Table 2. Botanical and common names of representative brown plants

Botanical name	Common name
<i>Anigozanthos</i>	<i>Kangaroo</i>
<i>Anthurium</i>	<i>Flamingo flower</i>
<i>Cordylina</i>	<i>Mountain cabbage</i>
<i>Cymbidium</i>	<i>Cymbidium orchid</i>
<i>Gerbera</i>	<i>Barberton daisy</i>

Native plants that produce green dye are *Butterfly Milkweed*, *Texas Paintbrush*, *Basket flower*, *Sagebrush*, *Stinging Nettle* and *Goldenrod*. Probably the most common color of plants in the world due to chlorophyll which emparts a green coloring. *Aloe*, which is used in countless beauty and medicinal products around the world, is the one of the most well-known green plants.

**Table 3.** Botanical and common names of representative green plants

Botanical name	Common name
<i>Adiantum</i>	Maidenhair
<i>Alocasia</i>	Elephant's ear plant
<i>Aloe</i>	Barbados aloe
<i>Anigozanthos</i>	Kangaroo paw
<i>Anthurium</i>	Flamingo flower
<i>Asparagus</i>	Ming fern
<i>Asplenium</i>	Birds nest fern
<i>Beaucarnia</i>	(Nolina) Elephant's foot
<i>Blechnum gibbum</i>	Tree fern
<i>Calathea makoyana</i>	Cathedral windows
<i>Calathea zebrine</i>	Zebra plant
<i>Capsicum</i>	Ornamental pepper
<i>Ceropegia woodii</i>	Rosary vine
<i>Chamaedorea</i>	Parlour palm
<i>Chlorophytum</i>	Spider plant
<i>Codiaeum</i>	Joseph's coat croton
<i>Cordyline</i>	Mountain cabbage
<i>Crassula</i>	Money tree
<i>cryptanthus</i>	Earth star
<i>Ctenanthe</i>	Never-never plant
<i>Cymbidium</i>	Cymbidium orchid
<i>Cyperus</i>	Papyrus
<i>Dieffenbachia</i>	Dumbcane
<i>Dionaea</i>	Venus fly trap
<i>Dracaena fragrans</i>	Corn lily
<i>Euphorbia trigona</i>	Tree euphorbia
<i>Ficus benjamina</i>	Weeping fig
<i>Ficus elastic</i>	Rubber plant
<i>Ficus lyrata</i>	Fiddle-leaf fig
<i>Ficus pumila</i>	Creeping fig
<i>Fittonia</i>	Snakeskin plant
<i>Heptapleurum (chefflera)</i>	(Chefflera), Umbrella plant
<i>Hedera</i>	Ivy
<i>Hypoestes</i>	Polkadot plant
<i>Monstera</i>	Swiss cheese plant
<i>Musa</i>	Banana
<i>Nephrolepis</i>	Boston fern
<i>Nolina recurvata</i>	Elephant's foot
<i>Opuntia</i>	Bunny's ear cactus
<i>Peperomia</i>	Green-ripple plant
<i>Philodendron scandens</i>	Sweetheart vine
<i>Philodendron selloum</i>	Lacy philodendron
<i>Phoenix</i>	Date palm
<i>Platyserium</i>	Staghorn fern
<i>Rhipsalis cassutha</i>	Mistletoe cactus
<i>Sarracenia</i>	Pitcher plant
<i>Schefflera</i>	Umbrella plant
<i>Sedum</i>	Stonecrop
<i>Syngonium</i>	Goosefoot plant
<i>Tolmiea</i>	Piggyback plant
<i>Tradescantia</i>	Wandering jew

**Table 4.** Botanical and common names of representative orange plants

Botanical name	Common name
<i>Anthurium</i>	Painter's palette
<i>Begonia</i>	Painted leaf
<i>Capsicum</i>	Ornamental pepper
<i>Clivia</i>	Kaffir Lily
<i>Cybidium</i>	Cymbidium orchid
<i>Euphorbia pulcherrima,</i>	Poinsettia
<i>Gerbera</i>	Barberton daisy
<i>Gloriosa</i>	Flame lily
<i>Guzmania</i>	Scarlet star
<i>Hibiscus</i>	China rose
<i>Hippeastrum</i>	Amaryllis
<i>Impatiens</i>	Busy Lizzie
<i>Ixora</i>	Flame of the woods
<i>Kalanchoë blossfeldiana</i>	Flaming Katy
<i>Lilium</i>	Lily
<i>Oncidium</i>	Dancing orchid
<i>Primula veris</i>	Primrose
<i>Ranunculus</i>	Turban buttercup
<i>Solanum capsicastrum</i>	Winter cherry
<i>Vriesea splendens</i>	Flaming sword
<i>Zantedeschia</i>	Calla lily, arum

Plants that grow vegetables also fall into this category such as *Asparagus* or *Onion*. Shades of green in plants are as varied as any other color and you can have tones ranging from deep jade to light mint (Table 3).

It has to be said that orange plants get some of the coolest common names out of all plant colors. Trees and plants that grow orange colored fruits and vegetables, like ornamental peppers or *Pyracantha* are a popular choice for gardeners who wish to inject a bit of sunshine into their allotments. Native plants for orange dye extraction include: *Western Comandra*, *Prairie Bluets*, *Bloodroot*, *Sassafras* and *Eastern Cottonwood*. Below a list of orange plants by botanical name and common name (Table 4).

One of the most delightful plant colors is pink. A presentation of white with pink color gives the impression of freshness. Brighter shades of purple also compatible in the company of white color. Those gardeners fond of contrasts can try to connect pink with gold or orange (Table 5).

Purple plants can fit into a garden with any color scheme to add a dramatic touch to any garden landscape. They come in many shades and tones, from pale lilac to a vibrant velvety rich violet. Here below a list of purple plants by botanical name and common name (Table 6).

Using *Ozark chinkapin*, *Sumac*, *Chokecherry*, *Prairie parsley*, *Slippery elm* and *Black Willow*, red dyes were obtained for textile dyeing. Red plants can vary from pale, almost pink varieties to intense rich red shades and there are a number of species that you can grow in your



**Table 5.** Botanical and common names of representative pink plants

Botanical name	Common name
<i>Aechmea</i> ,	Urn plant (bromeliad family)
<i>Anigozanthos</i>	Kangaroo paw
<i>Anthurium</i> ,	Flamingo flower
<i>Begonia</i>	Painted leaf
<i>Cineraria</i>	Dusty miller
<i>Cyclamen</i>	Sowbread
<i>Cymbidium</i>	Cymbidium orchid
<i>Euphorbia pulcherrima</i>	Poinsettia
<i>Fittonia</i>	Snakeskin plant
<i>Fuchsia</i>	Lady's eardrops
<i>Gerbera</i>	Barberton daisy
<i>Hibiscus</i>	China rose
<i>Hippeastrum</i>	Amaryllis
<i>Hyacinthus</i>	Hyacinth
<i>Hypoestes</i>	Polkadot plant
<i>Impatiens</i>	Busy Lizzie
<i>Jasminum</i>	Jasmine
<i>Kalanchoë blossfeldiana</i>	Flaming Katy
<i>Lilium</i>	Lily
<i>Medinilla magnifica</i>	Rose grape
<i>Pelargonium</i>	Geranium
<i>Phalaenopsis</i>	Moth orchid
<i>Primula veris</i>	Primrose
<i>Primula</i>	Polyanthus
<i>Rhododendron simsii</i>	Azalea
<i>Saintpaulia</i>	African violet
<i>Sedum</i>	Stonecrop
<i>Schlumbergera</i>	Christmas cactus
<i>Streptocarpus</i>	Cape primrose
<i>Tradescantia</i>	Wandering jew
<i>Zantedeschia</i>	Calla lily, arum

**Table 6.** Botanical and common names of representative purple plants

Botanical name	Common name
<i>Achimenes</i>	Hot water plant
<i>Campanula</i>	Bell flower
<i>Cineraria</i>	Dusty miller
<i>Cymbidium</i>	Cymbidium orchid,
<i>Dendrobium</i>	Dendrobium orchid
<i>Dianthus</i>	Pink
<i>Exacum</i>	Persian violet
<i>Gerbera</i>	Barberton daisy
<i>Hyacinthus</i>	Hyacinth
<i>Impatiens</i>	Busy Lizzie
<i>Kalanchoë blossfeldiana</i>	Flaming Katy
<i>Pelargonium</i>	Geranium
<i>Primula veris</i>	Primrose
<i>Primula</i>	Polyanthus
<i>Rhipsalidopsis</i>	Easter cactus
<i>Saintpaulia</i>	African violet
<i>Schlumbergera</i>	Christmas cactus
<i>Sinningia</i>	Gloxinia
<i>Streptocarpus</i>	Cape primrose
<i>Zantedeschia</i>	Calla lily, arum

**Table 7.** Botanical and mmon names of representative red plants

Botanical name	Common name
<i>Anigozanthos</i>	Kangaroo paw
<i>Anthurium</i>	Flamingo flower
<i>Begonia</i>	Painted leaf
<i>Apsicum</i>	Ornamental pepper
<i>Codiaeum</i> ,	Joseph's coat, croton
<i>Cryptanthus</i>	Earth star
<i>Cyclamen</i>	Sowbread
<i>Cymbidium</i>	Cymbidium orchid
<i>Dionaea</i>	Venus fly trap
<i>Euphorbia milii</i> ,	Crown of thorns
<i>Fittonia</i>	Snakeskin plant
<i>Gerbera</i>	Transvaal daisy
<i>Gloriosa</i>	Flame lily
<i>Guzmania lingulata</i>	Scarlet star
<i>Hibiscus</i>	China rose
<i>Hippeastrum</i>	Amaryllis
<i>Hypoestes</i>	Polkadot plant
<i>limpatiens, busy Lizzie</i>	Busy Lizzie
<i>Ixora</i>	Flame of the woods
<i>Kalanchoë blossfeldiana</i>	Flaming Katy
<i>Lilium</i>	Lily
<i>Neoregelia</i>	Crimson cup
<i>Primula veris</i>	Primrose
<i>Ranunculus</i>	Buttercup
<i>Rhipsalidopsis</i>	Easter cactus
<i>Rhododendron simsii</i>	Aazalea
<i>Sarracenia</i>	Pitcher plant
<i>Schlumbergera</i>	Christmas cactus
<i>Solanum capsicastrum</i>	Winter cherry
<i>Vriesea splendens</i>	Flaming sword

garden or keep as houseplants. Below we have a list of the flowers you can find blooming in red (Table 7).

White is a popular color, however, a native white dye is unknown. Only *White Iris*, *Butternut* and *Can-aigre Dock* are able to produce light grey to silver color dye. White is a winter color and white plants can look amazing when distributed through a lush green garden. We have compiled a list of the white flowers (Table 8).

Bright bold and yellow plants inject a good dose of sunshine into garden. Yellow gives a feeling of warmth and sunshine. The sky maybe reflected in a combination of yellow with blue.

It is also interesting to combine yellow blossoming flowers with plants with gray leaves. *Yarrow*, *Honey Locust*, *Golden wild-indigo*, *Tall cinquefoil*, *Pecan*, *Indian-grass* produced yellow color. Botanical and common names of representative yelllow plants are presented in Table 9.

A variety of colors can be obtained from different parts of the one plant. Roots, nuts and flowers are common natural ways to get many colors from the entire spectrum.

**Table 8.** Botanical and common names of representative white plants

Botanical name	Common name
<i>Agapanthus</i>	African lily
<i>Anthurium</i>	Painter's palette
<i>Begonia</i>	Painted leaf
<i>Campanula</i>	Bell, flower
<i>Chrysanthemum</i>	Frutescens marguerite
<i>Cyclamen</i>	Sowbread
<i>Cymbidium</i>	Cymbidium
<i>Dendrobium</i>	Dendrobium orchid
<i>Euphorbia milii</i>	Crown of thorns,
<i>Euphorbia</i>	Pulcherrima poinsettia
<i>Exacum</i>	Persian violet
<i>Gardenia</i>	Cape jasmine
<i>Gerbera</i>	Barberton daisy
<i>Guzmania</i>	Scarlet star
<i>Hippeastrum</i>	Amaryllis,
<i>Hyacinthus</i>	Hyacinth
<i>Hypoestes</i>	Polkadot plant
<i>Impatiens</i>	Busy Lizzie
<i>Jasminum</i>	Jasmine
<i>Kalanchoë blossfeldiana</i>	Flaming Katy
<i>Lilium</i>	Lily
<i>Muscari</i>	Grape hyacinth
<i>Narcissus tazetta</i>	Paperwhite
<i>Phalaenopsis</i>	Moth orchid
<i>Primula veris</i>	Primrose
<i>Primula</i>	Polyanthus
<i>Ranunculus turban</i>	Buttercup uttercup
<i>Rhododendron</i>	Simsii azalea
<i>Saintpaulia</i>	African violet
<i>Schlumbergera</i>	Christmas cactus
<i>Spathiphyllum</i>	Peace lily
<i>Stephanotis</i>	Madagascar jasmine
<i>Zantedeschia</i>	Calla lily

**Table 9.** Botanical and common names of representative yellow plants

Botanical name	Common name
<i>Anigozanthos</i>	Kangaroo paw
<i>Anthurium</i>	Flamingo flower
<i>Begonia</i>	Painted leaf,
<i>Capsicum</i>	Ornamental pepper
<i>Codiaeum</i>	Joseph's coat, croton,
<i>Cymbidium</i>	Cymbidium orchid
<i>Euphorbia milii</i>	Crown of thorns
<i>Euphorbia pulcherrima</i>	Poinsettia
<i>Gerbera</i>	Barberton daisy
<i>hibiscus</i>	China rose
<i>Ixora</i>	Flame of the woods
<i>Kalanchoë blossfeldiana</i>	Flaming Katy
<i>Lilium</i>	Lily
<i>Narcissus,</i>	Paperwhite,
<i>Oncidium,</i>	Dancing orchid
<i>Phalaenopsis</i>	Moth orchid
<i>Primula veris</i>	Primrose,
<i>Vriesea splendens</i>	Flaming sword
<i>Zantedeschia</i>	Calla lily, arum

**Examples of applied phytotherapy**

Ryeong and coworkers analyze the effects of *Eucalyptus* aroma therapy on relieving allergic rhinitis symptoms among university students and found that *Eucalyptus* aroma therapy is effective and enhancing the quality of life of university students.<sup>6</sup> The purpose of the next study was to understand the role of pollen allergy in Taiwan. It was shown that pollen allergy is believed to be less common in East Asia, Latin America, and other tropical areas.<sup>7</sup> In this study all individuals received a 30-item skin test panel that included perennial allergens (house dust mix, Dermatophagoides pteronyssinus, Dermatophagoides farinae, dog epithelium, cat hairs, cockroach mix, and Candida albicans) and pollen allergens (acacia, pine mix, *eucalyptus*, beefwood, juniper mix, willow, mulberry mix, pepper tree, cedar, Johnson grass, Bermuda grass, ragweed mix, Timothy grass, spiny pigweed, cocklebur, sage mix, sheep sorrel, dog fennel, pigweed mix, English plantain, castor bean, alfalfa, and dandelion).<sup>7</sup> Most patients with allergic rhinitis in Taiwan are sensitive to perennial allergens, and pollens are a less common allergen.<sup>7</sup> Immunological approach to extra-mural environmental naso-bronchial allergy was also investigated.<sup>8</sup>

**Garlic in laryngology**

The most important observation is that allicin, the main biologically active compound derived from *Garlic*, could prevent hearing loss induced by other drug such as cisplatin.<sup>9</sup> There is still growing interest in alternative medicine with the use of *Garlic* to treat common illnesses like the common cold and asthma.<sup>1</sup>

**Ginkgo biloba in laryngology**

*Ginkgo biloba* extract treatment was used to treat tinnitus. Since there is no objective method to measure the symptom, the search for an effective drug can only be made on an individual basis.<sup>10</sup> This study aims to investigate the efficacy of trimetazidine, betahistine and *ginkgo biloba* extract in the treatment of tinnitus.<sup>11</sup> To investigate the clinical efficacy of *Ginkgo biloba* injection combined with traditional therapy in the treatment of explosive deafness.<sup>12</sup> Compared with traditional therapy alone, combined *Ginkgo biloba* extract injection and traditional therapy can significantly improve tinnitus symptom and overall response rate in the treatment of explosive deafness in coal miners, which suggests that the combination therapy is worthy of clinical application.<sup>13</sup> Oxidative stress is involved in the development and progression of otitis media. In this study, we investigated the effect of *Ginkgo* leaf parenteral solution on blood and cochlea antioxidant and immunity index in rats.<sup>14</sup> The patient's subjective assessment of the treatment with regard to improvement in hearing and reduction in tinnitus suggested that *Ginkgo biloba* ex-

tract was more beneficial than pentoxifylline.<sup>15</sup> *Ginkgo biloba* does not benefit patients with tinnitus.<sup>15</sup> It was noticed the effect of *Ginkgo biloba* on the expression of intermediate-early antigen (c-fos) in the experimentally induced anosmic mouse.<sup>16</sup> Kumar and coworkers studied the role of *ginkgo biloba* extract in acquired sensorineural hearing loss.<sup>17</sup> The effect of blood flow promoting drugs on cochlear blood flow, perilymphatic pO<sub>2</sub> and auditory function in the normal and noise-damaged hypoxic and ischemic guinea pig inner ear.<sup>18</sup> The effect of blood flow promoting drugs, such as hydroxyethyl starch either of low or high molecular weight pentoxifylline, *Ginkgo biloba*, naftidrofuryl and betahistine, and various combinations of the drugs was studied in unexposed and noise-exposed.<sup>18</sup> The efficacy systemic injection of *Ginkgo biloba* extract, EGb761, in idiopathic sudden sensorineural hearing loss was also investigated.<sup>19</sup> Steroids are currently the most frequently accepted agents for idiopathic sudden sensorineural hearing loss.<sup>19</sup> The effect of Korean red *Ginseng* on Symptoms and Quality of Life in Chronic Tinnitus shows that the major mechanism of inner ear cell damage is the production of reactive oxygen species (ROS).<sup>20</sup> Korean red *Ginseng* has an anti-ROS effect; thus we hypothesized that KRG may be of use for the treatment of chronic idiopathic tinnitus.<sup>20</sup> These results suggest that Korean Red *Ginseng* may improve tinnitus symptoms and mental wellbeing in chronic tinnitus patients. Since Korean Red *Ginseng* has been proven to protect against gentamicin-induced vestibular and hearing dysfunction, the effects of KRG on age-related inner ear disorder in C57BL/6 mice were investigated.<sup>21</sup> Numerous studies of Korean Red *Ginseng* attempts to improve radiation-induced oral mucositis.<sup>22</sup> The protective effects of Korean Red *Ginseng* were caused by inhibition of the apoptotic signal transduction pathway linked to caspase-3. In conclusion, Korean Red *Ginseng* protects the oral mucosa and SMG from radiation-induced damage by inhibiting caspase-mediated apoptosis in rats.<sup>22</sup> Radiation-induced oral mucositis is a dose-limiting toxic side effect for patients with head and neck cancer.<sup>22</sup> *Ginseng* polysaccharide has multiple immunoprotective effects.<sup>22</sup> The authors evaluated the protective effects of Korean red *ginseng* against gentamicin induced unilateral vestibular and hearing dysfunction and investigated its effective mechanism using in vitro cell cultures.<sup>21</sup> Quantitative analysis of hair cell damage in the scanning electron microscopy was closely related with vestibular and hearing functional results. Korean red *ginseng* is reported to have anti-allergic properties, including beneficial effects on asthma and atopic dermatitis.<sup>23</sup> 3-Nitropropionic acid, a mitochondrial toxin, has been reported to induce an acute cochlear damage. Korean red *ginseng* is known to have protective effects from some types of hearing loss.<sup>21,22</sup> *Ginseng* extract is known to have many

beneficial effects, including ischemia, stress, and aging. Cisplatin, an effective antineoplastic drug, can cause irreversible sensorineural hearing loss and serious tinnitus in humans; thus cisplatin-induced ototoxicity is a useful experimental model for ototoxicity.<sup>24</sup>

### Pelargonium

The antibacterial effect of the drugs with active ingredients of *Pelargonium sidoides* on different bacterial species (72 Streptococci, 48 Staphylococcus, 32 Neisseriae spp, 20 Moraxella catarrhalis, and 20 Haemophilus) isolated from the throat cultures of patients with upper airway infection was observed.<sup>25</sup> The roots of *Pelargonium sidoides* were used in the cold showed that all patients (100%) in the active treatment group judged the subjective tolerability of *Pelargonium sidoides* as good or very good.<sup>26</sup> *Pelargonium sidoides*, is a herbal remedy thought to be effective in the treatment of acute.<sup>27,28</sup> Bachert *et al.* evaluate the efficacy and safety of the herbal drug preparation from the roots of *Pelargonium sidoides*. Patients with sinonasal symptoms of at least 7 days duration, and radiographically and clinically confirmed acute rhinosinusitis of presumably bacterial origin with a Sinusitis Severity Score of at least 12 out of 24 points at inclusion.<sup>29</sup> Bereznay *et al.* seek to confirm that treatment with an extract of *Pelargonium sidoides* (EPs 7630) is superior to placebo for treatment of non-GABHS tonsillopharyngitis in children.<sup>30</sup>

### Rosemary

The aim of Sienkiewicz and coworkers was to characterize the ability of essential oils to support antibiotics against pathogenic bacteria in wounds. Gram-positive and Gram-negative bacteria obtained from wound infections were identified according to standard microbiological methods.<sup>31</sup>

