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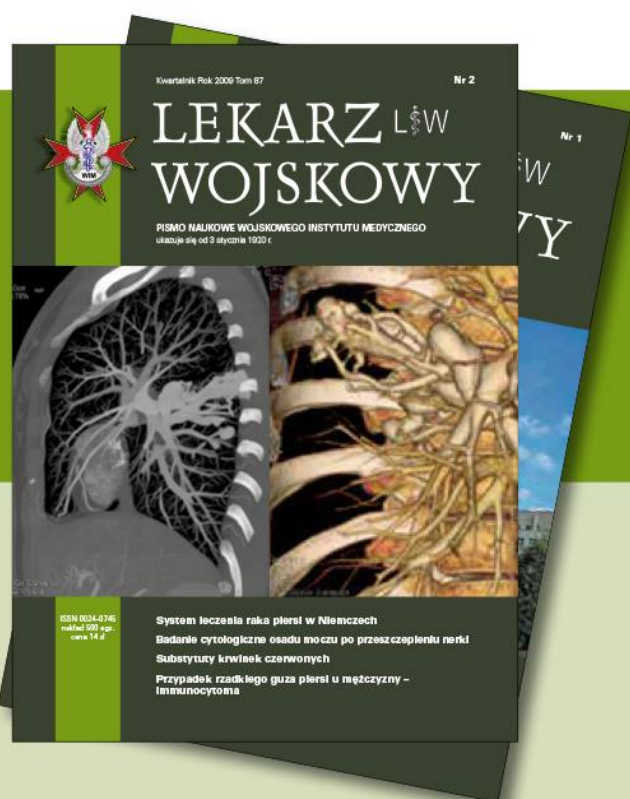
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# Suicide in the armed forces of NATO and partner states in the first decade of the 21<sup>st</sup> century

Samobójstwa w armiach NATO i państw partnerskich w pierwszej dekadzie XXI wieku

**Piotr Ilnicki, Stanisław Ilnicki**

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**Abstract.** In implementing the World Health Organisation's "Prevention of Suicide: A Global Imperative" program, NATO's Science & Technology Organization (STO NATO) established within the Health and Medicine (HFM) panel the RTG-218 Research Task Group. This sent questions to the Surgeons General of 34 NATO member states and partner states. The questions referred to the number and features of suicides, suicide surveillance and programs of suicide prevention in those states. The STO-TR-HFM-218 report was developed based on the responses obtained from half of the states invited, containing recommendations for both the leadership and commanders of NATO. This study compares the data from the report with the results of research conducted by Polish suicidologists, defining conclusions concerning the implementation of the report's recommendations in the Polish Armed Forces. Suicides are one of the primary causes of death in the NATO armed forces. Depression disorders as well as alcohol and psychoactive drug abuse are the most frequent medical suicide risk factors. False views on suicides, limited access to professional aid and a fear of stigmatisation are the main obstacles to effective prevention. Modern suicide prevention methods consist of a psycho-educational activity and regular monitoring of suicides based on a scientific basis. The recommendations of the NATO report should be implemented in the Polish Armed Forces.

**Key words:** suicides, NATO Armed Forces, prevention

**Streszczenie.** Realizując program Światowego Zgromadzenia Zdrowia „Prewencja samobójstw – globalnym imperatywem”, Organizacja ds. Nauki i Techniki NATO, w ramach panelu Zdrowie i Medycyna, utworzyła grupę badawczą RTG-218, która skierowała do szefów wojskowej służby zdrowia 34 państw NATO i państw partnerskich pytania dotyczące liczby oraz cech samobójstw, monitoringu suicydologicznego i programów prewencji samobójstw w tych państwach. Na podstawie odpowiedzi uzyskanych od połowy respondentów opracowano raport STO-TR-HFM-218 z rekomendacjami dla kierownictwa i dowódców NATO. Cel pracy. Konfrontacja danych raportu z wynikami badań polskich suicydologów. Uzasadnienie wdrożenia rekomendacji raportu w Wojsku Polskim. Wnioski. Samobójstwo jest jedną z głównych przyczyn śmierci żołnierzy w armiach NATO. Zaburzenia depresyjne oraz zaburzenia związane z używaniem alkoholu i środków psychoaktywnych są najczęstszymi medycznymi czynnikami ryzyka samobójczego. Fałszywe poglądy na temat samobójstw, ograniczony dostęp do fachowej pomocy oraz obawa przed stygmatyzacją są głównymi przeszkodami skutecznej profilaktyki. Psychoedukacja oraz systematyczny monitoring oparty na dowodach naukowych stanowią podstawę nowoczesnych programów prewencji suicydologicznej. Rekomendacje raportu NATO powinny być wdrożone w Wojsku Polskim.