### Spirulina

*Spirulina* represents a blue-green alga that is widely produced and commercialized as a dietary supplement for modulating immune functions, as well as ameliorating a variety of diseases.<sup>32</sup> To our knowledge, this is the first human feeding study that demonstrates the protective effects of *Spirulina* towards allergic rhinitis.<sup>32</sup> Ten different types of herbal supplements were identified, with stinging nettle (*Urtica dioica*), black elderberry (*Sambucus nigra*), and *Spirulina* being the most common (12.6%, 6.1%, and 5.7%, resp.). This study found a high prevalence of herbal treatment usage for the relief of allergic rhinitis symptoms in Turkey.<sup>33</sup> Compared to the control group, the tinnitus scores increased significantly, however, the salicylate-induced tinnitus could be reduced significantly by *spirulina* water extract.<sup>34,35</sup>

The study demonstrates that cancer regression is also accompanied by a significant induction of tumor necrosis factor in macrophages in the tumor area, sug-

gesting a possible mechanism of tumor destruction by algae extract.<sup>36,37</sup> The various agents were injected into the tumor bearing right buccal pouches twice-weekly for four weeks. Total tumor regression was found in 30% of phycotene animals, 20% of beta carotene animals and 15% of canthaxanthin animals after four weeks. Partial tumor regression was found in the remaining 70% of phycotene animals, 80% of beta carotene animals and 85% of canthaxanthin animals. None of the 13-cis-retinoic acid animals had total tumor regression, but 70% showed partial regression.<sup>37</sup>

An enhancement of IgA antibody production by *Spirulina* extract was also observed in culture supernatant of lymphoid cells, especially in the spleen and mesenteric lymph node from mice treated with *Spirulina* extract for 4 weeks before antigen stimulation. These results suggest that *Spirulina* may at least neither induce nor enhance allergic reaction such as food allergy dependent on an IgE antibody, and that when ingested both concurrently with antigen and before antigen stimulation, it may significantly enhance the IgA antibody level to protect against allergic reaction.<sup>38</sup>

### St John's wort

The results indicate that *St John's wort* (*Hypericum perforatum*) lowers blood concentrations of cyclosporin, amitriptyline, digoxin, indinavir, warfarin, phenprocoumon and theophylline; furthermore it causes intermenstrual bleeding, delirium or mild serotonin syndrome, respectively, when used concomitantly with oral contraceptives (ethinylestradiol/desogestrel), loperamide or selective serotonin-reuptake inhibitors (sertaline, paroxetine, nefazodone).<sup>38</sup> Phytomedicine uses remedies possessing significant pharmacological activity and, consequently, potential adverse effects and drug interactions. Several herbal medicines, such as aloe vera gel, contain pharmacologically active ingredients that may aid in wound healing.<sup>39-40</sup>

### Thyme

Chronic rhinosinusitis is a common disease which causes persisting inflammatory conditions of one or more sinuses. *Thyme honey* nasal spray seems to be a low-priced potential adjuvant remedy with excellent safety profile, to reduce inflammation and polyp formation and also fostering mucosal healing for patients suffering from chronic rhinosinusitis.<sup>41</sup> Antimicrobial properties of plants essential oils including *Thyme* have been investigated through several observations and clinical studies which purpose them as potential tools to overcome the microbial drug resistance problem.<sup>42</sup> The use of phytopharmaceuticals based on an investigated essential oil from *thyme* in the prevention and treatment of various human infections may be reasonable.<sup>43,44</sup> The viable counts of *Salmonella typhimurium* on nutrient agar decreased upon the addition

of either the essential oil of *thyme* or its constituent thymol, especially under anaerobic conditions. Antagonistic effects of thymol against *Staphylococcus aureus* were also greater under anaerobic conditions. In the presence of thymol, the viable counts of Salm. typhimurium obtained on a minimal medium were lower than those obtained on NA. Addition of bovine serum albumin neutralized the antibacterial action of thymol. It is suggested that the effects of BSA or Desferal are due to their ability to bind phenolic compounds through their amino and hydroxylamine groups, respectively, thus preventing complexation reactions between the oil phenolic constituents and bacterial membrane proteins.<sup>45</sup> Among other disorders, these alternative treatments are used in bronchitis and rhinitis, including some topical applications. *Thyme* oil did not affect CBF, whereas the presence of all other essentials oils resulted in an increase in CBF; the effect was higher at 0.2% than at 2%.<sup>46</sup> The antifungal effect of the essential oil from *Satureja montana* L., *Lavandula angustifolia* Mill., *Lavandula hybrida* Reverchon, *Syzygium aromaticum* (L.) Merrill and Perry, *Origanum vulgare* L., *Rosmarinus officinalis* L. and six chemotypes of *Thymus vulgaris* L. on *Candida albicans* growth were studied. The most efficiency was obtained with the essential oil from *Thymus vulgaris* thymol chemotype (MIC 80% = 0.016 microL/mL and Kaff = 296 microL/mL).<sup>47</sup> Essential oils extracted from ten Algerian plants were analyzed for their potential activity against *Candida albicans*. The highest efficiency was obtained with the essential oil from *Thymus numidicus* which showed antifungal effect 1357 fold stronger than that measured with amphotericin B.<sup>48</sup> Carvacrol, eugenol and thymol are major components of plants such as oregano, savory, clove and *thyme*. When applied to the tongue, these flavors elicit a warm sensation.<sup>49</sup> The results show aromatherapy to be a safe and effective treatment for alopecia areata.<sup>50</sup> *Thymus* oil and its components are becoming increasingly popular as naturally occurring antimicrobial and antioxidant agents. Histologic examination results show that the formation of new tissue in rats receiving thymus oil was more than other burned groups, and this finding supports our hypothesis.<sup>51</sup> The antioxidant activity was evaluated as a free radical scavenging capacity. A significant rate of antifungal activity of all of the examined essential oils was also exhibited.<sup>52</sup>

### Conclusions

This review includes studies on plants material. The properties of various plants physiology were discussed with the option for the use in phytotherapy.

### Acknowledgements

Dorota Bartusik-Aebischer acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).





## References

- Shakeel M, Trinidad A, Ah-See KW. Complementary and alternative medicine use by otolaryngology patients: a paradigm for practitioners in all surgical specialties. *Europ Arch Otorhinolaryngol*. 2010;267(6):961-971.
- Wahl RA, Aldous MB, Worden KA, Grant KL. Echinacea purpurea and osteopathic manipulative treatment in children with recurrent otitis media: a randomized controlled trial. *BMC Complement Altern Med*. 2008;8:56.
- Schapowal A, Berger D, Klein P, Suter A. Echinacea/sage or chlorhexidine/lidocaine for treating acute sore throats: a randomized double-blind trial. *Europ J Med Res*. 2009;14(9):406-412.
- Cohen HA, Varsano I, Kahan E, Sarrell EM, Uziel Y. Effectiveness of an herbal preparation containing echinacea, propolis, and vitamin C in preventing respiratory tract infections in children: a randomized, double-blind, placebo-controlled multicenter study. *Arch Pediatr Adolesc Med*. 2004;158(3):217-221.
- MacDavid K, Aebischer D. A Review of Sunlight Induced Cellular DNA Damage. *Am J Cancer Ther Pharmacol*. 2014;2(1):48-55.
- Ryeong SM, Kyung KE. Effects of Eucalyptus Aroma Therapy on the Allergic Rhinitis of University Students. *J Kor Biol Nurs Sci*. 2014;16(4):300-308.
- Liang KL, Su MC, Shiao JY, Wu SH, Li YH, Jiang RS. Role of pollen allergy in Taiwanese patients with allergic rhinitis. *J Formos Med Assoc*. 2010;109(12):879-885.
- Anand P, Agashe SN. Immunological approach to extramural environmental naso-bronchial allergy. *Indian J Otolaryngol*. 1984;36(2):39-44.
- Wu X, Li X, Song Y, et al. Allicin protects auditory hair cells and spiral ganglion neurons from cisplatin - Induced apoptosis. *Neuropharmacology*. 2017;116:429-440.
- Holgers KM, Axelsson A, Pringle I. Ginkgo biloba extract for the treatment of tinnitus. *Audiology*. 1994;33:85-92.
- Orhan I, Aydın S, Altın G, Yılmaz F. An efficacy comparison of betahistin, trimetazidine and ginkgo biloba extract in patients with tinnitus. *J Ear Nose Throat*. 2013;23(3):143-147.
- Tan J, Peng H. Clinical analysis of Ginkgo biloba injection combined with traditional therapy in treatment of explosive deafness. *Chinese J Ind Hyg Occup Diseases*. 2015;33(4):279-281.
- Zhao J, Su Y, Chen A, Yuan H, Liu L, Wu W. Effect of Ginkgo leaf parenteral solution on blood and cochlea antioxidant and immunity indexes in OM rats. *J Syn Chem Natural Prod Chem*. 2011; 16(12):10433-42.
- Jang CH, Cho YB, Kim JS, Cho SW, Yang HC, Jung KH, Kim JY, Choi CH, Lim Y, Park H, Kang SI. Effect of Ginkgo biloba extract on endotoxin-induced labyrinthitis. *Int J Pediatr Otorhinolaryngol*. 2011;75(7):905-909.
- Reisser CH, Weidauer H. Ginkgo biloba extract EGb 761 or pentoxifylline for the treatment of sudden deafness: a randomized, reference-controlled, double-blind study. *Acta Oto-Laryngol*. 2001;121(5):579-584.
- Lee NY, Chung KS, Jin JS, et al. Effect of Chicoric Acid on Mast Cell-Mediated Allergic Inflammation in Vitro and in Vivo. *J Nat Prod*. 2015;78(12):2956-2962.
- Kumar A, Raizada RM, Chaturvedi VN. Role of ginkgo biloba extract in acquired sensorineural hearing loss. *Indian J Otolaryngol Head Neck Surg*. 2000;52(3):212-219.
- Lamm K, Arnold W. The effect of blood flow promoting drugs on cochlear blood flow, perilymphatic pO<sub>2</sub> and auditory function in the normal and noise-damaged hypoxic and ischemic guinea pig inner ear. *Hearing Res*. 2000;141(1-2):199-219.
- Koo JW, Chang MY, Yun SC, et al. The efficacy and safety of systemic injection of Ginkgo biloba extract, EGb761, in idiopathic sudden sensorineural hearing loss: a randomized placebo-controlled clinical trial. *Eur Arch Otorhinolaryngol*. 2016;273(9):2433-2441.
- Kim TS, Lee HS, Chung JW. The Effect of Korean Red Ginseng on Symptoms and Quality of Life in Chronic Tinnitus: A Randomized, Open-Label Pilot Study. *J Audiol Otolaryngol*. 2015; 19(2):85-90.
- Tian C, Kim YJ, Lim HJ, Kim YS, Park HY, Choung YH. Red ginseng delays age-related hearing and vestibular dysfunction in C57BL/6 mice. *Experiment Gerontol*. 2014;57:224-232.
- Chang JW, Choi JW, Lee BH, et al. Protective effects of Korean red ginseng on radiation-induced oral mucositis in a preclinical rat model. *Nutr Cancer* 2014;66(3):400-407.
- Jung JH, Kang IG, Kim DY, Hwang YJ, Kim ST. The effect of Korean red ginseng on allergic inflammation in a murine model of allergic rhinitis. *J Ginseng Res*. 2013;37(2):167-175.
- Im GJ, Chang JW, Choi J, Chae SW, Ko EJ, Jung HH. Protective effect of Korean red ginseng extract on cisplatin ototoxicity in HEI-OC1 auditory cells. *Phytother Res*. 2010; 24(4):614-621.
- Uslu H, Yoruk O, Ayyıldız A, Aktan B. Antibacterial spectrum of umckaloabo (Pelargonium Sidoides) on upper airway infection agents. *Europ J General Med*, 2009; 6(4):245-248.
- Lizogub VG, Riley DS, Heger M. Efficacy of a pelargonium sidoides preparation in patients with the common cold: a randomized, double blind, placebo-controlled clinical trial. *J Sci Healing*. 2007;3(6):573-584.
- Timmer A, Günther J, Rücker G, Motschall E, Antes G, Kern WV. Pelargonium sidoides extract for acute respiratory tract infections. *Cochrane Database Syst Rev*. 2008; (3):CD006323.
- Conrad A, Jung I, Tioua D, et al. Extract of Pelargonium sidoides (EPs 7630) inhibits the interactions of group A-streptococci and host epithelia in vitro. *Int J Phytother Phytopharmacol*. 2007;14(6):52-59.
- Bachert C, Schapowal A, Funk P, Kieser M. Treatment of acute rhinosinusitis with the preparation from Pelargo-

- nium sidoides EPs 7630: a randomized, double-blind, placebo-controlled trial. *Rhinology*. 2009;47(1):51-58.
30. Bereznoy VV, Riley DS., Wassmer G, Heger M. Efficacy of extract of Pelargonium sidoides in children with acute non-group A beta-hemolytic Streptococcus tonsillopharyngitis: A randomized, double-blind, placebo-controlled trial. *Altern Ther Health Med*. 2003;9(5):68-79.
  31. Sienkiewicz M, Łysakowska M, Denys P, Kowalczyk E. The antimicrobial activity of thyme essential oil against multidrug resistant clinical bacterial strains. *Microbial Drug Resist*. 2012;18(2):137-148.
  32. Mao TK, Van de Water J, Gershwin ME. Effects of a Spirulina-based dietary supplement on cytokine production from allergic rhinitis patients. *J Med Food*. 2005;8(1):27-30.
  33. Sayin I, Cingi C, Oghan F, Baykal B, Ulusoy S. Complementary therapies in allergic rhinitis. *Int Schol Res Network Allergy*. 2013;938751.
  34. Hwang JH, Chan YC. Expressions of ion co-transporter genes in salicylate-induced tinnitus and treatment effects of spirulina. *BioMed Central Neurol*. 2016;16:159.
  35. Hwang JH, Chen JC, Chan YC. Effects of C-phycocyanin and Spirulina on salicylate-induced tinnitus, expression of NMDA receptor and inflammatory genes. *PLoS One*. 2013; 8(3):e58215.
  36. Shklar G, Schwartz J. Tumor necrosis factor in experimental cancer regression with alphatocopherol, beta-carotene, canthaxanthin and algae extract. *Europ J Cancer Clin Oncol*. 1988;24(5):839-850.
  37. Schwartz J, Shklar G. Regression of experimental hamster cancer by beta carotene and algae extracts. *J Oral Maxillofacial Surg*. 1987;45(6):510-515.
  38. Hayashi O, Hirahashi T, Katoh T, Miyajima H, Hirano T, Okuwaki Y. *J Nutritional Sci Vitaminol*. 1998;44(6):841-851.
  39. Izzo AA, Ernst E. Interactions Between Herbal Medicines and Prescribed Drugs. *Drugs*. 2001;61(15):2163-2175.
  40. Pribitkin ED, Boger G. Herbal therapy: what every facial plastic surgeon must know. *Arch Facial Plastic Surg*. 2001;3(2):127-132.
  41. Hashemian F, Baghbanian N, Majd Z, Rouini MR, Jahan-shahi J, Hashemian F. The effect of thyme honey nasal spray on chronic rhinosinusitis: a double-blind randomized controlled clinical trial. *Eur Arch Otorhinolaryngol*. 2015;272(6):1429-1435.
  42. Tohidpour A, Sattari M, Omidbaigi R, Yadegar A, Naze-mi J. Antibacterial effect of essential oils from two medicinal plants against Methicillin-resistant Staphylococcus aureus (MRSA). *Intern J Phytother Phytopharmacol*. 2010;17(2):142-145.
  43. Sienkiewicz M, Łysakowska M, Kowalczyk E, et al. The ability of selected plant essential oils to enhance the action of recommended antibiotics against pathogenic wound bacteria. *J Intern Society Burn Injur*. 2017;43(2):310-317.
  44. Mahboubi M, Bidgoli FG. Antistaphylococcal activity of Zataria multiflora essential oil and its synergy with vancomycin. *Int J Phytother Phytopharmacol*. 2010;17(7):548-550.
  45. Juven BJ, Kanner J, Schved F, Weisslowicz H. Factors that interact with the antibacterial action of thyme essential oil and its active constituents. *J Appl Bacteriol*. 1994;76(6):626-631.
  46. Neher A, Gstöttner M, Thaurer M, Augustijns P, Reinelt M, Schobersberger W. Influence of essential and fatty oils on ciliary beat frequency of human nasal epithelial cells. *Am J Rhinol*. 2008;22(2):130-134.
  47. Giordani R, Regli P, Kaloustian J, Mikail C, Abou L, Portugal H. Antifungal effect of various essential oils against Candida albicans. Potentiation of antifungal action of amphotericin B by essential oil from Thymus vulgaris. *Phytother Res*. 2004;18(12):990-995.
  48. Giordani R, Hadeif Y, Kaloustian J. Compositions and antifungal activities of essential oils of some Algerian aromatic plants. *Fitoterapia*. 2008;79(3):199-203.
  49. Xu H, Delling M, Jun JC, Clapham, DE. Oregano, thyme and clove-derived flavors and skin sensitizers activate specific TRP channels. *Nature Neuroscience*. 2006;9(5):628-635.
  50. Hay IC, Jamieson M, Ormerod AD. Randomized trial of aromatherapy. Successful treatment for alopecia areata. *Arch Dermatol*. 1998;134(11):1349-1352.
  51. Dursun N, Liman N, Ozyazgan I, Güneş I, Saraymen R. Role of thymus oil in burn wound healing. *J Burn Care Rehab*. 2003;24(6):395-399.
  52. Bozin B, Mimica-Dukic N, Simin N, Anackov G. Characterization of the volatile composition of essential oils of some lamiaceae spices and the antimicrobial and antioxidant activities of the entire oils. *J Agric Food Chem*. 2006;54(5):1822-1828.



## REVIEW PAPER

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# The potential of phytotherapy in otorhinolaryngology

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## Abstract

**Introduction.** The objective of this paper is to review the evidence of the use of herbs in phytotherapy.

**Aim.** To discuss plant properties and applications in otorhinolaryngology.

**Materials and methods.** We analysed literature and collected information of phytotherapy in otorhinolaryngology.

**Results.** The databases were searched using various keywords such as phytotherapy, otorhinolaryngology, and herbs such as: echinacea, eucalyptus, garlic, ginkgo, ginseng, kava, pelargonium sidoides, rosemary, spirulina, St John's wort, and thyme.

**Conclusions.** Due to the beneficial impact of medicinal plants in medicine there is a growing interest in analytical identification and quantification for clinical medicine and forensic toxicology.

**Keywords.** phytotherapy, medicinal plants, otorhinolaryngology

## Introduction to Phytotherapy

The world of plants surrounding us is invariably rich and diverse. Plants serve as a source of food for people and many are known to contain therapeutic phytochemicals. Plants, with the help of assimilatory dyes, can produce organic substances from water and carbon dioxide and other inorganic substances. From year to year, the number of new varieties of plants on the market is growing. In the 18th century, botanist Carl Linnaeus developed an internationally accepted system for nam-

ing each plant and wrote the first International Code of Botanical Nomenclature. The botanical name identifies each plant kingdom, sub-kingdom, division, class, order, family, and species divided into two names which are a genus and species epithet. Botanical names are convenient in communicating plant identification internationally.<sup>1</sup>

Thanks to over several thousand years of observation and experience, people have learned to distinguish edible plants from the inedible and even poisonous. Experience also taught them to use the healing properties

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Received: 28.09.2018 | Accepted: 16.10.2018

Publication date: September 2018

of certain species. Many medicinal plants were identified by the ancient Sumerians, Assyrians and Egyptians. The Middle Ages did not favor discoveries in the field of herbal medicine as during this period, numerous excesses and beliefs existed in relation to certain plants.

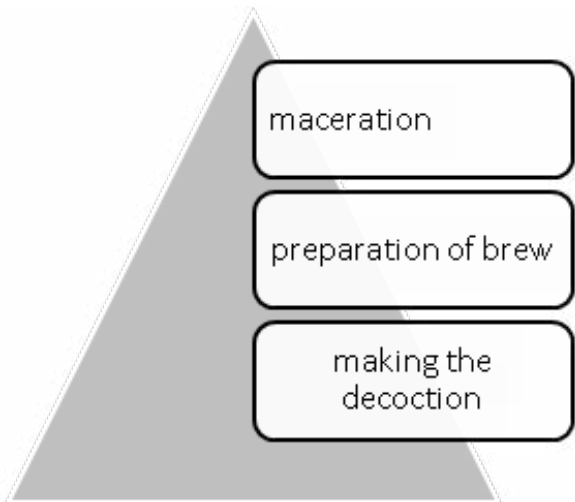


Fig. 1. Three ways to prepare herbal extracts

The healing properties of plants have been known since recorded history. Phytotherapy is a scientific medical method that recently, as part of a return to nature, millions of people around the world are be-

ginning to become interested in. Treatment using phytotherapy should be used wisely and properly under the direction of an experienced doctor or phytotherapist. Little data is available on complementary and alternative medicine use in children attending otolaryngology services.<sup>2</sup>

Most often, an herb is prepared in the form of freshly-made water extracts. In principle, there are three ways to prepare herbal tea, depending on the type of substances contained in the herbs (Figure 1).

1. maceration – the herbs are flooded with the prescribed amount of cold water and after some time the extract is drained
2. preparation of a brew – the herb is filled with boiling water and leaves under cover for 15 minutes
3. making the decoction – the herb in a covered dish is boiled over low heat.

Herbs consisting of various parts of plants and containing various substances are combined with a combination of, for example, decoction after maceration.

History of otolaryngology, laryngology and otorhinolaryngology

Table 1, Table 2 and Table 3 present a historical listing of a selection of main achievements in otolaryngology, laryngology and otorhinolaryngology respectively.

Table 1. History of otolaryngology

Year	Scientist	Achievements	References
1500 B.C.	-	published chapter titled: "Medications for the hard of hearing"	Nogueira <i>et al.</i> 2007 <sup>1</sup>
-	Empedocles (490-430 B.C.)	described the cochlea as the part of the inner ear involved in hearing	Singer 1957 <sup>3</sup>
-	Aristotle (384-322 B.C.)	created a theory on hearing	Gitter 1990 <sup>4</sup> , Nogueira <i>et al.</i> 2007 <sup>1</sup>
-	Galeno (129-201 d. C.)	dissected the ears of dogs and monkeys	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1543	Versalio (1514-1564)	described the structure of the malleus and the incus	Nogueira <i>et al.</i> 2007 <sup>1</sup>
-	Gabriel Fallopius (1523-1562)	described the facial nerve canal	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1649	Riolanos	described the technique of mastoidectomy	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1761	Domenico Cotugno (1736-1822)	described the perilymph	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1772	Antonio Scarpa (1752-1832)	described the endolymph	Brackmann <i>et al.</i> 2016 <sup>4</sup>
1829	Jean Cruveilhier (1791-1874)	described a pearl-like tumor in the central nervous system	Nogueira <i>et al.</i> 2007 <sup>1</sup>
838	Toulemouche	described malignant external otitis	Karaman <i>et al.</i> 2012 <sup>5</sup>
1860	Evenberg	reported the first case of sudden hearing loss	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1860	Joseph Toynbee (1815-1866)	published "Diseases of the ear"	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1875	Mach	performed pioneering studies on the vestibular excitability threshold	Nogueira <i>et al.</i> 2007 <sup>1</sup>



1883	Adam Politzer (1835-1920)	described auditory dystrophies	Lasmar and Seligman 2004 <sup>6</sup>
1885	Hermann Schwartz (1837-1910)	published papers systematizing the mastoidectomy technique	Hawkins 2004 <sup>7</sup>
1889	Emanuel Zaufal (1837-1910) and Stacker	described the radical mastoidectomy	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1892	Ernst Julius Richard Ewald (1855-1921)	established the labyrinthine origin of nystagmus	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1894	Adam Politzer (1835-1920)	described the hypoacusis	Lasmar and Seligman 2004 <sup>6</sup>
1901	Perry	opened the inner ear canal of a patient with Ménière's disease	Lasmar and Seligman 2004 <sup>6</sup>
1910	Gustave Bondy (1870-1954)	described a surgical technique for apical cholesteatoma with ossicular chain preservation and perforation of the tympanic pars flacida	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1910	Robert Bárány (1876-1936)	successfully trephinated the posterior semicircular canal without opening the antrum	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1912	Harold Albert Kisch (XIX-XX)	described a tympanoplasty for the first time, in a paper published in the "Proceedings of Royal Society"	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1913	Jenkins	trephinated the horizontal semi-circular canal, in an attempt dry the labyrinth	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1914	Robert Bárány (1876-1936)	received the Nobel Prize because of his work on vestibular apparatus physiology and pathology	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1918	Diniz Borges	published a pioneering thesis in Brazil on topics related to the vestibule	Lasmar and Seligman 2004 <sup>6</sup>
1919	Marcel Lermoyez (1858-1929)	described the syndrome that carried his name with the symptoms	Lasmar and Seligman 2004 <sup>6</sup>
1920	Harold Gillies (1882-1960)	was the first to use cartilage in remodeling the framework in cases of pinna reconstruction	Chauhan and Guruprasad 2012 <sup>8</sup>
1921	Carl Nylen (1892-1978)	introduced the monocular microscope for ear surgeries	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1922	Fletcher and Wegel	introduced the audiometric exam in screening patients for hearing loss	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1929	Lüscher	described the middle ear acoustic muscle activity	Møller 1974 <sup>9</sup>
1932	Charles Ballance (1856-1936) and Arthur Duel (1870-1936)	introduced the facial nerve decompression technique by opening its temporal bone canal	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1934	Schuster	measured for the first time the middle ear impedances	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1940	Boettcher	introduced the electrical burr for mastoid surgery	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1953	Zeiss Optical Company	introduced modern microscopic ear surgery with the development of the binocular microscope	Lasmar and Seligman 2004 <sup>6</sup>
1954	Edwin Armstrong (1890-1954)	introduced a polyethylene tube in the tympanic membrane, in order to treat cases of serous otitis media	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1967	Sohmer and Feinmesse	attempted to record the electrical activity of the human brainstem	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1968	Aran and Lê Bel	established the basis for electrocochleography	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1970	Jewet, Romano and Wilinston	demonstrated the origin of brainstem potentials	Jewett <i>et al.</i> 1970 <sup>10</sup>
1978	Charles Williams Vaughan (1926-2014)	Laboratory experiments of transoral laryngeal surgery using the CO <sub>2</sub> laser	Vaughan 1978 <sup>11</sup>
1980	Wolfgang Steiner (1942- )	transoral laser microsurgery (TLM) in laryngeal carcinoma	Harris <i>et al.</i> 2017 <sup>12</sup>
2008	Paolo Macchiarini (1958- )	conducted a transplant of a donated trachea colonized with the stem cells of the recipient	Macchiarini <i>et al.</i> 2008 <sup>13</sup>
2012	Fatma Tülin Kayhan (1967- )	first successful transoral robotic resection of a laryngeal paraganglioma	Tülin Kayhan <i>et al.</i> 2012 <sup>14</sup>

Table 2. History of Laryngology

Year	Scientist	Achievements	References
1545	Leonardo da Vinci (1452-1519) and Michelangelo di Lodovico Buonarroti Simoni (1475-1564)	performed detailed descriptions of laryngeal function	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1741	Giovanni Battista Morgagni (1682-1771)	described “vocal cords” in the paper “Adversaria Anatomica Prima”	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1745	Exupère-Joseph Bertin (1712-1781)	brought this new concept that the structures described by Ferrein were, in fact, folds, and not cords	Hawkins 2005 <sup>7</sup>
1806	Philipp Bozzini (1773–1809)	developed an angled speculum with a mirror, used to examine the most varied human cavities	Hawkins 2005 <sup>7</sup>
1829	Benjamin Ebbington (XVIII-XIX)	carried out a laryngoscopy with a device called “glottiscope”	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1837	Johannes Müller (1801–1858)	described the movement of vocal cords in cadavers	Weir 2000 <sup>15</sup>
1839	James Yearsley (1805-1869)	published the treaty “On throat deafness and the pathological connections of the throat, nose and ear”	Hawkins 2005 <sup>7</sup>
1865	Morell Mackenzie (1837-1892)	published “The use of the laryngoscope in diseases of the throat”	Hawkins 2005 <sup>7</sup>
1895	Arthur Schnitzler (1862-1931)	created an impressive atlas of laryngology, used until current times in the University of Vienna	Hawkins 2005 <sup>7</sup>
1954	Harold Horace Hopkins (1918-1994)	developed optic fibers endoscopes and use to examine the larynx, nasopharynx, nose and pharynx	Weir 2000 <sup>15</sup>
1970	Willard Sterling Boyle (1924-2011) and George Elwood Smith (1930-currently)	charge-coupled device (CCD) chip at the tip of the endoscope	Boyle and Smith 1970 <sup>16</sup>
1975	Mervyn Stuart Strong (1924) and Geza Julius Jako (1930-2015)	first use of CO <sub>2</sub> laser in patients with early laryngeal cancer	Tahir 2015 <sup>17</sup>
1976	Nobuhiko Isshiki (1930- )	published “Surgeries of the laryngeal framework, thyroplasties”	Weir 2000 <sup>15</sup>
2000	Alan Henry Shikani (XX-XXI) and Abraham Jacob Domb (XX-XXI)	new method of delivery of chemotherapy for the treatment of squamous cell carcinomas (SCCs) of the head and neck	Shikan and Domb 2000 <sup>18</sup>
2017	Abdul Latif Hamadan (XX-XXI)	the first case of a high-fidelity 3D-printed model of the vocal cords	Hamdan <i>et al.</i> 2017 <sup>19</sup>

Table 3. History of otorhinolaryngology

Year	Scientist	Achievements	References
1489	Leonardo da Vinci (1452-1519)	described the nasal conchae and the paranasal sinuses	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1597	Gaspare Tagliacozzi (1546-1599)	published the book “Treaty on Rhinoplasty”	Lascaratos 2003 <sup>20</sup>
1651	Nathaniel Highmore (1613–1685)	described the maxillary sinus	Feldmann 1998 <sup>21</sup>
1707	James Drake (1667–1707) and William Cowper (1666-1709)	described cases of halitosis caused by maxillary sinus suppuration	Feldmann 1998 <sup>21</sup>
1743	Louis Lamorier (1696–1777)	was already opening the maxillary sinus through the oral cavity	Tange 1991 <sup>22</sup>

1806	Philipp Bozzini (1773-1809)	created Rhinology name	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1806	Johann Nepomuk Czermak (1828-1873)	for the first time mentioned the term “rhinoscopy”	Feldmann 1998 <sup>21</sup>
1841	Friedrich Gustav Jakob Henle (1809-1885)	studied and differentiated various epithelia	Feldmann 1998 <sup>21</sup>
1870	Emil Zuckerkandl (1849-1910)	described details of the nose and paranasal sinuses in anatomical studies	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1886	Jan Mikulicz-Radecki (1850-1905)	was the first to describe the opening of the maxillary sinus through the inferior meatus	Nogueira <i>et al.</i> 2007 <sup>1</sup>
1893	George Walter Caldwell (1866-1946)	published his method, which consisted in opening the sinus through the canine fossa, removing the mucosal membrane	Feldmann 1998 <sup>21</sup>
1897	Henri Luc (1855-1925)	reported his own method, which was practically identical to Caldwell method	Feldmann 1998 <sup>21</sup>
1959	Walter Messerklinger (1920-2001)	developed the endoscopic technique for diagnosis and surgery of diseases of the nose, sinuses and skull base”	Feldmann 1998 <sup>21</sup>
1963	Gerard Guiot (1912-1998)	published his experience using the first endoscope with an external light source	Feldmann 1998 <sup>21</sup>
1970	Gerard Guiot (1912-1998)	the first to use endoscopy for a trans-sphenoidal approach in neurosurgery	Nogueira <i>et al.</i> 2007 <sup>1</sup>
2005	Kubo Shunsuke (XX-XXI)	applied the irrigation-suction straw sheath system originally developed for endoscopic sinus surgery in rhinology, for the endoscopic pituitary surgery	Kubo <i>et al.</i> 2005 <sup>23</sup>
2009	Hitier Martin (XX-XXI)	use of a computer-assisted system in transseptal pituitary surgery	Hitier <i>et al.</i> 2009 <sup>24</sup>

Medicinal qualities of plants

Many plants have medicinal qualities and have been used for centuries to cure ailments. Plants such as *Lavender*, *Dill*, *Eucalyptus*, *Marjoram*, *Rosemary*, and *Grape hyacinth* are often grown for scent and are among the most popular smells that people enjoy. *Mimosa* (*Acacia*), *Wax flower* (*Chamelaucium*), *Eucharis*, *Orange Blossom* and *Sweet Lemon* *Citrus* produce delicate lemon and marzipan scents which are bright and refreshing. *Gardenia*, *Oriental lily*, *Narcissus*, *Stephanotis* and *Tuberose* all have strong exotic scents. Flowers with a floral scent are *Freesia* (a popular flower with a delicate and summery fragrance), *Lily of the valley* (*Convallaria*) (a floral scent that is very popular in beauty products) and *Rose* (the classic floral fragrance). Flowers and plants which have a peppery smell often produce a warm scent. Spicy plants include *Chrysanthemum*, *Florists’ broom* (*Genista*), *Hypericum*, *Pink Dianthus* and *Stock*. Some plants aid in undesirable scent removal. Plants such as *Ficus*, *Spider plant* and *Peacy Lily* can filter out pollutants and leave the air fresh and clean. Plants can also remove chemicals from the air, such as those in paints, new carpets and furniture. A number of natural plant extracts are used for scent in beauty and cosmetic products. The most common medicinal plants are: *Eucalyptus*, *Aloe Vera* and *Chamomile*.<sup>25-34</sup>

The time of year is an important consideration when planning a scent garden. Some plants produce fragrance all year, such as evergreen. Planting and choosing scent-

ed plants for different seasons will assure a good balance. In order to have scent in garden twelve months of the year just like color, fragrance can be produced in different flowers.

Many of phytochemical constituents of medicinal plants demonstrate inhibition of tissue and bacterial hyaluronidase.<sup>35</sup> There is growing interest in use of complementary and alternative medicine among adult patients attending the ear, nose, and throat.<sup>36</sup> Echinacoside is a caffeoyl conjugate of *Echinacea* with known anti-hyaluronidase properties. Wound healing effects of *Echinacea* on vocal fold and functional voice outcomes have been investigated.<sup>37</sup> Histologically, treated vocal folds revealed stable hyaluronan content and no significant accumulation of collagen compared with controls. Findings provide a favorable outcome of anti-hyaluronidase treatment on acute vocal fold wound healing and functional measures of voice.<sup>35</sup> Chicoric acid (*Dicaffeoyl-tartaric acid*), is a natural phenolic compound found in a number of plants, such as chicory (*Cichorium intybus*) and *Echinacea* (*Echinacea purpurea*), which possesses antioxidant, anti-inflammatory, antiviral, and analgesic activities. Results suggest that chicoric acid has an antiallergic-related anti-inflammatory effect that involves modulating mast cell-mediated allergic responses. Therefore, chicoric acid could be an efficacious agent for allergy-related inflammatory disorders.<sup>36</sup> Herbal medicines are used worldwide by practitioners of traditional medicine to treat sore throat.<sup>37</sup> Based on research

done by Shi and coworkers, some Chinese herbal medicines for treating sore throat appeared efficacious. However, there is the lack of high quality results in clinical trials.<sup>38-40</sup>

## Conclusion

Due to the beneficial impact of medicinal plants in medicine there is a growing interest in analytical identification and quantification for clinical medicine and forensic toxicology.

## Acknowledgements

Dorota Bartusik-Aebischer acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).

## References

1. Nogueira JF Jr, Hermann DR, Américo RdosR, Filho ISB, Stamm AE, Pignatari SS. A brief history of otorhinolaryngology: otology, laryngology and rhinology. *Braz J Otorhinolaryngol.* 2007; 73(5):693-703.
2. Shakeel M, Trinidad A, Ah-See KW. Complementary and alternative medicine use by otolaryngology patients: a paradigm for practitioners in all surgical specialties. *Europ Arch Otorhinolaryngol.* 2010; 267(6):961-971.
3. Shakeel M, Trinidad A, Ah-See KW. Complementary and alternative medicine use by otolaryngology patients: a paradigm for practitioners in all surgical specialties. *Europ Arch Otorhinolaryngol.* 2010; 267(6):961-971.
4. Brackmann D, Shelton C, Arriaga MA. *Otologic Surgery.* Elsevier; 2016. ISBN: 978-0-323-299775. -9.
5. Karaman E, Yilmaz M, Ibrahimov M, Hacıyev Y, Enver O. Malignant otitis externa. *J Craniofac Surg.* 2012; 23(6):1748-1751.
6. Lasmar A, Seligman, J. *História (e histórias) da Otolgia no Brasil, Revinter.* Solvay Farma; 2014. ISBN 85-7309-801-5.
7. Hawkins JE. Sketches of Othistory: part 5 - Prosper Ménière: Physician, Botanist, Classicist, Diarist and Historian. *Audiol Neurotol.* 2005; 10:1-5.
8. Chauhan DS, Guruprasad Y. Auricular Reconstruction of Congenital Microtia Using Autogenous Costal Cartilage: Report of 27 Cases. *J Maxillofac Oral Surg.* 2012; 11(1): 47-52.
9. Møller AAGER. The Acoustic Middle Ear Muscle Reflex. Handbook of Sensory Physiology. *Springer Auditory Syst.* 1974; 5(1):519-548.
10. Jewett DL, Romano MN, Williston JS. Human auditory evoked potentials: possible brain stem components detected on the scalp. *Science.* 1970; 167(3924):1517-1518.
11. Vaughan CW. Transoral laryngeal surgery using the CO<sub>2</sub> laser: laboratory experiments and clinical experience. *Laryngoscope.* 1978; 88(9 Pt 1):1399-1420.
12. Harris AT, Tanyi A, Hart RD, et al. Transoral laser surgery for laryngeal carcinoma: has Steiner achieved a genuine paradigm shift in oncological surgery? *Ann R Coll Surg Engl.* 2018; 100(1):2-5.
13. Macchiarini P, Jungebluth P, Go T, et al. Clinical transplantation of a tissue-engineered airway. *Lancet.* 2008; 372(9655):2023-2030.
14. Tülin KF, Hakan KK, Altıntaş A, Fırat P, Sayın I. First successful transoral robotic resection of a laryngeal paraganglioma. *J Otolaryngol Head Neck Surg.* 2012; 41(6):E54-57.
15. Weir N. History of Medicine: Otorhinolaryngology. *Postgrad Med J.* 2000; 76:65-69.
16. Boyle WS, Smith GE. Charge coupled semiconductor devices. *Bell Syst Tech J.* 1970; 49:587-593.
17. Tahir A. The Evolution of Laser in Laryngology. *Intern. J Otolaryngol Head Neck Surg.* 2015; 4:137-140.
18. Shikani AH, Domb AJ. Polymer chemotherapy for head and neck cancer. *Laryngoscope.* 2000; 110(6):907-917.
19. Hamdan AL, Haddad G, Haydar A, Hamade R. The 3D Printing of the paralyzed vocal fold: added value in injection laryngoplasty. *J Voice.* 2017; 0892-1997(17)30269-2.
20. Lascaratos JG, Segas JV, Trompoukis CC, Assimakopoulos DA. From the roots of rhinology: the reconstruction of nasal injuries by Hippocrates. *Ann Otol Rhinol Laryngol.* 2003; 112(2):159-162.
21. Feldmann H. The maxillary sinus and its illness in the history of rhinology. Images from the history of otorhinolaryngology, highlighted by instruments from the collection of the German Medical History Museum in Ingolstadt. *Laryngorhinootologie.* 1998;77(10):587-595.
22. Tange RA. Some historical aspects of the surgical treatment of the infected maxillary sinus. *Rhinology.* 1991; 29(2):155-162.
23. Kubo S, Kikawada T, Hasegawa H, Tominaga S, Yoshimine T. Irrigation-suction straw sheath system for a rigid endoscope during endonasal endoscopic pituitary surgery. *Minim Invasive Neurosurg.* 2005; 48(6):373-375.
24. Gitter AH. A short history of hearing research. I. Antiquity. *Laryngorhinootologie.* 1990; 69(8):442-445.
25. Schwermer M, Längler A, Fetz K, Ostermann T, Zuzak TJ. Anthroposophic medicine in the treatment of pediatric pseudocroup: A systematic review. *Complement Ther Med.* 2018;40:185-19
26. Malcolm BJ, Tallian K. Essential oil of lavender in anxiety disorders: Ready for prime time? *Ment Health Clin.* 2018;7(4):147-155.
27. Henley-Smith CJ, Botha FS, Hussein AA, Nkomo M, Meyer D, Lall N. Biological Activities of *Heteropyxis natalensis* Against Micro-Organisms Involved in Oral Infections. *Front Pharmacol.* 2018;9:291.
28. Saleh AM, Selim S, Jaouni SA, Abdelgawad H. CO<sub>2</sub> enrichment can enhance the nutritional and health benefits of parsley (*Petroselinum crispum* L.) and dill (*Anethum graveolens* L.). *Food Chem.* 2018;269:519-526.
29. Mohammed FA, Elkady AI, Syed FQ, Mirza MB, Hakeem KR, Alkarim S. *Anethum graveolens* (dill) - A medicinal

- herb induces apoptosis and cell cycle arrest in HepG2 cell line. *J Ethnopharmacol*. 2018;219:15-22.
30. Osanloo M, Sereshti H, Sedaghat MM, Amani A. Nano-emulsion of Dill essential oil as a green and potent larvicide against *Anopheles stephensi*. *Environ Sci Pollut Res Int*. 2018;25(7):6466-6473.
31. Kamari A, Sepahvand A, Mohammadi R. Isolation and molecular characterization of *Cryptococcus* species isolated from pigeon nests and Eucalyptus trees. *Curr Med Mycol*. 2017;3(2):20-25.
32. Lapid D, Qureshi MA, Quresh IA, Afzal MR, Maud A, Rodriguez GJ, Khatri R. Possible Reversible Cerebral Vasoconstriction Syndrome Associated with Eucalyptus: Case Report *J Vasc Interv Neurol*. 2017;9(5):17-20.
33. Li Y, Xu YL, Lai YN, Liao SH, Liu N, Xu PP. Intranasal co-administration of 1,8-cineole with influenza vaccine provide cross-protection against influenza virus infection. *Phytomedicine*. 2017;34:127-135.
34. Dhakad AK, Pandey VV, Beg S, Rawat JM, Singh A. Biological, medicinal and toxicological significance of Eucalyptus leaf essential oil: a review. *J Sci Food Agric*. 2018;98(3):833-848.
35. Rousseau B, Tateya I, Lim X, Munoz-del-Rio A, Bless DM. Investigation of anti-hyaluronidase treatment on vocal fold wound healing. *J Voice*. 2006; 20(3):443-451.
36. Shakeel M, Little SA, Bruce J, Ah-See KW. Use of complementary and alternative medicine in pediatric otolaryngology patients attending a tertiary hospital in the UK. *Int J Ped Otorhinol*. 2007; 71(11):1725-1730.
37. Lee GS, Cho JH, Park CS, Jung SH, Lee DH, Jun BC, Song CE, Cho KJ. The effect of Ginkgo biloba on the expression of intermediate-early antigen (c-fos) in the experimentally induced anosmic mouse. *Auris Nasus Larynx*. 2009;36(3):287-291.
38. Shi Y, Gu R, Liu C, Ni J, Wu T. Chinese medicinal herbs for sore throat. *Cochrane Database Syst Rev*. 2007; (3):CD004877.
39. Hoseinifar SH, Sun YZ, Wang A, Zhou Z. Probiotics as Means of Diseases Control in Aquaculture, a Review of Current Knowledge and Future Perspectives. *Front Microbiol*. 2018;9:2429.
40. Wei F, Liao XF, Liu XF, Yang MH, Lu JH, Kong WJ. Research progress of pretreatment technology for mycotoxin detection in Chinese materia medica and complex matrices. *Zhongguo Zhong Yao Za Zhi*. 2018 ;43(17):3431-3443.