**Słowa kluczowe:** samobójstwa, Siły Zbrojne NATO, prewencja

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## Introduction

Suicide is a significant public health problem. According to World Health Organisation (WHO) data, over 800 thousand people committed suicide in 2012. It was the fifteenth most common cause of death globally, and the mean standardised suicide rate was 11.4 per 100,000 citizens. In the population aged 30-49 years old, suicide was the fifth most common cause, and in people aged 15-29 years old the second most common cause of death (following traffic accident) [1].

In 2013, the World Health Assembly initiated a global suicide prevention programme, comprising the systematic collection and analysis of data regarding suicidal behaviours, as well as an international exchange of experiences in their effective reduction [2].

Military service, especially involving foreign missions, is considered to be a suicidal risk factor. Therefore, in relation to the WHO suicide prevention programme, NATO Science & Technology Organization (NATO STO) created Research Task Group (RTG) 218 as part of the Human Factors and Medicine (HFM) panel, in order to:

- obtain information regarding suicidal behaviours in the member countries of NATO Partnership for Peace (PfP), and those cooperating with NATO (Other Military Cooperation – OMC),
- learn more about the suicide prevention programmes implemented in these countries.
- create a platform for continuous, international cooperation in this area,
- develop recommendations regarding effective preventive measures for NATO commanders at all levels, especially for Chiefs of Military Medical Services in NATO (COMEDS) [3].

In implementing the above goals, HFM-RTG-218 prepared a questionnaire regarding: (1) the number of active soldiers in a given state; (2) the position of suicide in the ranking of death causes in the military; (3) the adopted definition of suicide; (4) the suicide rate (s.r.) of soldiers, in total and separately (5) for men and (6) for women; (7) s.r. for veterans; (8) the definition of attempted suicide adopted in the military; (9) the rate of suicide attempts; (10) the body qualified to determine the cause of soldiers' deaths; (11) the body managing data regarding the causes of soldiers' deaths; (12) five most common causes of death among soldiers; (13) procedures of establishing and documenting causes of soldiers' deaths; (14) monitoring of suicides in the armed forces; (15) three most frequent suicide methods among military personnel; (16) factors specific for the armed forces preventing suicide (*protective factors*); (17) indicators specific for the armed forces concerning suicide risk (*risk indicators*); (18) three most common psychiatric diagnoses in suicide victims in the military; (19) the structure of the armed forces in a state; (20) the definition of deployment; (21) the duration of deployment (minimum, maximum, average); (22) the average interval between deployments; (23) three

most frequent places of deployment within the past 5 years; (24) the total number of suicides and s.r. during a deployment; (25) methods of effective reduction of suicidal behaviours (*best practices*) – in a given state, in the armed forces and among veterans; and (26) the expected forms of international co-operation in this area.

In 2013, the questionnaire, together with an invitation to participate in a survey and description of its purpose, was sent to Surgeon Generals in 34 NATO, PfP and OMC states; half of them responded. Based on the responses, a STO-TR (Science and Technology Organization Technical Report) HFM-218 report with consensual recommendations was developed [3].

## Aim of the study

The aim of the study was to compare the data in the HFM-218 report, in which the data regarding Poland is missing, with the results of studies concerning suicide in the Polish Armed Forces after joining NATO. Due to editorial restrictions, the article presents responses to some of the questions in the questionnaire. The remaining ones will be discussed in the next publication.

## Material and methods

We used the results of our own studies [4] and of the research conducted by Polish suicidologists [5, 6], information from Polish Statistical Yearbooks [7, 8], and statistical data obtained from the Human Resources Department of the Ministry of National Defence [9]. The outcomes are presented in the tables from the HFM-RTG-218 report, supplemented with data regarding Poland. Relatively complete tables, with few empty fields were selected.

## Results

Table 1 presents the structure of personnel in the Polish Armed Forces and in the armies of countries participating in the NATO STO HFM-218 project, according to the gender of the soldiers.