## REVIEW PAPER

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# How genetic predispositions may have impact on injury and success in sport

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### Abstract

**Introduction.** Studies investigating the determinants of physical endurance were initiated nearly 30 years ago. The research was inspired by the curiosity to find out about the nature of talent for sport and why some athletes are better than others, despite the same or even greater effort in training routine, diet and the supplementation. An attempt was therefore made to determine the genotype of a perfect athlete, but conducted research showed that it is a very difficult task. Although 140 genes were proposed to affect of ideal sportsman fitness, scientists are still far from formulating answers about the nature of physical abilities and genotype.

**Aim.** Our main goal was to review the literature about the selected genes and polymorphisms which are most often investigated in the context in relation to injury in sports.

**Materials and methods.** Analysis of literature from US National Library of Medicine, National Institutes of Health, PubMed, Google Scholar.

**Results.** We review the selected genes and polymorphisms which are most often investigated in the context in relation to injury in sports, we also present the function of genetic variants prevalent in athletes which are able to achieve better physiological adaptation during the training.

**Conclusions.** There are probably more than 140 genes involved in physical performance. Changes in even one nucleotide within the gene (SNP) can improve the body's adaptation to better physical performance and the frequency of injury to athletes.

**Keywords.** sport, genetic predisposition, endurance performance, aerobic capacity, injury

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 16.08.2018 | Accepted: 22.09.2018

Publication date: December 2018

### The list of abbreviations:

LDL – low density lipoprotein, SNPs – single nucleotide polymorphisms,  $VO_{2max}$  – maximal oxygen uptake, GDP – guanosine diphosphate, ATP – adenosine triphosphate, ADP – adenosine diphosphate, RLC – regulatory light chain, CK – creatine kinase, Mb- myoglobin, mTOR – mammalian target of rapamycin kinase, BMD – bone mineral density

### Introduction

Individuals who are able to master new movements during exercise within only few repetitions and who need little time to learn new motor skills are commonly referred to as physically gifted individuals.<sup>1</sup> A question arises what factors may influence the occurrence of such abilities in some people, while a complete lack of these abilities is observed in others. A similar question can be asked in relation to professional athletes, i.e. why do some athletes gain greater benefits from training than others? The explanation could be provided by Darwin's theory of natural selection declaring that people with more favourable traits have a better chance of survival and transfer the relevant trait to their offspring. It should also be noted that every person has certain limits in task execution. This is caused by the adaptation of the organism to the environment and the prevailing conditions. Phenotypes characterized by endurance, which may be linked with genetics, include: muscle performance, extensibility and strength of tendons and ligaments and physiological attitude towards training.<sup>2</sup> Increasing the performance of one function may impair the development of another. These assumptions were supported by research focusing on world-class athletes. In one of the experiments it was shown that persons cultivating a strictly defined sport on a daily basis may be predisposed by nature to succeed, yet the same individuals are not able to obtain equally good results in other disciplines.<sup>2</sup> It has also been shown that players who are very successful in static sports, such as weightlifting, cannot boast of equally good results in dynamic sports e.g. sprint running, and *vice versa*.<sup>3</sup> The importance of the genetic factor has long been studied in many laboratories worldwide. One of these projects is "the HERITAGE family study" focused on health, risk factors, training exercise and genetics, which began in 1992. This project was designed to determine the impact of individual genes on the performance of the cardio-respiratory system, metabolism, and hormone balance during aerobic exercise. The analysis also covered such parameters as: maximal oxygen uptake, blood pressure, concentration of glucose and concentration of free fatty acids. The results of this project have shown that changes in metabolic processes during training have influence on the results achieved by athletes and in some patients this increase amounted even 50%, but no relationship

between initial level of  $VO_{2max}$  and the change in this parameter after training was found. Changes in metabolic process are a result of the regulation of gene expression and the variability of non-protein and protein products.<sup>4</sup> Roth et al. suggests on an interest in a particular sport discipline is affected by genetic factors, and additionally, it was noted that the specific physical characteristics, such as body shape are important and unique for particular sport disciplines.<sup>5</sup> Hereditary traits were also examined in children whose parents were professional athletes. During this study the hereditary sport-related traits like skeletal muscle was shown to range from 55% to 65% frequency, but height frequency of the body was found to be the most hereditary trait of all, reaching the up to 85%. Aerobic capacity was measured in terms of a submaximal rate, of the measured value and as the maximum factor (eg.  $VO_{2max}$ ). This trait has proven to be much less heritable compared with the abovementioned genes, heredity oscillated in the range of 40-50% frequency. Each of the attributes described above can help to increase the endurance of the organism.<sup>5</sup> However, looking at the last 20 years, and the studies carried out during that time, it can be seen that they mostly focused on isolated genes, as well as a small number of chromosomal regions.<sup>6</sup>

Polymorphisms of genes described below may be associated with predispositions to various types of sports. Pescatello and Roth presented the relationship between gene tested in terms of predisposition for sport as overlapping parts of circles, which indicates that one gene does not affect only one function in the human body.<sup>7</sup> In addition, increasing number of scientific publications show a multigene character of performance *attainment* in sport, thereby departing from investigating isolated genes only.

### Genes and gene variants implicated in determination of endurance

#### Adrenergic- $\beta$ 2 receptor (ADRB2)

Adrenergic receptors are located in cell membranes, they are activated by adrenaline or noradrenaline, and are able to activate the G protein which is responsible (along with GPCRs) for activation and directing of B and T lymphocytes and monocytes towards immune response and for enhancing their proliferation and in addition phosphorylation of GDP. Beta receptors are involved also in cardiac and smooth muscle tone (in the muscle they are expressed in 99% of cells).<sup>4,8,9</sup> ADRB2 is responsible for the performance and endurance of the body because it regulates energy and lipid levels in human adipose tissue.<sup>10</sup> It is responsible for relaxation of the smooth muscle, strength and frequency of myocardial contractions, dilation of blood vessels and decrease of blood pressure.<sup>4</sup> Research also showed the inverse correlation between initial concentration of noradren-

aline and work performed or maximal oxygen uptake, and positive correlation between the expression of the *ADRB2* gene before training and work performed as well as maximal oxygen uptake.<sup>11</sup> Beta adrenergic receptor is the main target of illegal anabolic agents which are used by athletes. Agonists of these receptors cause e.g. expansion of the bronchi. In combination with corticosteroids the receptors significantly enhance the anti-inflammatory activity. Additionally people with the *Gly16* (*rs1042713*) variant show a rapid decrease in  $\beta 2$  receptor activity and loss of sensitivity to agonists. On the other hand people with the *27Glu* (*rs1042713*) allele will be resistant to these effects.<sup>12</sup> Wolfarth et al in their study mainly focused on the *Arg16Gly* polymorphism (*rs1042713*).<sup>13</sup> The study group included 313 athletes: runners, cyclists, rowers, triathlons and others. The results were compared with the control group of 297 male subjects. The findings showed that the *Gly16* allele was not responsible for the athletes' high endurance but for their strength. Tsianos et al. showed the *16Arg* allele influenced the results (times) obtained by marathon runners, whereas in gymnasts the *ADRB2* gene may be associated with low body weight and adipose tissue.<sup>14,15</sup>

### Guanine nucleotide binding protein $\beta$ polypeptide 3 (GNB3)

The *C825T* polymorphism (*rs5443*) in the *GNB3* gene, which encodes the  $\beta 3$  subunit of the G protein is associated with increased transduction signal between the receptors coupled to this protein and intracellular effectors presented in almost cells of the human body.<sup>16</sup> The product of the *GNB3* gene can also affect hypertension by enhanced exchange of  $\text{Na}^+/\text{H}^+$  activity which is mediated by G- protein.<sup>17</sup> The T allele of *GNB3* gene (*rs5443*) is associated with higher arterial blood pressure in Korean men.<sup>18</sup> There is also evidence that the T allele of this gene may enhance effectiveness of certain drugs, e.g. used as treatment of pulmonary hypertension.<sup>19</sup> This polymorphism has also been investigated in the context of sporting achievements.

A study of 155 Israeli athletes has demonstrated that there are no significant differences in the allele frequency in three groups (controls, endurance runners and sprinters), regardless of their proficiency level, for genotype distribution and for allele frequencies. However, Eynon et al. did not find the correlation of the *C825T* polymorphism of *GNB3* gene and the -9/+9 polymorphism of *BDKRB2* gene with the endurance performance.<sup>20</sup> Sawczuk et al. confirmed that the *C825T* polymorphism had no differences in genotype distribution between endurance oriented athletes and strength/power in Polish athletes.<sup>21</sup> However, previous studies, conducted by Eynon et al. demonstrated that TT genotype was more frequent in elite endurance athletes than in sprinters and that the *GNB3* gene was associated with

$\text{VO}_{2\text{max}}$  in people who were not athletes.<sup>22,23</sup> Additionally the results reported by Gülyaşar et al. suggest that the T allele can be used as a genetic marker of poor capacity for sporting achievement, because basketball players with this genotype obtained lower results related to muscle strength than the remaining study participants.<sup>24</sup>

### Genes and gene variants implicated in determination of muscle endurance

#### Creatine kinase (CK-MM)

Creatine kinase supplies ATP molecules to the heart and to the skeletal muscle.<sup>4</sup> It is a catalyst in the reversible transfer reaction of a phosphate group from phosphocreatine to ADP, which is produced during muscle contraction; as a result of this process ATP molecules are formed.<sup>25</sup> CK-M is associated with myofibrils M-line which is located in sarcomere. Creatine kinase also regenerates ATP molecules in that location.<sup>26</sup> Rivera et al. suggest that the *CK-MM* gene may contribute to individual differences in the  $\text{VO}_{2\text{max}}$  (which was measured during cycle ergometry test before and after 20 weeks of endurance training) response during training ( $n=495$ ).<sup>27</sup> The A/G (*rs8111989*) polymorphism of the *CK-MM* gene affects athletes' endurance.<sup>28</sup> The AA genotype may be associated with rhabdomyolysis.<sup>29</sup> A allele was detected with higher frequency in athletes' strength.<sup>30</sup> Additionally, the GG and GA genotypes in women ( $n=85$ ), who practice sports as well as aerobic and anaerobic exercise, are related with maximum oxygen uptake. The G allele in turn has a positive effect on  $\text{VO}_{2\text{max}}$ .<sup>31</sup> Moreover, as a more common gene variant can be associated with the mechanism protecting muscles against damage.<sup>29</sup> Studies of Russian athletes have shown that the AA genotype is more common in endurance athletes, e.g. in rowers, which may be associated with higher  $\text{VO}_{2\text{max}}$ . On the other hand the GG genotype was more frequent in weightlifting athletes.<sup>30</sup> In contrast to the study presented above, Döring et al. did not find a link between the A/T (*rs344816*), C/G (*rs10410448*), C/G (*rs432979*), T/C (*rs1133190*), T/C (*rs7260359*), G/T (*7260463*) and C/T (*rs4884*) polymorphisms and elite athletes.<sup>32</sup>

#### $\alpha$ -actinins-3 gene (*ACTN3*)

Alpha actinin belongs to a group of actin-binding proteins.<sup>33</sup> There are two genes that encode skeletal muscle alpha-actinin. In humans *ACTN2* which is expressed in all muscle fibres and *ACTN3* expressed only in Type 2 fibres. The genotypes associated with *ACTN3* are related to the size of the muscle mass and the use of glycogen during exercise.<sup>34</sup> Alpha actinins are responsible (as opposed to the CK-MM) for the Z-line in sarcomere, and play a role in the regulation of metabolism and signalling pathways.<sup>3,35</sup> Different genotypes of the *ACTN3* gene are associated with different physical fitness in hu-



mans relative to specific environmental conditions. The strength linked with type 2 muscle fibres (high speed and rate of movement) is expressed as the ability of an individual to adapt to training; moreover, a protein, which is a product of the *ACTN3* gene, is necessary for the normal structure and muscle function.<sup>8,3</sup> The *R577X* polymorphism (*rs1815739*) of the *ACTN3* gene is often described in the context of sporting achievements. Replacement of arginine at amino acids 577 causes a generation of a premature stop codon and result in complete lack of production of a protein in actinin 3.<sup>36,37</sup>

Lack of this protein is quite common (18% people have the XX genotype) and may impact the increase in calcineurin signalling in alpha actin 3.<sup>38,35</sup> The result is the release of the calcineurin from inhibitory effect of calsarcin 2 and leads to a reduction in strength, muscle mass and fast-twitch muscle fibres.<sup>35,39</sup> This increases the metabolism of the skeletal muscle and the quantity of slow-twitch fibres; additionally, exercise-induced increase of phosphorylation of mTOR (which is important signalling pathway in regulation of muscle mass) was lower in individuals with the XX genotype than in those with the RR or RX genotype.<sup>40</sup> This indicates a lower predisposition to hypertrophy in people with the XX genotype.<sup>34</sup> A study carried by Mills et al. on a group of Russian athletes which doing various types of sports, including volleyball, basketball, boating and others. The study found a correlation between the R allele and high level of serum testosterone in male group, in female. Moreover, the authors observed a deficiency in  $\alpha$  actinin 3 and muscle hypertrophy as well as power athlete status of the holders of these allele.<sup>40</sup> On the other hand a study of Japanese athletes has demonstrated the influence of the *R577X* polymorphism on muscle strength, but only in male subjects. The authors of this study suggest that the RR and RX genotypes are associated with significantly higher affects peak muscle power in men during anaerobic exercise then in athletes with XX genotype.<sup>41</sup> In another study on Japanese runners it has been shown that sprinters with the RR and RX genotypes achieve better timing than those with the XX genotype because the former genotypes give benefits which are linked with the endurance of the organism.<sup>33</sup> No such genetic relationship was identified in the case of runners who compete over a distance of 400m.<sup>42</sup>

#### Myosin light-chain kinase (MLCK)

RLC catalyzed by MLCK plays a significant role in the development of muscle strength. The binding of  $\text{Ca}^{2+}$  to tropin and tropomyosin is a fundamental regulator of skeletal muscle contraction.<sup>43</sup> It is possible that MLCK has the ability to change the phosphorylation of the RLC type 2 fibres, reducing the ability to withstand loads during long-lasting muscle contractions. The *MLCK* gene can be helpful in providing answers to the varia-

bility of muscle injury during exercise. The studies presented below investigated two polymorphic sites *C49T* (*rs2700352*) and *C37885A* in this gene. The first of these is responsible for the increase in CK (creatin kinase) and Mb (myoglobin) after four-day exercise. It was observed that the largest increase and activity in the above proteins was demonstrated in carriers of the TT genotype. The second polymorphism is associated with higher concentrations of CK, however only after 7 days of effort. But heterozygotes exhibit greater concentration of this protein than homozygotes after 10 days of training; on the other hand the *C37885A* polymorphism was associated with decreased strength (which was determined by level of Mb) during training. Additionally, heterozygotes showed greater loss of strength after training, compared to the homozygous individuals.<sup>44</sup> People with the *37885A* allele are more susceptible to rhabdomyolysis than homozygotes with the C allele, however, it may also happen that individual carriers of the *49T* and *37885A* genotypes may in the future be affected by this muscle disease.<sup>44,45</sup>

#### Angiotensin I converting enzyme (ACE)

Angiotensin I converting enzyme gene (*ACE-I*) was one of the frequent studied genes in regards to the physical performance because their physiological function.<sup>46</sup> *ACE* is located on chromosome 17, it is composed of 25 exons and 26 introns.<sup>47</sup> This gene impacts the renin-angiotensin system (RAS). It plays an important role in the regulation of blood pressure, sodium, water and an increase in muscle tissue.<sup>48</sup> The reduced amount and activity of ACE circulating in serum may be associated with an insertion polymorphism (inserting 287 bp of Alu sequences) in intron 16 of the *ACE* gene.<sup>49</sup> Angiotensin I converting enzyme is a genetic marker which is also used in determining the risk of kidney or cardiovascular disorders. With regard to this gene there may be the following genotypes: homozygous I/I or D/D and heterozygote I/D (*rs4646994*).<sup>50</sup> The insertion (the I allele) is associated with an improvement in the organism's performance in response to an applied endurance training. It has also been shown that the polymorphism is associated with prolonged exercise capacity at high altitudes. This was demonstrated during surveys of British mountaineers (who had ascended beyond 8,000m without oxygen) no one was homozygous with for D allele. Similar studies were carried out taking into account rowers, runners, and cyclists which have most frequently I allele compared with controls.<sup>51,48</sup> The I/I genotype is characterized by low activity of this enzyme in the tissues and allows to keep a positive energy balance during long and intense exercises. It turned out that the athletes with an insertion allele obtained better results at distances longer than 200m. In contrast to the I allele, individuals with the D allele obtain better results in short-distance

sports, which require greater muscle strength and more rapid shrinkage of type II muscle fibres these findings were confirmed e.g. for swimmers and sprinters running at a distance of 200m.<sup>48,50,52</sup> Researchers also found that the D allele is a factor contributing to the uniqueness of some players, because its significant part participates in the conversion of angiotensin I to II. The latter is prevalent in the skeletal muscle but it is also found in the myocardium; it has also been demonstrated that angiotensin II is involved in the repair of this tissue.<sup>53</sup> The I/D polymorphism may be associated with vascular diseases such as hypertension, myocardial infarction, and left ventricular hypertrophy. This polymorphism has no effect on the level of oxygen uptake or regulation of muscle contraction but it is associated with the increase in the size of type I muscle fibre. The D allele is associated with higher production of angiotensin II and aldosterone, as well as decreased half-life of bradykinin in comparison with the I allele.<sup>5</sup>

In contrast to the I/I genotype, the D/D genotype is more common in athletes who have to deal with anaerobic exercise (sprinters, short-distance swimmers). In these individuals the ACE levels in tissues is more than twice as large as in people with the I/I genotype.<sup>49</sup>

In general, left ventricular hypertrophy is a common trait of athletes. Exercise activates the renin-angiotensin system, which can regulate the growth of the heart muscle. Angiotensin II stimulates the synthesis of proteins in this muscle, whereas bradykinin, which plays the opposite part, inhibits this process. It has been proven that the increase in the left ventricular mass in each of the subjects was different; this suggests that the genetic factors can regulate this trait. Moreover the D allele is associated with the ACE protein concentration and thus angiotensin II in plasma and tissues.<sup>54</sup> The highest concentration of this protein was demonstrated in individuals with the D/D genotype and the lowest in those with the I/I genotype.<sup>55</sup> Increasing the ACE level in the organism can promote angiotensin II; the consequences include an increase in the amount of superoxide anions decomposing nitric oxide (which regulates the cardiovascular system and more specifically is directly related to vascular relaxation; it retains a resting tension of blood vessels); additionally, ACE can promote the degradation of bradykinin.<sup>54,56</sup>

### Bradykinin $\beta$ 2 receptor (BDKRB2)

*BDKRB2* encodes the bradykinin  $\beta$ 2 receptor responsible for increased glucose uptake in the skeletal muscle during exercise. Activation of bradykinin leads to the production of nitric oxide (NO) from arginine. Under the physiological conditions NO regulates mitochondrial metabolism and optimizes the ratio of oxygen consumption to the produced energy.<sup>57</sup> *BDKRB2* is responsible for the regulation of arterial blood pres-

sure and for the performance of muscle contraction; it may be associated with bradykinin which is activated by *BDKRB2* (B2R).<sup>58,59</sup> The polymorphism investigated in this context -9/+9 (*rs5810761*), located in exon 1. The -9 allele, in contrast to the +9 allele, is associated with increased expression of *B2R* gene; moreover, this allele is associated with higher muscle metabolism efficiency and enhanced performance and endurance in athletes.<sup>55</sup> Additionally, the -9/-9 genotype is more frequent in Caucasian triathletes than in the control group and also together with the G allele of the *NOS3* gene impacts better results at the finish compared with the control subjects.<sup>60</sup> Furthermore, the homozygous -9/-9 genotype showed associated with better muscle growth after short force-training in comparison with the homozygous +9/+9.<sup>58</sup> On the other hand a study of 125 Israeli athletes by Eynon et al. showed that the -9/+9 polymorphism was not related to endurance in athletes.<sup>20</sup> A study on Greek athletes showed a predominance of the +9/+9 genotype; moreover Sgourou et al. suggested that the joint influence of the D/D genotypes of the *ACE* gene, +9/-9 *BDKRB2* and G/A *LEP* gene may be associated with better feat achieved by athletes.<sup>61</sup> On the other hand a study of Polish swimmers (157 subjects) suggested that the -9/+9 *BDKRB2* gene polymorphism had no effect on sport achievements.<sup>62</sup>

### Insulin-like growth factor-1 (IGF-1)

Insulin-like growth factor 1 (IGF-1) is redundant and structurally similar to the insulin receptors. Just like myostatin, IGF-1 is produced in the skeletal muscle and liver; it is also a modulator promoting muscle growth and strength. IGF-1 impacts the anabolic effects such as the increase in the level of protein synthesis.<sup>63</sup> An increase of IGF-1 in the bloodstream following physical effort may be an evidence of effective training and good health; moreover, free form of IGF-1 may be absorbed by the tissues which are involved in exercise.<sup>64</sup> The potential benefits possibly caused by IGF-1 include: an increase in lipolysis, lipid oxidation, glycogen synthesis, a decrease in muscle degrading proteins, an increase in the opposing, synthesizing proteins and an increase in the synthesis of collagen in tendons.<sup>65</sup> The polymorphism of this gene, potentially associated with the genetic determined sporting accomplishment is *C1245T* (*rs35767*) which is located in the *IGF-1* gene promoter. This polymorphism was investigated in the context of the muscle size and function. It has been shown that in elderly women the C/C genotype is associated with increased body fat compared with the C/T genotype; in addition people with the C/C genotype have lower level of muscle tissue and fat-free mass than those with the T/T genotype.<sup>66</sup> The T/T genotype is only found in athletes, but not in the control group. It may also be associated with athletes' strength and endurance. Moreover,

the T allele occurred only in top athletes.<sup>67</sup> The polymorphism associated with the P1 region in the *IGF-1* gene promoter is characteristic for endurance athletes, and it may also be associated with the organisms' adaptation to performance.<sup>68,66</sup> Thesecond investigated polymorphism is A275124C (*rs1464430*); the study published by Ben-Zaken et al. shows that the incidence of the A/A genotype is much higher in the control group than in whole swimming athletes group, this is due to reduce of frequency A/A genotype in short-distance swimmers.<sup>67</sup> On the other hand, there was no difference in the prevalence of this genotype in athletes competing in national and international tournaments, but in top athletes this genotype occurred less frequently than in athletes competing in national events only.

### Myostatin (MSTN)

Myostatin is a highly conserved member of the TGF- $\beta$  family (transforming growth factor- $\beta$ ), functioning as a negative regulator of muscle size and mass, moreover it is often expressed in skeletal muscle but lesser in adipose tissue and cardiac muscle.<sup>69-71</sup> Polymorphism of *Lys(K)153Arg(R)* in (*rs1805086*) myostatin gene consist in replacement nucleotide 2379>G, which causes the exchange of amino acids included in mature myostatin protein. This may affect the proteolytic processing or binding affinity to the extracellular activin type II receptor which causes activation of the SMAD pathway, inducing myoblast proliferation and muscle mass growth.<sup>72</sup> Studies of untrained individuals suggest that this polymorphism is associated with influences muscle strength and an increase in the thickness of triceps and biceps. Another study involving a group of 316 Caucasian endurance athletes has shown that the K153R polymorphism influences an increase in the thickness of the biceps and quadriceps muscle, but the gene in question cannot be considered as a marker of organism's endurance.<sup>72,73</sup> On the other hand a study of a young African-American population proved that the 153R allele influenced the maximum isometric contraction in both sexes.<sup>74</sup> On the other hand, Seibert et al. conducted research focusing on people aged 70-79 and the study yielded different results: people with the 153R allele had less muscle strength than the other participants of the study.<sup>75</sup>

### Susceptibility to injury

Mutations in the *COL1A1* gene coding the alpha 1 chain of type 1 collagen, which is the principal protein component of connective tissue, can cause many diseases such as e.g. *osteogenesis imperfecta*, excessive bone fracture or Ehlers-Danlos syndrome.<sup>76</sup> Single-nucleotide polymorphism in the *COL1A1* gene is associated with connective tissue disorders such as increased risk of shoulder dislocation, Achilles tendon rupture, verte-

bral fractures due to diseases causing low bone mineral density (BMD) and anterior cruciate ligament rupture. The latter injury is associated with the +1245 G/T polymorphism (*rs1800012*) of the *COL1A1* gene. A study conducted on Polish skiers showed that the probability of rupture in the anterior cruciate ligament is 1.43 times lower in individuals with the G allele compared with the subjects with the T allele. Moreover the authors found the difference in the genotype distribution (GG vs GT and TT) between injured skiers and controls.<sup>77</sup> Another polymorphism of this gene which is described in the literature with regard to the same injury is -1997 G/T (*rs1107946*). A study about football players has shown that the higher frequency of the GT haplotype in both of these polymorphisms (-1997G/T and +1245 G/T) acted protectively against a possibility of injury involving anterior cruciate ligament rupture.<sup>78</sup> On the other hand the *COL5A1* gene encodes the alpha chain of type V collagen.<sup>79</sup> Moreover, similar to *COL1A1*, it may be associated with Achilles tendon injuries and joint hypermobility (Ehlers-Danlos syndrome).<sup>76</sup>

Polymorphism-/AGGG(*rs71746744*) is associated with adaptation to running, while AGGG/AGGG genotype was significantly over-represented in the group of fast and least flexible runners compared with the -/AGGG and -/- genotypes.<sup>80</sup> Genetic predisposition to and a higher risk of tendon injury is also associated with the genetic variation in the gene encoding the protein MMP3 (matrix metalloproteinase3) and TNC (tensacine C). The 5A/6A polymorphism (*rs3025028*) in the promoter of the *MMP3* gene, like the *COL1A1* gene polymorphisms, may be linked with cracks in the anterior cruciate ligament. Moreover, the 5A genotype may be associated with susceptibility to this type of injury comparing patients from contact sports and non-contact.<sup>81</sup> These genes are also responsible for Achilles tendon injuries in physically active people.<sup>82</sup> Furthermore, the variant of the G allele of the *MMP3* gene and T allele of the *COL5A1* gene interact and increase the risk of Achilles tendon injuries.<sup>83</sup>

### Conclusion

The article is a review of research papers discussing selected locations of markers used to study genetic determine to sport achievements and to predispose to sustaining injuries.

Another important aspect described here is the psychological adaptation. While considering these issues, it is possible to raise a question regarding the genetic factors which might be responsible for contestants' will to compete, their desire to win, capacity for self-denial, persistence in aiming for a particular purpose, or for the phenomenon in sport frequently referred to as a one-day-predisposition. Despite the positive findings of the many studies, the authors suggest the multi-ge-

netic nature of physical capacity and the dependence of the tested alleles responsible for the organism's strength on this function. The same conclusion which was presented above can also be drawn in the context of muscle performance and susceptibility to injury. Therefore, other genetic markers associated with strength, injury proneness and psychological adaptation tested jointly, can provide new and interesting information about the predisposition to succeed in sport. However, these genes should be investigated in relation to specific sports rather than taking into account similar disciplines jointly. This is because each sport has its own unique characteristics; therefore the training in an obvious way focuses on different domains, which as a consequence are the underlying factors of the competitors' success. Considering the genetic markers of sport achievements we also have to take into account the differences between populations.

New available technologies such as microarrays and new generation sequencing (NGS) could provide new insights on the genetic determinants of sports achievements and predisposition to injury. The role of association studies concerned on human disease is huge and well established. The significance of genetic study focused on physical performance may be useful to the decision by subjects, who do not reached satisfactory results or sustained injuries during training/competition, on which discipline they should concentrate to reach the better results and which efforts they should avoid. However there are probably more than 140 genes involved in physical performance what nowadays makes it difficult to use them in laboratory tests. In addition, besides the SNPs, epigenetic changes like DNA methylation and microRNA expression can modified the ability to athletic effort and sport achievements. There is much probability that in the future the epigenetic and functional study will develop in this science field.

## References

1. Maszczyk A. Analiza dynamiki zmian sprawności siłowej oszczepników z wykorzystaniem szeregów czasowych. *Zeszyty Medyczno-Naukowe AWF w Katowicach*. doi:0867-7751
2. Lippi G, Longo UG, Maffulli N. Genetics and sports. *Br Med Bull*. 2010;93(1):27-47.
3. Yang N, MacArthur DG, Gulbin JP, et al. ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet*. 2003;73(3):627-631.
4. Sysoeva OV, Maluchenko NV, Timofeeva MA, et al. Aggression and 5HTT polymorphism in females: Study of synchronized swimming and control groups. *Int J Psychophysiol*. 2009;72(2):173-178.
5. Roth SM. Critical overview of applications of genetic testing in sport talent identification. *Recent Pat DNA Gene Seq*. 2012;6(3):247-255.
6. Pescatello LS, Roth SM, eds. *Exercise Genomics*. Totowa, NJ: Humana Press; 2011.
7. Pescatello LS, Roth SM. A Synopsis of Exercise Genomics Research and a Vision for its Future Translation into Practice. In: *Exercise Genomics*. Totowa, NJ: Humana Press; 2011:231-254.
8. Lewandowicz AM, Kowalski ML, Pawliczak R. [RGS proteins (regulators of G protein signaling) and their roles in regulation of immune response]. *Postepy Hig Med Dosw (Online)*. 2004;58:312-320.
9. Liggett SB, Shah SD, Cryer PE. Characterization of beta-adrenergic receptors of human skeletal muscle obtained by needle biopsy. *Am J Physiol Metab*. 1988;254(6):795-798.
10. Wells DJ. Gene doping: the hype and the reality. *Br J Pharmacol*. 2008;154(3):623-631.
11. Kochanska-Dziurawicz AA, Janikowska G, Bogacz A, et al. Catecholamines and  $\beta$ 2-adrenoreceptor gene expression before and after maximal incremental cycle test in young ice hockey players: relation to work performed. *Biol Sport*. 2013;30(2):85-90.
12. Davis E, Loiacono R, Summers RJ. The rush to adrenaline: drugs in sport acting on the beta-adrenergic system. *Br J Pharmacol*. 2008;154(3):584-597.
13. Wolfarth B, Rankinen T, Mühlbauer S, et al. Association between a  $\beta$ 2-adrenergic receptor polymorphism and elite endurance performance. *Metabolism*. 2007;56(12):1649-1651.
14. Tsianos GI, Evangelou E, Boot A, et al. Associations of polymorphisms of eight muscle- or metabolism-related genes with performance in Mount Olympus marathon runners. *J Appl Physiol*. 2010;108(3):567-574.
15. Tringali C, Brivio I, Stucchi B, et al. Prevalence of a characteristic gene profile in high-level rhythmic gymnasts. *J Sports Sci*. 2014;32(14):1409-1415.
16. Cabrera-Vera TM, Vanhauwe J, Thomas TO, et al. Insights into G Protein Structure, Function, and Regulation. *Endocr Rev*. 2003;24(6):765-781.
17. Zeltner R, Delles C, Schneider M, Siffert W, Schmieder RE. G-protein beta(3) subunit gene (GNB3) 825T allele is associated with enhanced renal perfusion in early hypertension. *Hypertension*. 2001;37(3):882-886.
18. Lee J, Lee S, Shin S, Kang H-S. Association between the GNB3 polymorphism and blood pressure in young Korean men. *Med Sci Sports Exerc*. 2005;37(7):1138-1143.
19. Sekine A, Tanabe N, Sugiura T, et al. Polymorphism of the G protein  $\beta$ 3 subunit gene influences the efficacy of sildenafil in patients with pulmonary hypertension. *Intern Med*. 2014;53(4):291-297.
20. Eynon N, Meckel Y, Alves AJ, Nemet D, Eliakim A. Is there an interaction between BDKRB2 -9/+9 and GNB3 C825T polymorphisms and elite athletic performance? *Scand J Med Sci Sports*. 2011;21(6):242-246.
21. Sawczuk M, Maciejewska-Karłowska A, Cięszczyk P, Leońska-Duniec A. Is GNB3 C825T polymorphism associated with elite status of Polish athletes? *Biol Sport*. 2014;31(1):21-25.






22. Eynon N, Oliveira J, Meckel Y, et al. The guanine nucleotide binding protein  $\beta$  polypeptide 3 gene C825T polymorphism is associated with elite endurance athletes. *Exp Physiol*. 2009;94(3):344-349.
23. Faruque MU, Millis RM, Dunston GM, et al. Association of GNB3 C825T polymorphism with peak oxygen consumption. *Int J Sports Med*. 2009;30(5):315-319.
24. Gülyaşar T, Öztürk L, Sipahi T, et al. GNB3 gene c.825C>T polymorphism and performance parameters in professional basketball players. *Acta Physiol Hung*. 2014;101(2):176-184.
25. Brancaccio P, Maffulli N, Limongelli FM. Creatine kinase monitoring in sport medicine. *Br Med Bull*. 2007;81-82(1):209-230.
26. Hornemann T, Kempa S, Himmel M, Hayess K, Fürst DO, Wallimann T. Muscle-type creatine kinase interacts with central domains of the M-band proteins myomesin and M-protein. *J Mol Biol*. 2003;332(4):877-887.
27. Rivera MA, Pérusse L, Simoneau JA, et al. Linkage between a muscle-specific CK gene marker and VO<sub>2</sub>max in the HERITAGE Family Study. *Med Sci Sports Exerc*. 1999;31(5):698-701.
28. Rivera MA, Dionne FT, Wolfarth B, et al. Muscle-specific creatine kinase gene polymorphisms in elite endurance athletes and sedentary controls. *Med Sci Sports Exerc*. 1997;29(11):1444-1447.
29. Heled Y, Bloom MS, Wu TJ, Stephens Q, Deuster PA. CM-MM and ACE genotypes and physiological prediction of the creatine kinase response to exercise. *J Appl Physiol*. 2007;103(2):504-510.
30. Fedotovskaya ON, Popov DV, Vinogradova OL, Akhmetov II. Association of muscle-specific creatine kinase (CKMM) gene polymorphism with physical performance of athletes. *Hum Physiol*. 2012;38(1):89-93.
31. Gronek P, Holdys J, Kryściak J, Stanislawski D. CKM Gene G (NcoI-) Allele Has a Positive Effect on Maximal Oxygen Uptake in Caucasian Women Practicing Sports Requiring Aerobic and Anaerobic Exercise Metabolism. *J Hum Kinet*. 2013;39:137-145.
32. Döring F, Onur S, Fischer A, et al. A common haplotype and the Pro582Ser polymorphism of the hypoxia-inducible factor-1 $\alpha$  (HIF1A) gene in elite endurance athletes. *J Appl Physiol*. 2010;108(6):1497-1500.
33. Gunel T, Gumusoglu E, Hosseini MK, Yilmazyildirim E, Dolekcap I, Aydinli K. Effect of angiotensin I-converting enzyme and  $\alpha$ -actinin-3 gene polymorphisms on sport performance. *Mol Med Rep*. 2014;9(4):1422-1426.
34. Norman B, Esbjörnsson M, Rundqvist H, Österlund T, Glenmark B, Jansson E. ACTN3 genotype and modulation of skeletal muscle response to exercise in human subjects. *J Appl Physiol*. 2014;116(9):1197-1203.
35. Seto JT, Quinlan KGR, Lek M, et al. ACTN3 genotype influences muscle performance through the regulation of calcineurin signaling. *J Clin Invest*. 2013;123(10):4255-4263.
36. Quinlan KGR, Seto JT, Turner N, et al.  $\alpha$ -Actinin-3 deficiency results in reduced glycogen phosphorylase activity and altered calcium handling in skeletal muscle. *Hum Mol Genet*. 2010;19(7):1335-1346.
37. Vincent B, De Bock K, Ramaekers M, et al. ACTN3 (R577X) genotype is associated with fiber type distribution. *Physiol Genomics*. 2007;32(1):58-63.
38. Mills M, Yang N, Weinberger R, et al. Differential expression of the actin-binding proteins,  $\alpha$ -actinin-2 and -3, in different species: implications for the evolution of functional redundancy. *Hum Mol Genet*. 2001;10(13):1335-1346.
39. MacArthur DG, Seto JT, Raftery JM, et al. Loss of ACTN3 gene function alters mouse muscle metabolism and shows evidence of positive selection in humans. *Nat Genet*. 2007;39(10):1261-1265.
40. Ahmetov II, Donnikov AE, Trofimov DY. Actn3 genotype is associated with testosterone levels of athletes. *Biol Sport*. 2014;31(2):105-108.
41. Kikuchi N, Nakazato K, Min S, Ueda D, Igawa S. The ACTN3 R577X Polymorphism Is Associated With Muscle Power in Male Japanese Athletes. *J Strength Cond Res*. 2014;28(7):1783-1789.
42. Mikami E, Fuku N, Murakami H, et al. ACTN3 R577X Genotype is Associated with Sprinting in Elite Japanese Athletes. *Int J Sports Med*. 2013;35(02):172-177.
43. Pawlak G, McGarvey TW, Nguyen TB, et al. Alterations in tropomyosin isoform expression in human transitional cell carcinoma of the urinary bladder. *Int J Cancer*. 2004;110(3):368-373.
44. Clarkson PM, Hoffman EP, Zambraski E, et al. ACTN3 and MLCK genotype associations with exertional muscle damage. *J Appl Physiol*. 2005;99(2):564-569.
45. Deuster PA, Contreras-Sesvold CL, O'Connor FG, et al. Genetic polymorphisms associated with exertional rhabdomyolysis. *Eur J Appl Physiol*. 2013;113(8):1997-2004.
46. Bray MS, Hagberg JM, Pérusse L, et al. The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update. *Med Sci Sports Exerc*. 2009;41(1):35-73.
47. Nowakowska A. [The influence of I/D polymorphism of the angiotensin I converting enzyme (ACE) gene and 4G/5G polymorphism of plasminogen activator inhibitor (PAI-1) gene promoter on the haemostatic system in patients with essential hypertension and dyslipidemia]. *Ann Acad Med Stetin*. 2005;51(1):95-105.
48. Collins M, Xenophontos SL, Cariolou MA, et al. The ACE gene and endurance performance during the South African Ironman Triathlons. *Med Sci Sports Exerc*. 2004;36(8):1314-1320.
49. Rigat B, Hubert C, Alhenc-Gelas F, Cambien F, Corvol P, Soubrier F. An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. *J Clin Invest*. 1990;86(4):1343-1346.

50. Holdys J, Kryściak J, Stanisławski D, Gronek P. ACE I/D gene polymorphism in athletes of various sports disciplines. *Hum Mov.* 2011;12(3):223-231.
51. Alvarez R, Terrados N, Ortolano R, et al. Genetic variation in the renin-angiotensin system and athletic performance. *Eur J Appl Physiol.* 2000;82(1-2):117-120.
52. Nazarov IB, Woods DR, Montgomery HE, et al. The angiotensin converting enzyme I/D polymorphism in Russian athletes. *Eur J Hum Genet EJHG.* 2001;9(10):797-801.
53. Weber KT. Angiotensin II and connective tissue: homeostasis and reciprocal regulation. *Regul Pept.* 1999;82(1-3):1-17.
54. Bitigen A, Cevik C, Demir D, et al. The frequency of angiotensin-converting enzyme genotype and left ventricular functions in the obese population. *Congest Heart Fail.* 13(6):323-327.
55. Hernández D, de la Rosa A, Barragán A, et al. The ACE/DD genotype is associated with the extent of exercise-induced left ventricular growth in endurance athletes. *J Am Coll Cardiol.* 2003;42(3):527-532.
56. Ufnal M, Zera T. Rola tlenku azotu, siarkowodoru oraz tlenku węgla w regulacji układu krążenia i ich potencjał farmakoterapeutyczny. *Kardiologia Pol.* 2010;68(5):436-440.
57. Saunders CJ, de Milander L, Hew-Butler T, et al. Dipso-genic genes associated with weight changes during Ironman Triathlons. *Hum Mol Genet.* 2006;15(20):2980-2987.
58. Wang J, Mougey EB, David CJ, et al. Determination of human beta(2)-adrenoceptor haplotypes by denaturation selective amplification and subtractive genotyping. *Am J Pharmacogenomics.* 2001;1(4):315-322.
59. Williams AG, Dhamrait SS, Wootton PTE, et al. Bradykinin receptor gene variant and human physical performance. *J Appl Physiol.* 2004;96(3):938-942.
60. Saunders CJ, Xenophontos SL, Cariolou MA, Anastasiades LC, Noakes TD, Collins M. The bradykinin  $\beta$ 2 receptor (BDKRB2) and endothelial nitric oxide synthase 3 (NOS3) genes and endurance performance during Ironman Triathlons. *Hum Mol Genet.* 2006;15(6):979-987.
61. Sgourou A, Fotopoulos V, Kontos V, Patrinos GP, Papatzopoulos A. Association of genome variations in the renin-angiotensin system with physical performance. *Hum Genomics.* 2012;6(1):24.
62. Grenda A, Leońska-Duniec A, Ciężczyk P, Zmijewski P. Bdkrb2 gene -9/+9 polymorphism and swimming performance. *Biol Sport.* 2014;31(2):109-113.
63. Guler HP, Zapf J, Froesch ER. Short-term metabolic effects of recombinant human insulin-like growth factor I in healthy adults. *N Engl J Med.* 1987;317(3):137-140.
64. Di Paolo S, Teutonico A, Leogrande D, Capobianco C, Schena PF. Chronic Inhibition of Mammalian Target of Rapamycin Signaling Downregulates Insulin Receptor Substrates 1 and 2 and AKT Activation: A Crossroad between Cancer and Diabetes? *J Am Soc Nephrol.* 2006;17(8):2236-2244.
65. Guha N, Erotokritou-Mulligan I, Nevitt SP, et al. Biochemical markers of recombinant human insulin-like growth factor-I (rhIGF-I)/rhIGF binding protein-3 (rhIGFBP-3) misuse in athletes. *Drug Test Anal.* 2013;5(11-12):843-849.
66. Kostek MC, Devaney JM, Gordish-Dressman H, et al. A polymorphism near IGF1 is associated with body composition and muscle function in women from the Health, Aging, and Body Composition Study. *Eur J Appl Physiol.* 2010;110(2):315-324.
67. Ben-Zaken S, Meckel Y, Nemet D, Eliakim A. Can IGF-I polymorphism affect power and endurance athletic performance? *Growth Horm IGF Res.* 2013;23(5):175-178.
68. Krych-Garsztka K, Mizgajska-Wiktor H, Goździcka-Józefiak A. An Analysis of the Regulatory Region of the IGF1 Gene in Professional Athletes in Youth Sports Teams. *Hum Mov.* 2011;12(3).
69. Schuelke M, Wagner KR, Stolz LE, et al. Myostatin Mutation Associated with Gross Muscle Hypertrophy in a Child. *N Engl J Med.* 2004;350(26):2682-2688.
70. Allen DL, Hittel DS, McPherron AC. Expression and Function of Myostatin in Obesity, Diabetes, and Exercise Adaptation. *Med Sci Sport Exerc.* 2011;43(10):1828-1835.
71. White TA, LeBrasseur NK. Myostatin and Sarcopenia: Opportunities and Challenges - A Mini-Review. *Gerontology.* 2014;60(4):289-293.
72. Santiago C, Ruiz JR, Rodríguez-Romo G, et al. The K153R Polymorphism in the Myostatin Gene and Muscle Power Phenotypes in Young, Non-Athletic Men. Calbet JAL. *PLoS One.* 2011;6(1):e16323.
73. Döring F, Onur S, Kürbitz C, et al. Single nucleotide polymorphisms in the myostatin (MSTN) and muscle creatine kinase (CKM) genes are not associated with elite endurance performance. *Scand J Med Sci Sports.* 2011;21(6):841-845.
74. Kostek MA, Angelopoulos TJ, Clarkson PM, et al. Myostatin and Follistatin Polymorphisms Interact with Muscle Phenotypes and Ethnicity. *Med Sci Sport Exerc.* 2009;41(5):1063-1071.
75. Seibert MJ, Xue QL, Fried LP, Walston JD. Polymorphic variation in the human myostatin (GDF-8) gene and association with strength measures in the Women's Health and Aging Study II cohort. *J Am Geriatr Soc.* 2001;49(8):1093-1096.
76. Collins M, Raleigh SM. Genetic Risk Factors for Musculoskeletal Soft Tissue Injuries. In: *Genetics and Sports.* Vol 54. Basel: KARGER; 2009:136-149.
77. Stępien-Słodkowska M, Ficek K, Eider J, et al. The +1245g/t polymorphisms in the collagen type I alpha 1 (col1a1) gene in polish skiers with anterior cruciate ligament injury. *Biol Sport.* 2013;30(1):57-60.
78. Ficek K, Cieszczyk P, Kaczmarczyk M, et al. Gene variants within the COL1A1 gene are associated with reduced anterior cruciate ligament injury in professional soccer players. *J Sci Med Sport.* 2013;16(5):396-400.
79. Posthumus M, September A V., Schwellnus MP, Collins M. Investigation of the Sp1-binding site polymorphism within the COL1A1 gene in participants with Achilles tendon injuries and controls. *J Sci Med Sport.* 2009;12(1):184-189.