In 2012, among the 18 countries compared, Poland was 12th (*ex aequo* with Germany, Lithuania, Latvia and the United Kingdom) in the percentage of citizens in active military service, at 0.25% (the mean is 0.36%) [7]. As for the percentage of women in the military, Poland was ranked last at 2.5% (the mean was 9.8%). Polish female soldiers were younger compared to the women in other armies (except for the US military), at 31 (the mean was 34.6) [9].

Table 2 presents the data regarding the absolute number of suicidal deaths and suicide rates (s.r.) of soldiers in the compared countries, according to the gender of the victims, as well as information about the monitoring of suicide in the military.

**Table 1. Military population demographics by gender as reported by Poland and other states participating in the study**  
**Tabela 1. Struktura demograficzna Wojska Polskiego i armii państw uczestniczących w projekcie badawczym wg płci**

Country	Year	Total number of employees	% of general population	Male soldiers			Female soldiers		
				n	%	Mean age	n	%	Mean age
Australia	2010	50,049	0.2	–	–	–	–	–	–
Austria	2012	30,000	0.4	–	–	–	–	–	–
Belgium <sup>1</sup>	2012	35,934	0.3	33,015	91.9	42.5	2,919	8.1	41.7
Denmark	2013	15,800	0.28	14,770	93.5	–	1,030	6.5	–
Estonia	2012	5800	0.43	5,104	88.0	33.0	696	12.0	40.0
Finland <sup>1</sup>	2011	8,844	0.16	8,526	96.4	–	318	3.6	–
France	2012	325,583	0.5	275,297	85.0	32.9	50,286	15.0	31.9
Netherlands	2011	53,130	0.32	48,630	91.0	–	4,500	9.0	–
Canada <sup>1</sup>	2012	67,449	0.4	58,116	86.2	35.0	9,332	13.8	35.0
Lithuania <sup>1</sup>	2012	7,382	0.25	6,696	90.7	32.0	686	9.3	36.0
Latvia <sup>1</sup>	2012	5,008	0.25	3,956	79.0	–	1,052	21.0	–
Germany	2011	205,149	0.25	187,191	91.0	–	17,958	9.0	–
Poland	2012	95,318	0.25	92,934	97.5	33.5	2,384	2.5	31.0
Romania <sup>1</sup>	2011	80,000	0.37	73,600	92.0	–	6,400	8.0	–
Slovenia <sup>1</sup>	2011	7,500	0.36	6,300	85.0	–	1,200	15.0	–
Turkey	2013	593,708	0.77	–	–	–	–	–	–
UK <sup>1</sup>	2014	159,620	0.25	143,780	90.0	27.0	15,840	10.0	32.0
USA <sup>3</sup>	2012	2,270,127	0.74	1,907,693	84.0	30.0	362,434	16.0	29.4

– signifies a lack of data

<sup>1</sup> United Kingdom (UK) – the data refers to soldiers in active service.

<sup>2</sup> With military police and military reserve forces; without their formations, the French Armed Forces comprise 222,215 soldiers.

<sup>3</sup> Median is used as the mean value.

In the analysed period, in 27.8% of countries the s.r. was >20.0/100,000 soldiers, in 16.7% of states it was 15.0–19.9/100,000 soldiers, in 22.2% of countries it was 10.0–14.9, in 5.5% of countries it was <10.0, and 27.8% of countries did not provide any data in this area. At the same time Poland, next to Denmark, Germany and Turkey, demonstrated one of the lowest s.r. in the military: 11.8, with a mean total s.r. of 18.0. It was also characterised (together with 6 other countries) by the absence of suicide among women in military service [4]. 66.7% of countries implemented the regular monitoring of suicides [3, 4].

Table 3 presents the ranking of the main causes of death among soldiers in the compared armies.

Only 9 (52.9%) countries provided answers regarding the main causes of death among soldiers in active military service. In 77.8% of the states, suicide was one of three

most common causes of soldiers' deaths. The United Kingdom (UK) and Canada were ranked 7th and 5th, respectively, regarding suicide as the cause of death in the military. In the Polish Armed Forces in 2012 suicide was the 3rd most frequent cause of death among soldiers [9]. The above data, together with the ranking of the main causes of death in the compared countries, indicate that suicidal deaths in the armed forces of these states were more frequent than among civilians [1, 8].