80. Abrahams S, Posthumus M, Collins M. A Polymorphism in a Functional Region of the *COL5A1* Gene: Association with Ultraendurance-Running Performance and Joint Range of Motion. *Int J Sports Physiol Perform.* 2014;9(3):583-590.
81. Malila S, Yuktanandana P, Saowaprut S, Jiamjarasrangsri W, Honsawek S. Association between matrix metalloproteinase-3 polymorphism and anterior cruciate ligament ruptures. *Genet Mol Res.* 2011;10(4):4158-4165.
82. Pokrywka A, Kaliszewski P, Majorczyk E, Zembroń-Łacny A. Genes in sport and doping. *Biol Sport.* 2013;30(3):155-161.
83. Raleigh SM, van der Merwe L, Ribbans WJ, Smith RKW, Schwellnus MP, Collins M. Variants within the MMP3 gene are associated with Achilles tendinopathy: possible interaction with the *COL5A1* gene. *Br J Sports Med.* 2009;43(7):514-520.



## CASUISTIC PAPER

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# Multistage treatment of a patient with developmental dysplasia of the hip: A case study

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## Abstract

**Introduction.** Developmental dysplasia of the hip (DDH) concerns about 5 per cent of the newborn population, and congenital hip dislocation (1%) is considered a challenge in child orthopedics due to the risk of further complications. Recently, the occurrence of this illness has been decreasing due to early hip diagnostics in newborns and fast implementation of proper treatment.

**Aim.** To describe multi-annual treatment and multiplicitous complications in a 15 years old patient diagnosed with DDH.

**Description of the case.** Complications occurring, despite the treatment conducted in accordance with accepted standards, induced the necessity of surgical procedures. This paper describes applied surgical techniques, physiotherapy treatment, the functional status of patient during particular stages of treatment as well as current results of gait analyses.

**Conclusions.** In spite of early diagnosis and treatment of DDH, surgical intervention does not always bring the expected result.

**Keywords.** developmental dysplasia of the hip, complications, gait assessment, pelvic osteotomy

## Introduction

Developmental dysplasia of the hip (DDH) is considered the most frequent disorder of motor organs in Poland (it affects 4-6 % of infants). Early diagnostics of hip joints in newborns and infants as well as swift implementation of proper treatment significantly decreases the frequency of total luxation (dislocation) that requires surgical intervention.<sup>1-4</sup> Available literature widely describes the risk factors of congenital defects of hip joint, treatment possibilities, complications and secondary effects including joint mobility limitations, necro-

sis of blood vessels within the head of femur (5-15% of cases), secondary dislocation of the joint and hip arthritis.<sup>4,5</sup> Early diagnosis and undertaking the proper treatment are the most important factors in preventing subsequent pathological changes.

Despite the fact that DDH is considered one of the most researched diseases, there are still many controversies regarding its etiology, diagnostics and treatment. One of them considers the timing of surgical treatment initiation in late diagnosed DDH in infants aged 6-8 months.<sup>6</sup> Some doctors recommend to start the treatment as soon as the disease is diagnosed, due to joint

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 28.06.2018 | Accepted: 28.09.2018

Publication date: December 2018



plasticity, as the joints of infants are mainly built from cartilage which ensures better modeling capabilities.<sup>7,8</sup> On the other hand, many orthopedists claim that the treatment should be undertaken after the appearance of ossification nucleus of femoral head, to decrease the risk of development of necrosis of femur.<sup>4,8,9</sup>

Early diagnosis and treatment of DDH in newborns and infants enables application of nonsurgical treatment methods such as orthopedic appliances, over head extension and plaster casts.<sup>10</sup> Still, the optimal treatment result is not always obtained and treated infants remain with so called residual dysplasia.

### Case study

A 14 year old patient accompanied by guardians was admitted to the Children's Orthopedic Clinic with significant right lower limb shortening (PKD) of about 6.5 cm due to congenital DDH and multiple surgeries of the pelvis and right femur. The girl, a third child pregnancy was born naturally in good general condition (Apgar 9), weight – 2390 g, with no complications during the perinatal period. Right, total DDH was diagnosed in the first month of her life and the treatment was undertaken in the second month. The family history did not show any cases of dysplasia or DDH. Over next 14 years, the patient was hospitalized 16 times due to treatment of motor organs undertaking 13 surgical procedures on the pelvis and right lower limb with several complications such as reoccurring threefold joint luxation, delayed bone union after femur osteotomy, displacement of bone fragments, fracture of internal stabilization and contractures in right lower limb joints. Up to the age of 5, the patient was treated orthopedically without any physiotherapy treatment. After twofold luxation and subsequent surgery of right hip, post - surgery and ambulatory physiotherapy was applied. Such a treatment regimen for this patient was systematically continued from the age of 8.

In 2016, at the age of 13, the patient underwent right femur lengthening with the use of a monotube apparatus. Before that procedure, orthopedic and physiotherapy examination showed a right lower limb shortening of 6.5 cm with active and passive movement limitations of the right hip. ROM of abduction and adduction amounted to 20-0-25 with passive mobility of 25-0-25, ROM of active flexion and extension equaled 20-0-25 with passive mobility of 25-0-25, ROM of flexion and active extension 10-0-120 with passive mobility of -5 -0-110, ROM of hip rotation was difficult to assess while ROM of active flexion and extension of knee joint totaled -5-0-125 with passive mobility of -5-0-130. The right lower limb muscle strength assessed in Lovett scale was weak. Right hip joint flexors produced the result of 4+ while extensors 3, abductors 2+ and adductors 5. Additionally, the quadriceps femoris atrophy (2.5 cm dif-

ference while compared with left thigh) was noticed. For about a year the patient has been walking without elbow crouches while the limb shortening was compensated by orthopedic insole and shoe lining. Gait phases were incorrect showing waddling gait and positive Trendelenburg-Duchenne symptom. The patient also showed functional shortening of her Achilles tendon on the right side and fixed diagonal pelvis and lumbar spine position. After orthopedic examination and image diagnostics (Fig. 1), the patient was qualified for right lower limb lengthening.



**Fig. 1.** X-ray of the patient's silhouette on admission to orthopedic clinic for assessment of the length difference in lower limb before the application of Monotube apparatus (May 25<sup>th</sup> 2016)

## Surgical techniques

The patient has been treated from the age of 1 month, at first with conservative treatment with the use of over-head extension. Five weeks later, unsuccessful closed reposition of hip with arthrography was performed, followed by open, simple hip joint reposition and “human position” plaster cast. At the age of 5 the girl underwent reposition and reconstruction of right hip with osteotomy stabilized with Kirschner wires and plate due to joint luxation followed by hip plaster cast. One year later, the arthrography of right hip was performed and internal fixation (Kirschner wires) was removed from ala of ilium. At the age of 8 the luxation of the operated joint reoccurred. Subsequent surgery was necessary and the following procedures were applied: the plates and screws were removed, valgus osteotomy of femur was performed, stabilization with PHP plate was done and pelvis osteotomy according to Dega with the use of allogenic bone graft was performed. Three years later, the third right hip joint luxation occurred. The plates were removed, open reposition of hip was performed, valgus osteotomy of proximal femur with its shortening was done with PHP plate stabilization, pelvis osteotomy according to Dega was performed and hip plaster cast was applied. In the same year, due to delayed femur bone union, Gravitational Platelet Separation System (GPS) factor was applied. The patient continued physiotherapy including gait learning without weightbearing on right lower limb. At the age of 12 the subsequent complication occurred in the shape of fracture of internal implants. The subsequent surgery of proximal femur was performed; PHP plate and fractured implants were removed and intramedullary stabilization of subtrochanteric area was performed with the use of aLFN Expert blocked nail. With doctor’s permission, gradual weightbearing of right lower limb was started (February 2015). One year later, due to an increasing length difference of right lower limb (shortening of about 6.5 cm) the external Monotube apparatus was put on. During the lengthening process, the dislocation of bone fragments in sagittal plane occurred.

The Monotube apparatus was urgently repositioned what led to its earlier removal with simultaneous blockage of nail in distal femur (Fig 2). As a consequence, the lengthening of 4 cm was obtained. Orthopedic and functional examination showed the following: decrease of muscle strength of right lower limb and pelvis, the need to use elbow crutches while walking, passive and active limitation of ROM of hip and knee joints.

After the consultation with the doctor, the patient participated in kinesiotherapy to minimize post-surgery effects in motor organ. Three months after the removal of apparatus (age 14), the intramedullary nail in distal femur got broken (Fig. 3). The nail was urgently removed and reposition of fracture with SYNTHES intramed-

ullary nail was performed (Fig. 4). The physiotherapy was continued and included anti-swelling exercises increasing active and passive ROM of joint of right lower limb and improving strength of gluteal muscles, teaching gradual weight bearing of the limb, gait learning (with insole compensating the length difference), knee-cap mobilization, stretching of quadriceps and hip joint adductors and posture control exercises. After 5 months the achieved ROM of hip joint was the same as before the use of Monotube apparatus. The only differences concerned the limitations of active ROM of knee joint -5-0-118, passive 0-0-125. Meanwhile, the control X-Ray done 3 months after the surgery confirmed proper course of treatment and stability of bone fragments.



**Fig. 2.** X-ray of right femur before the removal of Monotube apparatus ( June 13<sup>th</sup> 2016).



**Fig. 3.** Fracture of intramedullary osteosynthesis (November 3<sup>rd</sup> 2016)



**Fig. 4.** X-ray after the replacement of broken intramedullary nail with SYNTHES (November 11<sup>th</sup> 2016)

At the age of 15, 6 months since the last surgery, the girl has not been feeling any pain or unwellness. ROM of hip and knee joints are the same like before the lengthening process and muscle strength improved what made hip joint stability better and positively influenced the gait of the patient. Despite the difference in length of limbs, the girl started exercising on an exercise bike and learning how to walk with full weight bearing of right lower limb. Her quality of life has improved dramatically, as well as her balance and gait, however still done with the use of elbow crouches, what justifies the continuation of further physiotherapy

Lab gait analyses

In order to assess the gait pattern of patient, the gait analyses with the use of BTS Smart was conducted in May 2017. The analyses showed weight bearing asymmetry of both limbs, the duration of stance phase was shorter on operated limb – 58.7% of gait cycle, compared with healthy -66% of gait cycle. The significant decrease of gait pace was also noticed (Tab. 1). The pelvis of patient was set up in anteversion of 9-15° and tilted in relation to gait direction. Its right side was positioned frontally, diagonally and upward (Fig. 5). During all gait cycles both hip joints were abducted. Left hip joint was internally rotated while the right one (operated) was externally rotated up to 50% of stance and at the end of terminal swing. Diagonal position of pelvis imposed excessive flexion of hip and knee joints as well as excessive dorsiflexion of the left foot in whole gait cycle (Fig. 5). The right foot was touching the surface with forefoot. At the beginning and the end of swing phase, right

foot was positioned in plantarflexion while in the mid swing in dorsiflexion up to 4 degrees. Left foot during whole swing phase was in dorsiflexion up to 12 degrees. In stance, right foot was externally over rotated up to 25 degrees while the left one was properly positioned in regard to gait direction.

**Table 1.** Summary of temporo-spatial gait parameters of patient

Temporo-spatial parameters	Operated limb		Non-operated limb	
	Value	SD	Value	SD
Stane phase [%]	58.7	0.6	66	0.3
Swing chase[%]	41.2	0.6	34	0.3
Step length [m]	0.49	0.02	0.48	0.01
		Value	SD	
Initial double support [%]	12.1		0.4	
Terminal double support [%]	12.1		0.9	
Cadence [step/min]	110.4		1.2	
Mean Speed [m/s]	0.67		0.04	

Discussion

According to recommendation of Children Orthopedics Division of Polish Orthopedics and Traumatology Association, the compulsory standard to detect congenital defects of hip joint in children is their clinical examination and USG evaluation. The screening program of hip joints conducted in pre-luxation clinics considerably lowered the percentage of late diagnosis of hip dysfunctions. The majority of unstable hips get stabilized by themselves by 2-6 week of life while every hip that remains luxated or unstable requires immediate orthopedic intervention.<sup>12,13</sup> The infants under 6 months are being treated by not-surgical methods.<sup>13,14</sup> The lack of effectiveness of conservative treatment and late diagnosis of DDH impose the necessity to apply surgical methods including closed reposition of hip joint followed by “human position” cast and in older children open reposition and joint stabilization.<sup>16</sup> In children aged 18-24 months additional osteotomy of femur and/or pelvis is often required.<sup>6,16</sup> In hereby case study, considerable number of complications occurring despite the treatment conducted in accordance with standards imposed the necessity of surgical interventions. Therefore the authors decided to address the issues of multiple complications in the process of DDH treatment. Many authors emphasize occurrence of complications in the process of DDH treatment.<sup>17-19</sup> During conservative treatment Pavlik harness, “Koszli” harness or splints are considered hazardous as their usage may lead to ischemia of head of femur leading to its necrosis or reversible palsy of femoral nerve.<sup>20</sup> In turn, the dislocation of head of fe-

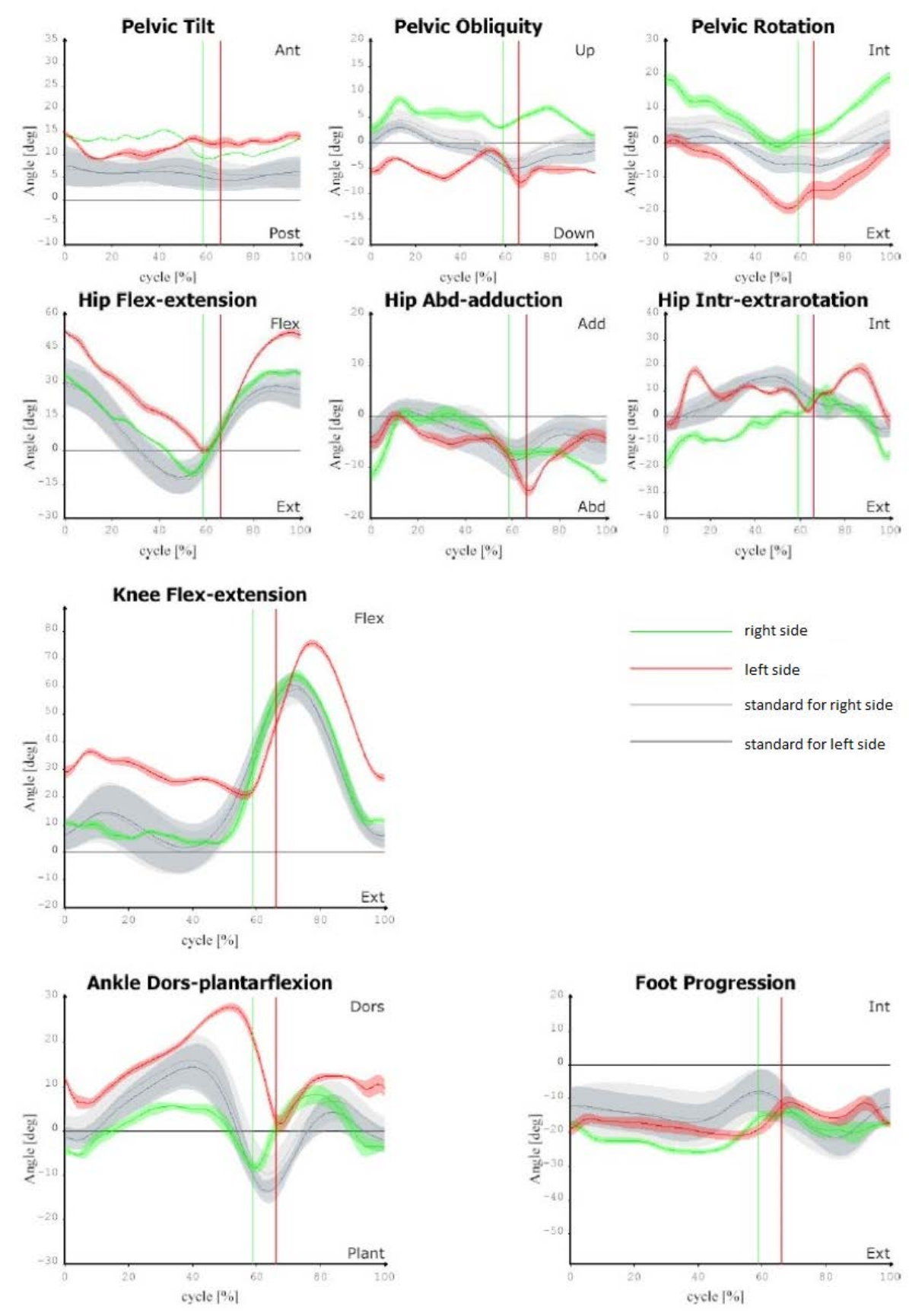


Fig. 5. Kinematic gait parameters

mur and pelvis, joint stiffness, necrosis of head of femur or subsequent joint dislocation can become post-surgical complications. Another possible complication includes dysmorphia of the head of femur, its necrosis or weakening of hip joint muscle strength as observed in our patient.<sup>20</sup> In this case study, in spite of early diagnosis and undertaken treatment the complications such as dislocation of femoral head, incorrect development of acetabulum or delayed bone union have been occurring systematically. Many authors underline the correlation between risk factors and treatment methods and the age of patient when luxation or DDH was diagnosed.<sup>17-20</sup> Our patient initially was treated conservatively, but ineffectiveness of surgical methods imposed open reposition. This surgery was repeated over the years with additional osteotomies. Wenger et al. suggest the application of conservative methods in small patients while in older children they recommend implementation of surgical methods including osteotomy.<sup>9</sup> Those surgical methods focus on recreation of proper bio-mechanics of joint and are very crucial for further prognosis. Osteotomy within femur and/or pelvis should minimize the risk of dislocation and necrosis. The authors propose to decrease the number of surgical procedures on bones as they negatively influence circumarticular soft tissue.<sup>9,21</sup>

Such an option did not concern our patient due to constant, ineffective treatment results. Recurring dislocation of head of femur imposed the utilization of open methods. Ahamed Sami Barakat et al. in the research stated that in a part of 20 patients with DDH treated with closed reposition method with tenotomy of adductors there was the necessity to perform the next procedure with the use of open reposition.<sup>21</sup> Naeem ur Razaq M et al. diagnosed the necrosis of femoral head in 8,3% patients treated with open reposition with osteotomy. Moreover, 5 % of patients showed residual dysplasia of hip joint and subsequent luxation and 3,3% of patient suffered from joint infection.<sup>22</sup> By analyzing literature and treatment history of our patient, above mentioned complications cannot be excluded, but due to lack of sufficient diagnostics they cannot be confirmed. Open reposition of luxated hip joint is considered risk factor of femoral head necrosis.<sup>23-24</sup> Barakat et al. noted several cases of necrosis of the head of femur after aggressive joint manipulation. Their research shows that tenotomy does not prevent the necrosis.<sup>21</sup> Schur et al. obtained opposite results. The analyses of treatment results of 82 patients with closed reposition done in operating theatre did not produce significant difference in occurrence of necrosis of the head of femur (AVN).<sup>25</sup> It also concerned the cases with previous use of Pavlik harness, joint traction or tenotomy of adductors. They stated, however, that in male patients treated with closed reposition, secondary AVN may occur more frequently. The research conducted by Mulpuri K et al. showed that in DDH patients

diagnosed between 6 -18 months, hip dislocation was more frequent than in patients diagnosed before 3 month of life.<sup>26</sup> Our patient suffered from joint decentralization, although she was diagnosed with DDH in the second month of her life. Both, initial treatment with extension and closed reposition failed. Roposch underlines negative influence of necrosis on formation of joint surface regardless the treatment method. He states that swift improvement of function concerns joints without AVN.<sup>27</sup> Kothari analyzed the treatment results of patients treated by open method or without osteotomy. Based on evaluation of radiological effects, clinical examinations and percentage of complications (AVN) he stated that open reposition with osteotomy should be considered one of the most appropriate treatment methods, ensuring durable results.<sup>28</sup> Analyses of the literature leads to the conclusion that complication in DDH treatment are not rare in spite of properly conducted treatment.<sup>29</sup> Therapy and desired functional results are complicated due to secondary effects such as uneven length of lower limbs, persistent luxation of head of femur or incorrect joint structure.<sup>30</sup> In the presented case, drawing the conclusion about the reasons of occurring complications is quite difficult due to lack of sufficient diagnostics. Orthopedic treatment was completed and patient has been undergoing physiotherapy due to functional deficits. The deficits and dysfunctions in her motor organ include trunk asymmetry, features of scoliosis, gait pattern disorders, gait with help of elbow crutches, difference in length of lower limbs, weakening of muscle strength and ROM of joints of right lower limb.

To assess the results of two years long physiotherapy process and long orthopedic treatment, the gait analyses was performed. Gahramanov et al. performed similar analyses in patients after the osteotomy of hip joint. The authors claim that gait pattern of patients treated with osteotomy is partly similar to the gait pattern of healthy people; however it still cannot be considered a proper one. The functional effects of surgeries frequently differ from theoretical assumptions.<sup>30</sup> Gait analyses performed by authors indicate severe disorders.

Based on obtained results of both clinical examination and gait analyses it seems essential to include physiotherapy procedures into orthopedic treatment. Such an approach assures complexity of the treatment and improves life quality of DDH patients. The physiotherapy procedures performed on patient included: gait reeducation (with or without orthopedic appliances), proprioception and balance improvement, PNF posture correction, application of Kaltenborn – Evjenth manual therapy on soft tissue and fascia to improve the (slide in the joint), range of movement and contracture reduction. In the next stage, the obtained effects were used in functional therapy aimed at the patient's goals (riding a bicycle, scooter, walking without elbow crutches).

## Conclusion

1. Despite an early diagnosis and treatment of hip luxation in DDH, surgical treatment does not always bring anticipated results and can cause unwanted compensations in motor organ.
2. Obtained improvement seen in both clinical examination and gait analyses confirms the grounds for conjunction between individual physiotherapy and orthopedic treatment. This unified process should be initiated as early as possible, preferably on the day of DDH diagnosis, what will enable to avoid many complications such as wrong gait patterns, wrong trunk compensations, risk of scoliosis and reoccurrence of joint destabilization in further treatment and recovery process. In the next stage, the obtained effects were used in functional therapy aimed at the patient's goals (riding a bicycle, scooter, walking without elbow crutches).

## References

1. Pietrzak Sz, Czubak J. Jak się wykonuje badanie przesiewowe stawów biodrowych u noworodków i niemowląt. *Pediatr Dypl.* 2012;16(6):42-45.
2. Maciałyzyk – Paprocka K. Epidemiologia wad postawy u dzieci i młodzieży. Praca doktorska. Poznań 2013 r. Uniwersytet Medyczny im. Karola Marcinkowskiego w Poznaniu.
3. de Hundt M, Vlemmix F, Bais JM, et al. Risk factors for developmental dysplasia of the hip: a meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* 2012;165(1):8-17.
4. Randall T, Loder, Elaine N, Skopelja. The Epidemiology and Demographics of Hip Dysplasia. *International Scholarly Research Network ISRN Orthopedics.* 2011; 238607,46 pages. doi:10.5402/2011/238607
5. Noordin S, Umer M, Hafeez K, Nawaz H. Developmental dysplasia of the hip. *Orthop Rev.* 2010;2(2):73-78.
6. Clarke NM. Developmental dysplasia of the hip: diagnosis and management to 18 months. *Instr Course Lect.* 2014;63:307-311.
7. Razaq MN, Younas M, Awan AS, Waqas, Alam MI. Risk factors leading to developmental complications after open reduction In developmental dysplasia of the hip. *J Ayub Med. Coll Abbottabad.* 2016;28(1):26-28.
8. Storer SK, Skaggs DL. Developmental dysplasia of the hip. *Am Fam Physician.* 2006; 15;74(8):1310-1316.
9. Wenger DR. Surgical treatment of developmental dysplasia of the hip. *Instr Course Lect.* 2014;63:313-323.
10. Sewell MD, Rosendahl K, Eastwood DM. Developmental dysplasia of the hip. *BMJ.* 2009;24:339:b4454
11. Laborie LB, Engesæter IØ, Lehmann TG, Eastwood DM, Engesæter LB, Rosendahl K. Screening strategies for hip dysplasia: long-term outcome of a randomized controlled trial. *Pediatrics.* 2013;132(3):492-501.
12. Choudry Q, Goyal R, Paton RW. Is limitation of hip abduction a useful clinical sign in the diagnosis of developmental dysplasia of the hip? *Arch Dis Child.* 2013;98(11):862-866.
13. Dezateux C, Rosendahl K. Developmental dysplasia of the hip. *Lancet.* 2007;369 (9572):1541-1552.
14. Shorter D, Hong T, Osborn DA. Cochrane Review: Screening programmes for developmental dysplasia of the hip in newborn infants. *Evid Based Child Health.* 2013;8(1):11-54.
15. Holman J, Carroll KL, Murray KA, Macleod LM, Roach JW. Long-term follow-up of open reduction surgery for developmental dislocation of the hip. *J Pediatr Orthop.* 2012;32(2):121-124.
16. Waško MK, Pietrzak S, Szarejko A, Przybysz W, Parol T, Czubak J. Wyniki radiologiczne leczenia rozwojowej dysplazji stawów biodrowych wyciągiem ponad głowę u dzieci niechodzących. *Ortop Traumatol Rehabil.* 2017;19(2):127-136.
17. Tsukagoshi Y, Kamegaya M, Kamada H, et al. The correlation between Salter's criteria for avascular necrosis of the femoral head and Kalamchi's prognostic classification following the treatment of developmental dysplasia of the hip. *Bone Joint J.* 2017;99-B(8):1115-1120.
18. Eastwood DM, de Gheldere A. Clinical examination for developmental dysplasia of the hip in neonates: how to stay out of trouble. *BMJ.* 2010;340:c1965.
19. Sankar WN, Young CR, Lin AG, Crow SA, Baldwin KD, Moseley CF. Risk factors for failure after open reduction for DDH: a matched cohort analysis. *J Pediatric Orthop.* 211;31(3):232-239.
20. Sionek A, Czubak J, Kornacka M, Grabowski B. Określenie czynników ryzyka rozwojowej dysplazji stawów biodrowych u dzieci urodzonych z ciąż wielopłodowych. Ocena w badaniu ultrasonograficznym z zastosowaniem metody Grafa. *Ortop Traumatol Rehabil.* 2008;10(2):115-130.
21. Barakat AS, Zein AB, Arafa AS, et al. Closed reduction with or without adductor tenotomy for developmental dysplasia of the hip presenting at walking age. *Curr Orthop Pract.* 2017;28(2):195-199.
22. Naeem ur Razaq M, Risk factors leading to developmental complications after open reduction In developmental dysplasia of the hip. *J Ayub Med Coll Abbottabad.* 2016;28(1):26-28.
23. Roposch A, Protopapa E, Cortina-Borja M. Weighted diagnostic criteria for developmental dysplasia of the hip. *J Pediatr.* 2014;165(6):1236-1240.
24. Carrera N, Colmonero E, Castelo JL, Guisan A, Naviera E, Lorenzo JR. Risk of developmental dysplasia of the hip in patients subjected to the external cephalic version. *An Pediatr (Barc).* 2018;88(3):136-139.
25. Schur MD, Lee C, Arkade A, Catalano A, Choi PD. Risk factors for avascular necrosis after closed reduction for developmental dysplasia of the hip. *J Child Orthop.* 2016;10:185-192.
26. Mulpuri K, Schaeffer EK, Andrade J, et al. What risk factors and characteristics are associated with late-presenting dislocations of the hip in infants? *Clin Orthop Relat Res.* 2016;474(5):1131-1137.

27. Roposch A, Ridout D, Protopapa E, Nicolaou N, Gelfer Y. Osteonecrosis complicating developmental dysplasia of the hip compromises subsequent acetabular remodeling. *Clin Orthop Relat Res.* 2013;471(7):2318-2326.
28. Kothari M, Grammatopoulos G, Hopewell S, Theologis T. How does bony surgery affect results of anterior open reduction in walking-age children with developmental hip dysplasia? *Clin Orthop Relat Res.* 2016;474(5):1199-1208.
29. Farsetti P, R. CateriniR, Potenza V, Ippolito E. Developmental dislocation of the hip successfully treated by pre-operative traction and medial open reduction: A 22-year mean followup. *Clin Orthop Relat Res.* 2015;473(8):2658-2669.
30. Gahramanov A, Inanici F, Caglar O. Functional results in periacetabular osteotomy: is it possible to obtain a normal gait after the surgery? *Hip Int.* 2017;27(5):449-454.





## CASUISTIC PAPER

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# A comparative analysis of the rehabilitation course of two patients after the implantation of an artificial hip joint

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### Abstract

**Introduction.** Endoprosthetics is the most effective method of returning to a normal way of life without pain. The key element is the post-operative rehabilitation program where a patient has to comply with certain rules and principles. The rehabilitation also includes the family of the patient. Each person, after any surgery requires an individual approach, and no patient can be commonly treated.

**Aim.** The aim of the article is to compare the effects of an early rehabilitation after the implantation of an artificial hip joint in two patient cases.

**Description of the cases.** This research was conducted at Bodden-Klinken GmbH. An individual case study was used, based on an example of two patients at the age of 59 who had implantation of an artificial hip joint. The carried out rehabilitation of the patients was conducted without any disruptions. Patients were able to freely walk on crutches nine days after the procedure.

**Conclusions.** In the cases analyzed, the rehabilitation course was described until the ninth day after implantation of an artificial hip joint. High results in terms of patient rehabilitation were achieved. Furthermore, in order to continue their therapy, they were referred to the sanatorium.

**Keywords.** artificial hip joint, rehabilitation, post-surgical rehabilitation

### Introduction

Femurs are very thick and at the same time, highly strong bones. In order to break it, as far as young and healthy persons are concerned, an extremely high force is required, which mostly occurs in terms of traffic accidents. However, it is significant that the majority of people who suffer from a broken femur are not young or healthy. A wide range of pathologies which determine a reduced durability of bones can be distin-

guished. Among others, those include: osteoporosis, tumors, and bone disorders that are connected with renal failure.<sup>1</sup>

The treatment of such fractures should begin as quickly as possible. However, fracture of a hip bone does not result in detrimental life changes due to the fact that the fractures are surrounded with a thick layer of muscle and the risk of critical organ damage as well as the risk of open fracture is at a really low level.<sup>1-4</sup>

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**Participation of co-authors:** A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 3.06.2018 | Accepted: 2.09.2018

Publication date: December 2018



An effective and at the same time, the most widely used method of treatment of such fractures is endoprosthetics of the hip joint which refers to the operational change of the damaged femoral neck and end, as well as in some cases – the acetabulum, into ceramic-metal or metal-plastic prosthesis. The reason behind the popularity of this method is strictly connected with the fact that fusing of bone takes significantly more time and during such time, a clot can occur resulting in patient mortality. On the contrary, after endoprosthetics, a patient is able to stand up after a few days and after a total healing of the wound, he or she can entirely walk on his or her own. The healing effects occur significantly faster. What is more, part of the femoral neck located closer to the hip as well as the femoral neck are irrigated from the side of the femoral diaphysis. Therefore, if a fracture takes place, the blood vessels are extinguished and, as a result of that, a neck and end remain without blood supply. Necrosis occurs and the acceleration is no longer possible. Among the most significant complications after this type of operation may include: anemia, losing a prosthesis, infection as well as thromboembolic complications.<sup>5</sup> Taking this into consideration, heparin is injected under the stomach skin of each patient. Nonetheless, the rehabilitation process pays significant attention to putting a patient on its feet and beginning the process of walking. Mostly, a rehabilitant, whose work and effort contribute directly to saving life of suffering people, aids in rehabilitation. For an elderly person, each downfall is potentially life-threatening. Therefore, taking care of the environment, prevention, as well as contracting the described fractures are of great importance.<sup>6-8</sup>

However, there are certain factors which considerably increase the risk of hip fracture:

- Osteoporosis,
- Benign and malicious bone cancers,
- Using immunosuppressive treatment (such as steroid medication),
- Innate fragility of bones and brittleness of bones,
- Hormonal changes,
- Improper eating (especially calcium and protein deficiencies),
- Too low level of physical activity.<sup>9-12</sup>

At the initial phase of treatment, after the procedure, limited physical activity is recommended in order not to overtire the hip as well as the operated leg. If using operational treatment was not possible, for example due to a bad health condition, then an additional derotation-al leg plaster is used. Due to a high risk of thrombosis, people suffering from hip fracture are administrated anticoagulants. Patients are also provided with painkillers. A part of injured patients require blood transfusion.<sup>13-15</sup>

Before starting a surgical procedure, an overall internal assessment and additional examinations should be conducted. The surgical treatment mostly includes:

- Connection of broken bones parts with the use of special screws, nails and angular boards,
- Substitution of the broken part of bone with an artificial element – endoprosthesis which can be partial or total (total hip replacement).<sup>16</sup>

In majority of cases, the prosthesis of hip joint includes the following elements: acetabulum (globular element attached to pelvis one), cylinder (“bearing” of the moving end), end (ball located on the mandrel) and mandrel (a part of prosthesis located in the hip bone).

Among prosthesis, one may distinguish: unicondylar, complete (cemented and uncemented). An unicondylar endoprosthesis is of an old type, however it is still widely used. A complete endoprosthesis can be divided into cemented and uncemented. Sometimes, especially during a revision surgery, during a change of an old endoprosthesis into new one, hybrid solutions are used (one part is cemented whereas the other one is not).

The cemented endoprosthesis is located in the bone using an acrylic bone cement, whereas the uncemented endoprosthesis is stabilized at the bone stock mechanically.

Mostly, the acetabulum of the diameter of 50 to 54 mm are integrated. However, extreme sizes such as 38 mm and 72 mm occurs. Similar situation can be observed in reference to mandrels which occur at the variety of sizes (the set includes 7–10 sizes). At the pre-operational planning stage, exact measurements are made on radiograms, using dedicated templates including the bio-mechanical conditions that occur after the procedure.<sup>17</sup>

The aim of the operation is to achieve stability of the end of endoprosthesis in an acetabulum, to reproduce the axis of rotation of joint in a physiological point, to sustain the tension of the periarticular tissues, to situate a hip bone in proper distance with reference to pelvis (so-called offset) and to create conditions that enable a proper range of motion.

In case of surgeries, the post-isometric relaxation of the muscle within a pelvis is used (analgesic activity increasing the range of joint motion). Functional massage is used, such as the massage of gluteus medius muscle, tensor fasciae latae muscle, quadriceps femoris muscle, adductor magnus muscle. The main assumption of this action is to decrease pain and to retain the total passive mobility of hip joint at any direction.<sup>18</sup>

The aim of the article is the comparative analysis of the effects of the early rehabilitation after the procedure of injection of an artificial hip joint, focusing on two patients.

### Description of the cases

The research was conducted at Bodden-Kliniken GmbH. The method of an individual case study was used. The participants were two patients at the age of 59 who had

injected an implant at the same day. The physical operations were conducted in accordance to the standards of the Clinics, what will be further described including the conducted procedures.

Both patients were diagnosed with degenerative hip disease. After no symptomatic treatment, patients were referred for surgery. Patient no. 1 underwent surgery - implantation of the endoprosthesis of the right hip. Additional blood and urine tests were performed. The operation was performed without complications. During the stay, breathing exercises were carried out, the lower limb was massaged, the correct posture was learned while walking on crutches, and the patient and his family were informed how to proceed after leaving the hospital. After the procedure pain medications were administered at the patient's request such as painkillers by intravenous injection. Two blood units "AB" Rh (+) were transfused to the patient. Blood was absorbed without negative reactions from the body. During the stay in the ward, the patient also had a X-ray of the hip joint and gastroscopy performed. Surgery for patient no. 2 was performed - cementless prosthesis of the right hip. Additional blood and urine tests were performed. The operation was performed without complications. After the procedure, pain medications were administered at the patient's request, such as: painkillers in intravenous injection.

The characteristics of the patients are presented in the Table 1.

Effects of post-hospital rehabilitation

Since the first post-operational day, the physiotherapist began the work with each patient individually, in accordance to the physiotherapy standards established in the Implantology Center Bodden – Kliniken GmbH. In both cases of the two patients postoperative observation was performed in which every two hours the pulse and heart rate were checked, the general condition of the patient, the level of pain, blood supply, limb staining, feeling.

During the first visit of the therapist, the instructions concerning what movements and in what scope can be done by a patient were given. The next stage included a mobilization of patients into a sitting position, taking the necessary safety precautions. Patient no. 1 did not find it difficult and completed the task almost on his own. On the contrary, Patient no. 2 required a considerable help of the physiotherapist, suffering from nausea and vertigo. The next stage included a preparation of medical supplies for patients - crutches with an anatomic handle providing comfort for both of them. Both patients managed to complete this task in an excellent way and each one, in turn, began to learn the three-point gait. The first steps were took at the Patient's room.

Table. 1. Characteristics of the patients

Specification	Patient no. 1	Patient no. 2
Age	59 y/o	59 y/o
Professional activity	Professionally active, willing to return to work	Due to a persistent pain – professionally inactive and rather does not declare return to work
Profession	Restaurant worker	Real estate agent
Type of works	Constantly moving	Mostly sitting behind his desk or in the car
Body parameters	Weight:78 kg, Height: 182 cm.	Weight: 117 kg, Height: 179 cm
Sporting activity	Biking, swimming	Lack of sporting activity (walking with wife or dog alternatively)
Hip joint degeneration (family)	No problems connected with hip or knee joint degeneration observed in the family	No problems connected with hip or knee joint degeneration observed in the family
Moving before surgery	Moving in the last hours, however, due to increasing degeneration of hip joint experienced a persistent pain. While sitting at the scale from 1 to 10, it often amounted to 8, however it decreased to 4 during movement. However, it was too persistent that it required the use of pharmacology.	Moving in the last hours, however often using crutches and large amounts of painkillers. While sitting and walking the high discomfort was experienced which at the scale from 1 to 10 amounted to 9.
Mobility of the joint	Despite a persistent pain, the scope of mobility in the joint did not change significantly due to the fact that the patient did not observe any changes in this scope.	The scope of mobility of the patient decreased by the internal rotation of the limb, lifting the limb during laying as well as during abduction.
Execution of the surgery	The patient was admitted to the clinic in order to have an implantation of the right hip point made in general anesthesia in January 2018	The patient was admitted to the clinic in order to have an implantation of the right hip point made in general anesthesia in January 2018

The next stage included kinesis therapy which took place at the bed of the Patient – laying on his back. Those were breathing and circulatory exercises. Activation of the healthy limb in first place, including abduction and bending in hip and knee joint, was a crucial element. This exercise was performed by both patients without any problems. However, as far as the Patient no. 2 is concerned, it elicited iliopsoas muscle spasm. Then, both patients performed the isometric and isotonic exercises of both limbs as well as gluteus muscles. The next stage concerned an alternate work with limbs by way of long lever of straightening the knee joint in order to activate the thigh muscle. Those two exercises were performed excellent by both of the patients. However, during abduction (the active supporting exercises) as well as bending in the hip joint up to 90 degrees of the operated limb, the Patient no. 1 was the leader. On the contrary, the Patient no. 2 suffered from muscle spasms and pains of the hip.

In order to improve the efficiency of hip, the decision regarding conduction of rehabilitation splint (*Continuous Passive Motion* - CPM) - twice a day was made, trying to achieve a flexion in the knee and hip joints up to 90 degrees, obviously not from the beginning. Then, both patients were informed about the necessity of laying on their back and lack of possibility of making a flexion in their hip larger than 90 degrees. They can go to the toilet with help of nurses or therapist and sit on the bed on their own, of course from the operated side. After a few hours it turned out, that the Patient no. 2 is unable to conduct this activity on this own.

Two days after the operation, both patients seemed to be in good shape. At the beginning, the exercises conducted on the previous day were repeated, however the number of repetitions and intensity increased. The overweight patient suffered from higher pains during the mobilization and the exercise concerning bending and abduction in hip. Rehabilitation splint which was mentioned before was activated. The bend allowed only for 55 degrees. The procedure lasted 30 minutes. It can be added that the same activity was conducted after six hours and bending in knees amounted to 75 degrees. After conduction of the exercises, both patients began an individual mobilization in order to sit on the bed. Then, without any significant problems, using two elbow crutches they stood up and began to learn a proper three-point gait. Better results were achieved by the Patient no. 1 who had a normal weight.

At the third, fourth and fifth day after the operation, the amount and intensity of exercises was extended. Rehabilitation splint used in case of the Patient no. 2 showed 80 degrees after fifth day of the rehabilitation. What is more, the patient experienced a smaller discomfort. Both patients continued the gait training concerning previously provided rules. However, the distances were

getting longer. Nonetheless, the Patient no. 2 suffered from larger problems than before since his heart rate and blood pressure raised.

On the sixth day after the operation the same exercises as on the fifth day were conducted. The additional element constituted the two-point gait learning, alternate and similar to the physiological gait. Patient no. 1 completed the exercise in an excellent way, however, the Patient no. 2 with his obesity and different lifestyle had a problem with a ballast received by his newly-embed joint. Therefore, he remained at the three-point cycle of gain. However, the rehabilitation splint work showed 90 degrees of bending both knee and hip joints what took place without any considerable problems.