Table 4 presents the ranking of methods of suicide used by soldiers of the compared armies.

Among the 12 states that provided answers to the questionnaire, in 6 soldiers the most often method of suicide was shooting or hanging (equal frequency). It is noteworthy that in Belgium all suicides in the military involved hanging, and in Turkey there were no such cases [3].

## ORIGINAL WORKS

**Table 2. Military suicide data by gender in Poland and the states participating in the study**  
**Tabela 2. Samobójstwa żołnierzy wg płci w Polsce i w państwach uczestniczących w projekcie badawczym**

Country	Year	Total		Male soldiers		Female soldiers		Monitoring of suicide in the military
		Number	s.r.	Number	s.r.	Number	s.r.	
Australia	2013	92	–	85	–	7	–	Yes
Austria	2012	–	27,0	–	27,0	–	0.0	Yes
Belgium	2012	13	36.0	12	33.0	1	34.0	No
Denmark	1990–2009	41	10.0	41	10.0	0	0.0	Yes
Estonia	–	–	–	–	–	–	–	No
Finland <sup>1</sup>	2011	3	17.2	3	17.2	0	0.0	Yes
France <sup>2</sup>	2012	69	20.6	62	22.6	7	8.4	Yes
Netherlands	–	–	–	–	–	–	–	No
Canada	2010	12	17.6	12	20.4	0	0.0	Yes
Lithuania	2012	3	23.0	3	25.8	0	0.0	Yes
Latvia	2003-2011	9	20.0	9	20.0	0	0.0	No
Germany	2011	18	8.5	18	9.3	0	0.0	Yes
Poland	2012	11	11.5	11	11.5	0	0.0	Yes
Romania	–	–	–	–	–	–	–	No
Slovenia	–	–	–	–	–	–	–	No
Turkey	2013	64	10.8	64	10.8	–	–	Yes
UK	1994–2013	408	13.5	391	14.3	17	10.7	Yes
USA <sup>3</sup>	2013	259	18.7	244	20.7	15	4.1	Yes

– signifies a lack of data

s.r. – suicide ratio per 100,000 soldiers

<sup>1</sup> The data refers to conscripted soldiers

<sup>2</sup> Mean data from 2002–2012

<sup>3</sup> Updated results from 2013 – the Centers for Disease Control and Prevention's Web-based Injury Statistics Query and Reporting System

In 2012, in Poland, 89.5% of suicides were committed by hanging, and only 1.8% by shooting [4].

Table 5 presents the ranking of the mental disorders with which the soldiers in the compared armies were diagnosed.

In ten countries participating in the survey, the most frequently established diagnoses were depression in the course of affective disorders (F30-39), and neurotic and stress-related disorders (F40-48). The next most frequent diagnosis involved disorders associated with the use of alcohol and other psychoactive substances (F10). The distribution of the most common psychiatric disorders in the Polish military was similar: F32 (50.0%), F43.2 (30.4%), and F10 (19.6%) [5, 6].

## Discussion

The HFM-RTG-218 report is the first attempt in the history of NATO to present the scale and conditions of suicidal

behaviour in soldiers, as well as to present the recommendations regarding its prevention. The fact that half of the 34 Surgeons General of the NATO and PfP states invited to participate in the project failed to answer the survey questions, and the incomplete answers provided by some participants demonstrate the obstacles in the area of international cooperation in military suicidology.

In most countries participating in the survey, suicide was the second or third most frequent cause of death among soldiers. However, statistically significant comparisons cannot be based on differences in s.r. values between these states, as there are considerable differences in the identification and classification of suicidal behaviour in various armies, and the data presented in the survey are only from the last reported year. Moreover, the structure of the armed forces varies (professional military or conscription), as well as culture, and the requirement regarding the duration of deployment, for example.