On the eighth day both patients without large problems, were able to complete the total set of exercises and Patient no. 2 began and successfully finished learning of two-point gait. The next exercise included learning on climbing stairs with the help of handrail and one crutch. Both patients efficiently managed to climb 27 steps of stairs downwards and upwards. However, the Patient no. 2 suffered from lack of oxygen (he suffered from a breathlessness probably caused by an increase of air pressure). The next exercise was completed only by the patient no. 1. It was connected with climbing stairs using two crutches. Patient no. 2 argued that he is not able to maintain such balance.

On the ninth day, both patients were discharged from the hospital with given instructions. At the same day, they were admitted to the orthopedic sanatorium for three weeks in order to continue the more advanced therapy.

## Discussion

Hip is one of the largest joints in human organism, which join pelvis together with femur. It constitutes of acetabulum of pelvis and end of femur. The entire joint is surrounded with the strong and thick articular capsule, enhanced with ligament apparatus. Endoprosthetics (hip replacement) is currently a widely accepted standard of treatment in case of joint destruction with an annual systematic increase of the number of conducted operations.

The progress of the current medicine provides novel and better opportunities concerning restoring of fitness of people suffering from osteoarthritis who previously were condemned to life with strong pain. After the operation of implantation of an endoprosthesis, the early introduction of rehabilitation activities is recommended in order to recover patient's proper motion range as well as the potential full fitness as a result of the decrease of pain. On the first day after the operation, the patient is prepared to walk on his or her own.

The source literature includes certain recommendations regarding rehabilitation for the patients after the

implantation of an artificial hip joint which comprises a wide scope of physical, kinesiotherapeutic procedures, planning of the treatment process including a variety of stages. However, majority of authors is focused on the aspect of kinesiotherapy.<sup>19-21</sup>

On the basis of the research conducted by M.S. Krastanov, E.M. Iliev i E.V. Danelin, it was proven that using a long-term kinesiotherapy program, with reference to the treatment of the patients after the implantation of an artificial hip joint, adjusted to the individual conditions of health care, can contribute to a faster recovery after an operation, especially in terms of electro-stimulation.<sup>22</sup>

The aim of the research conducted by J. Stanek et.al. was to rate the subject of hip arthroplasty and to assess the mobility of patients after hip replacement. The tests were carried out among patients after total hip replacement. The respondents were a group of 120 people, in which there were 76 women (63.3%) and 44 men (36.7%) using the specialist Rehabilitation Clinic of the Karłowice Medical Center "KAR-MED" in Wrocław from February to December 2013. Patients who underwent endoprosthesis were significantly improved in functional status and reduced pain. This favorable trend was found in all areas of life included in the research carried out by the authors of the work. The implantation of the endoprosthesis caused a statistically significant reduction in the number of patients with reduced walking efficiency (by 28.4%), as well as those experiencing hip, buttock and thigh pain (by 20.9%). After the surgery the percentage of patients who received rehabilitation increased from 57.5% to 95%. The percentage of patients with very severe pain decreased from 19.2% to 0.8%, and with severe pain from 47.5% to 8.3%. As a result arthroplasty, the degree of difficulty in performing all the analyzed activities significantly decreased ( $p < 0.0001$ ). Before the surgery, 21.7% of the subjects underwent rehabilitation treatment, while 75.9% followed the procedure for rehabilitation.<sup>23</sup>

When analyzing the data of the American health insurance system, it can be concluded that the number of total arthroplasty increases with age and above 75-79 years of age significantly decreases and more often affects women. In the own study, the group of women was also more numerous and accounted for 63% of the respondents, and the average age was 69 years.<sup>24</sup>

These results were confirmed in the Borowicz study.<sup>25</sup> After the procedure pain became much less annoying. According to Mańczak et al. the main assumptions of post-operative rehabilitation are to reduce pain, exudation and inflammation, achieve the greatest possible range of motion and regain muscular control as quickly as possible.<sup>26</sup> According to Pozowski, the most common cause of hip replacement is degeneration of articular cartilage and underlying subchondral bone layer they are a degenerative disease.<sup>27</sup>

## Conclusions

This paper describes the rehabilitation of two patients who differ among themselves primarily lifestyle (active and passive), which had impact on body weight subjects (normal body weight and obesity). Despite the improvement observed in both cases, patient No. 2 had more difficulties and worse results.

As far as the analyzed case studies are concerned, the process of rehabilitation until the ninth day after the completion of the operation of implantation of an artificial hip was described. Both patients achieved similar results in terms of improvement.

The rehabilitation took place without any major problems. What is more, no complications were observed. In order to continue the specialist therapy, both patients were admitted to sanatorium.

## References

1. Andrzejczak P. *Pierwsza pomoc przedmedyczna, Pierwsza Pomoc Przedmedyczna*. Warszawa: Wojewódzki Ośrodek Medyczny;2006:13-21.
2. Bednarenko M. Systemy klasyfikacyjne złamań krętarzowych kości udowej. *Kwart Ortop*. 2011;1:1-9.
3. Dziak A, Gusta A, Żuk T. *Podstawy ortopedii*. Warszawa: Wyd. PZWL; 1983.
4. Garcia J, Quintana-Domeque C. The evolution of adult height in Europe: A brief note. *Econom Hum Biolog*. 2007;5:340-349.
5. Gaździk T. *Crash Course - ortopedia i reumatologia*. Wrocław: Urban & Partner; 2007:45-49.
6. Greenman PE. *Principles of manual Medicine*. Philadelphia: Williams & Wilkins; 2003.
7. Impagliazzo A, Lispi A, Magistro L. *Inchiodamento endomidollare retrograde del femore. Lo Scapello*. 2009;22:158-164.
8. Marciniak J. *Biomateriały w chirurgii kostnej*. Gliwice: Wydawnictwo Politechniki Śląskiej;1992.
9. Marciniak J, Chrzanowski W, Krauze A. Gwoździowanie śródszpikowe w osteosyn-tezie. Gliwice: Wyd. Politechniki Śląskiej; 2006:117-131.
10. Nowacki J, Dobrzański LA, Gustavo F. Implanty śródszpikowe w osteoporozie kości długich. *Open Access Library*. 2011;11(7):13.
11. Ogrodzka K, Rodan T. Postępowanie rehabilitacyjne po złamaniach w obrębie nasady bliższej kości udowej. *Prakt Fizjoter Rehab*. 2013;2:59-63.
12. Okoński M, Piszczatowski S. Biomechaniczne aspekty deformacji porażennego stawu biodrowego. Warszawa: Materiały konferencyjne I Kongresu Mechaniki Polskiej; 2007.
13. Pozowski A. *Alloplastyka stawu biodrowego*. Wrocław: Wydawnictwo Medyczne; 2011:2-48.
14. Reicher M, Bochenek A. *Anatomia człowieka, t. 1, Anatomia ogólna. Kości, stawy i więzadła. Mięśnie*. Warszawa: Wyd. PZWL;2008.

15. Ruff C. Variation in human body size and shape. *Annual Review of Anthropology*. 2002;31:211-232.
16. Sznajd J. Profilaktyka przeciwzakrzepowa i leczenie zakrzepicy w różnych stanach klinicznych. Profilaktyka i leczenie żyłnej choroby zakrzepowo-zatorowej - VI Wytyczne American College of Chest Physicians. *Med Prakt*. 2001;7:23-48.
17. Szulc A. *Wiktor A. Degi ortopedia i rehabilitacja tom 1-2*. Warszawa: Wydawnictwo Lekarskie PZWL. 2003:23-29.
18. Tuchocka-Piotrowska A. Możliwości farmakoterapii w chorobie zwyrodnieniowej. *Przew Lekarza*. 2007;3:12-13.
19. Avery PP, Baker RP, Walton MJ. Total hip replacement and hemiarthroplasty in mobile, independent patients with a displaced intracapsular fracture of the femoral neck: a seven- to ten-year follow-up report of a prospective randomised controlled trial. *J Bone Joint Surg*. 2011;93(8):1045-1048.
20. Bodén H, Adolphson P. No adverse effects of early weight bearing after uncemented total hip arthroplasty. *Acta Orthop Scandinav*. 2003;5(1):21-29.
21. Kisner C. *Therapeutic Exercise 1915*. Philadelphia: Davis Company;2007.
22. Krastanova MS, Ilieva EM, Vachera DE. Rehabilitation of Patients with Hip Joint Arthroplasty (Late Post-surgery Period – Hospital Rehabilitation). *Folia Medica*. 2017;59:217-221.
23. Stanek J, Juzwizyn JM, Borek K et al. Kompleksowa ocena powrotu do sprawności ruchowej chorych po zabiegu endoprotezoplastyki stawu biodrowego. *Pielęgn Zdrowie Publ*. 2017;7:269-277.
24. Pop T, Dudek J, Bielecki A, Dudek W, Snela S. Stan funkcjonalny chorych po endoprotezoplastyce stawu biodrowego pochodzących z terenów wiejskich. *Prz Med Uniw Rzesz Inst Leków*. 2011;1:79-89.
25. Borowicz B, Cielicka M, Nadulska A, Teter M, Dec-Szlichtyng M. Codzienne funkcjonowanie i jakość chodu u pacjentów po całkowitej artroplastyce stawu biodrowego. *Pielęgn XXI w*. 2012;1:31-34.
26. Mańczak M, Kalinowski P, Pelc M. Rehabilitacja w chorobie zwyrodnieniowej stawu biodrowego. *THINK: Studenckie Naukowe Czasopismo Internetowe*. 2009;1:1-18.
27. Pozowski A. *Alloplastyka stawu biodrowego*. Wrocław: Wydawnictwo Medyczne Górnicki;2011.



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refuse to review the work without asking the reviewers for their opinion, if in the view of the Editorial Staff the paper's essential value or its form does not meet the requirements, or if the theme of the article does not comply with the journal's profile. An incomplete set of documents or articles which are not prepared accordingly to the standards will be sent back to the Authors before the reviewing process along with the information about the deficiencies.

Articles are reviewed by at least two independent reviewers. Manuscripts are accepted if both reviewers agree that the work can be published in its present form. In case of any discrepancies between the two reviewers the paper is directed to the third reviewer, whose decision is final.

The papers are not sent to reviewers working for the same institution as the Author or to people who can remain in conflict of interest with the Author. The papers sent for reviewing are confidential and anonymous (the so-called „double blind review”). Each article is given an editorial number allowing for further identification in the publishing process. The Authors are informed about the results of the reviewing process and receive the actual reviews. The Authors can log on to the system and check at what stage of the process their manuscript is.

Ultimately, the decision concerning accepting the article for publication, accepting for amending or rejecting the article is made by the Editor. The decision cannot be appealed.

A list of all of the reviewers of the published works is announced once a year (<http://www.ejcem.ur.edu.pl/en/reviewers-list>).

It is required to present a written consent for reprint from a previous publisher for any materials that were published previously (tables, figures). If information in the case description, illustrations or the text allow for identifying any people, their written consent should be delivered.

## PREPARING THE ARTICLE

Technical requirements:

The text of a work: interline 1.5, font Times New Roman, 12 points.

Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Volume of original, systematic reviews/ reviews papers should not exceed 20 pages, and of clinical observations - 8 pages of a standard computer text (1800 signs on a page).

## THE TITLE PAGE

The following information should be given on the **TITLE PAGE**:

- A complete title of the article (max 50 words), titles and subtitles should not be put into quotation marks and ended with a full stop.
- Abbreviated title of the article (*Running Head*).
- Names, last names of the Authors (without degrees and titles).
- Affiliations and participation of all of the Authors (according to a pattern below\*\*).
- Detailed data: name, last name, address, telephone, and email address of the person responsible for preparation of the paper for publication and contact with the Editor.
- The title page should also give information about a source of funding the research (grants, donations, subventions etc.) and conflict of interest.

\*\* A participation in preparation of the article should be determines in accordance with the following categories:

- A. Author of the concept and objectives of paper
- B. collection of data
- C. implementation of research
- D. elaborate, analysis and interpretation of data
- E. statistical analysis
- F. preparation of a manuscript
- G. working out the literature
- H. obtaining funds

### Example:

Jan Kowalski<sup>1 (A,B,C,D,E,EG)</sup>, Anna Nowak<sup>1,2 (A,B,C,E,F)</sup>, Adam Wisniewski<sup>1 (A,B,E,F)</sup>

1. The Institute of Physiotherapy, University of Rzeszow, Poland
2. Centre for Innovative Research in Medical and Natural Sciences', Medical Faculty of University of Rzeszow, Poland

The **MAIN BODY** of the manuscript should contain:

- A full title of the article.
- 3–6 keywords, chosen in compliance with the MeSH system (Medical Subject Headings Index Medicus <http://www.nlm.nih.gov/mesh/MBrowser>.

html). Keywords cannot be a repetition of the title. Give a list of Abbreviations in alphabetical order.

- Abstract, which should be maximum 200 words and present a structural construction.

## ARRANGEMENT OF TEXT

An **original** article should contain the following elements:

- Introduction
- Aim of the study
- Material and methods
- Results (used statistical methods should be described in detail in order to allow for verifying the results)
- Discussion
- Conclusion
- References

**Case study** should contain the following elements:

- Introduction
- Case description
- Discussion
- A summary
- References

**Systematic review** should contain the following elements:

- Introduction
- Description of the subject literature (a source of publication, data range)
- Analysis of the literature
- A summary
- References

**Review article** should contain the following elements:

- Introduction
- Body of the subject matter (the problem)
- Conclusion
- References

## REFERENCES/ EXAMPLES OF CITATION

References should be prepared according to the AMA style. The list of references should be placed at the end of an article and prepared according to the order of citation in the text.

Citations in the article should be placed after a sentence ending with a full stop and edited as the so called 'superscript'. In-text citations should only be placed at the end of a sentence or a paragraph, not in the middle.

*Examples:*

- The degree of respiratory muscles fatigue depends on the applied exercise protocol and the research group's fitness level.<sup>1,2</sup> The greatest load with which a patient continues breathing for at least one minute is a measure of inspiratory muscles strength.<sup>3</sup>
- Diabetes mellitus is associated with a high risk of foot ulcers.<sup>4-6</sup>

A citation should contain a maximum of 6 authors. When an article has more than six authors, only the first three names should be given by adding 'et al.'. If the source

does not have any authors, the citation should begin with the title.

Journal titles should be given in brief according to the Index Medicus standard.

The number of sources cited for an opinion article/ a review article should be between 40 and 50, and from 20 to 40 for other articles. A minimum of 50 % of literature should come from the last 5 years.

The following are examples of individual citations made according to the required rules of editing and punctuation:

Article from a journal, number of authors from 1 to 6	Lee JC, Seo HG, Lee WH, Kim HC, Han TR, Oh BM. Computer-assisted detection of swallowing difficulty. <i>Comput Methods Programs Biomed.</i> 2016;134:79-88. de Kam D, Kamphuis JF, Weerdesteyn V, Geurts AC. The effect of weight-bearing asymmetry on dynamic postural stability in people with chronic stroke. <i>Gait Posture.</i> 2016;53:5-10.
Article from a journal, number of authors more than 6	Gonzalez ME, Martin EE, Anwar T, et al. Mesenchymal stem cell-induced DDR2 mediates stromal-breast cancer interactions and metastasis growth. <i>Cell Rep.</i> 2017;18:1215-28. Jordan J, Toplak H, Grassi G, et al. Joint statement of the European Association for the Study of Obesity and the European Society of Hypertension: obesity and heart failure. <i>J Hypertens.</i> 2016;34:1678-88.
Article from an online journal	Coppinger T, Jeanes YM, Hardwick J, Reeves S. Body mass, frequency of eating and breakfast consumption in 9-13-year-olds. <i>J Hum Nutr Diet.</i> 2012;25:43-9. doi: 10.1111/j.1365-277X.2011.01184.x. Cogulu O, Schoumans J, Toruner G, Demkow U, Karaca E, Durmaz AA. Laboratory Genetic Testing in Clinical Practice 2016. <i>Biomed Res Int.</i> 2017;2017:5798714. doi: 10.1155/2017/5798714.
Websites	Cholera in Haiti. Centers for Disease Control and Prevention Web site. <a href="http://www.cdc.gov/haiti-cholera/">http://www.cdc.gov/haiti-cholera/</a> . Published October 22, 2010. Updated January 9, 2012. Accessed February 1, 2012. Address double burden of malnutrition: WHO. World Health Organization site. <a href="http://www.searo.who.int/mediacentre/releases/2016/1636/en/">http://www.searo.who.int/mediacentre/releases/2016/1636/en/</a> . Accessed February 2, 2017.
Book	Naish J, Syndercombe Court D. <i>Medical Sciences.</i> 2nd ed. London, Elsevier;2015. Modlin J, Jenkins P. <i>Decision Analysis in Planning for a Polio Outbreak in the United States.</i> San Francisco, CA: Pediatric Academic Societies;2004.
Chapter in a book	Pignone M, Salazar R. Disease Prevention & Health Promotion. In: Papadakis MA, McPhee S, ed. <i>Current Medical Diagnosis &amp; Treatment.</i> 54th ed. New York, NY: McGraw-Hill Education; 2015:1-19. Solensky R. Drugallergy: desensitization and Treatment of reactions to antibiotics and aspirin. In: Lockey P, ed. <i>Allergens and Allergen Immunotherapy.</i> 3rd ed. New York, NY: Marcel Dekker; 2004:585-606.

**NOTE:** The editorial board requires consistent and carefully made references prepared according to the above-mentioned AMA standards. Otherwise, the work will be sent back to the authors.

TABLES AND FIGURES

All tables and figures should be inserted in the text. They must have captions.

Tables should have the Arabic Numerals and a caption inserted above a table, in the sequence of appearance of the first reference in the text. One should ensure whether every table is mentioned in the text. When constructing tables, avoid vertical separators.

Figures should have the Arabic Numerals and a caption placed under it. They should be numbered in a sequence of appearance of the first reference in the text. One should ensure whether every figure is mentioned in the text.

If a given figure has already been published, one should give a source and obtain a written consent from a person having copyrights for reprinting the material, with the exception of documents constituting public interest.

ABBREVIATIONS AND SYMBOLS

The Editorial Staff requires using only standard abbreviations. One should not use abbreviations in the title and in the abstracts. A full version of a term, for which a given abbreviation is used must be given before

the first appearance of the abbreviation in the text, with the exception of standard units of measurement.

The abbreviation used for European Journal of Clinical and Experimental Medicine is Eur J Clin Exp Med.

The Editorial Staff reserves itself a possibility to introduce amendments without contacting the Author.

The Authors and the reviewers do not receive any compensation for publishing the article.

The Editorial Office does not charge the Authors for publishing the article in the journal.

Papers written incompatibly with the rules determined in the hereby Instructions cannot be published in the European Journal of Clinical and Experimental Medicine.

INSTRUCTIONS FOR SUBMITTING THE MANUSCRIPT

The Editorial Office accepts articles English language. The Authors whose Polish-language article is qualified for



publications are required to translate it into English within 10 days following the date of receiving the information about the article being accepted for publication.

To send the article to the Editor one should use the system ScholarOne Manuscripts which can be found on <https://mc04.manuscriptcentral.com/pmur>

To submit an article the Author has to be signed in the aforementioned system. The account can be created by clicking on *Register here*.

During the registration one should state his or hers scientific degree, first name, last name, email address. Next one should give his or hers address country, city and postal code. Finally one should set a password and click *Finish*. If the user already has an existing account it is enough to log in at the journal's web site and enter the Author Center.

After logging on to the system, the Authors are obliged to fill standard declarations (check list) concerning funding source, a declaration not to publish the article in other journals, complying with ethical guidelines, consents from all the Authors, transferring copyright, declaration confirming reading the instructions for Authors as well as declaration of revealing any conflict of interest.

The instruction and help can be found on the website: <http://mchelp.manuscriptcentral.com/gethelpnow/training/author> (Author User Guide file).

## SUBMITTING AN ARTICLE

To start sending a new article log in to your user account and click on *Click here to submit a new manuscript* in *Author Resources*.

### Step 1. The type, Title & Abstract

At this stage you should choose the type of the article, type in the title, abbreviated title (*Running Head*) and the abstract.

### Step 2: Attributes

You should insert 3 key words related to the article.

### Step 3: Authors & Institutions

Optionally, you can give the names of all the Authors (it is not necessary). In *Add Author* you should find a co-author by typing his or hers email address. If the co-author does not have an existing account in the system you should click on *Create a new co-author* and follow the instructions.

### Step 4: Reviewers

You should pinpoint **four** proposed recommended Reviewers (name, institution and email address). The reviewers **cannot be** in any conflict of interest with the

Authors and **cannot** come from the same facility as the Authors. To add a proposed reviewer click on *Add Reviewer*.

### Step 5: Details & Comments

During this stage you can add a *Cover Letter*. If there are any funding sources you should list them in *Funding*. In the Check List you should give information concerning: the number of figure, the number of tables, the word count, and confirmation of the declarations: no previous publications of the article, fulfilling ethical requirements, consent of all the Authors for publishing, transferring the copyright, familiarizing with the Instruction for Authors, translating the paper to English and revealing any conflict of interest.

### Step 6: File Upload

You should send the article in **two files**. In *FILE DESIGNATION* you should choose *Title Page*, then click *Select File 1* and choose the appropriate document. In *FILE DESIGNATION* you should choose *Main Document*, then click *Select File 2* and choose the main body document. Then click: *Upload Selected Files*.

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You should check if the information concerning the metadata is correct. You should click *View PDF proof* and then confirm by clicking *Submit*.

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To send an amended manuscript click *'Manuscripts with Decision'* in *My Manuscripts* and then click *Click here* to submit a revision.

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