**Table 3. Main causes of in the military and the general population in the compared states**  
**Tabela 3. Główne przyczyny zgonów w wojsku i w generalnej populacji porównywanych państw**

Country	Year	Main causes of deaths in the military			Place of suicide		
		1.	2.	3.	In the military	In the general population	
Australia	2010	Traffic accident	Disease	Suicide	3	15	
Austria	2013	Traffic accident	Other accident	Suicide	3	13	
Belgium	2012	–	–	–	–	15	
Denmark	2011	–	–	–	–	10	
Estonia	2011	–	–	–	–	9	
Finland	2007	Traffic accident	Suicide	Other accident	2	7	
France	2011	Disease	Traffic accident	Suicide	3	8	
Netherlands	2011	–	–	–	–	4	
Canada	2006	Combat loss	Accident	Disease	5	7	
Lithuania	2012	Traffic accident	Suicide	Disease	2	6	
Latvia	2009	–	–	–	–	5	
Germany	2012	–	–	–	–	12	
Poland	2012	Traffic accident	Other accident	Suicide	3	13	
Romania	2011	–	–	–	–	11	
Slovenia	2009	–	–	–	–	–	
Turkey	2013	Suicide	Accidents involving weapons	Traffic accident	1	12	
UK	2013	Disease	Other accident	Traffic accident	7	22	
USA	2012	Accident	Combat loss	Suicide	3	10	

– signifies a lack of data

<sup>1</sup> The data refers only to conscripted soldiers

The validity of these objections is confirmed by changes in s.r. values in the Polish Armed Forces: in 2012 it was 11.5/100,000 soldiers, in the years 2000-2008, before the military became professional, it was 19.0/100,000, and after the professionalisation, in the years 2009-2011, it was 16.6 [4]. In 2012, suicide was the third most common cause of death of the military personnel, and in the 2009-2016 period, the second, following traffic accident [9].

In the year the report was prepared, in half of the states participating in the survey the most common suicide method among military personnel involved firearms, and in the other half it was hanging. Before professionalisation, in the Polish Armed Forces 59.9% of suicides were committed by hanging, and 29.1% involved firearms. After the military was professionalised, 89.5% of suicides was committed by hanging, and 1.8% with firearms [4]. Based on the data in the report, it is not possible to determine the dominant suicide method in NATO armies.

In all the compared states, including Poland, the type of mental disorders ranked first in military suicide victims were depressive disorders, both in the course of affective disorders, and adjustment disorders. They were followed

by mental disorders associated with the use of alcohol and other psychoactive substances. The above problems together accounted for 90% of the diagnoses. Unfortunately, the report does not explain on what the assessments were based: data from medical records, from the central register of causes of death, or conclusions from a retrospective analysis of prosecution or court files.

The above controversies indicate the need for a standardised scientific basis for research on suicide in the military, to provide comparable results and enable international exchange of experiences regarding preventive measures.

Comments to the questions of the HFM-218 questionnaire suggest that in the majority of states that declare the monitoring of suicide, including Poland, it is limited to recording suicidal deaths, with a limited scope of information useful for scientific studies. Only in the Scandinavian countries [10], Canada [11], and United States are individual circumstances of suicide analysed, i.e. the sociodemographic, biological and psychological factors, or situational aspects related to service, medical or psychosocial issues.

**Table 4. Top 3 Suicide methods in soldiers of the compared states**  
**Tabela 4. Trzy najczęstsze sposoby popełniania samobójstwa przez żołnierzy porównywanych państw**

Country	Year	Main suicide methods %		
		1.	2.	3.
Australia	2009	–	–	–
Austria	2012	Firearms 46.0	Hanging 26.0	Vehicle impact 10.0
Belgium	2012	Hanging 100.0	–	–
Denmark	1990-2009	Firearms 41.0	Hanging 22.0	Poisoning 24.0
Estonia	–	–	–	–
Finland <sup>1</sup>	1991-2007	Firearms 60.4	Hanging 16.7	Jumping from a height 8.3
France	2002-2012	Firearms 44.7	Hanging 40.5	Poisoning 5.7
Netherlands	–	–	–	–
Canada	2011–	Hanging 63.2	Firearms 23.7	Poisoning 13.2
Lithuania	2012	Hanging 60.0		
Latvia	2003-2011	Hanging 77.8		
Germany	2011	Hanging 44.4	Vehicle impact 10.0	
Poland	2009-2012	Hanging 89.5	Firearms 1.8	Other 8.7
Romania	–	–	–	–
Slovenia	–	–	–	–
Turkey	2013	Firearms 80.8	Poisoning 13.7	Jumping from a height 2.7
UK	2014	Hanging 43.0	Firearms 22.0	Gas poisoning 13.0
USA	2011	Shot using private firearms 53.9	Hanging 29.4	Service weapons 6.5

– signifies a lack of data

<sup>1</sup> The data refers only to conscripted soldiers

In the years 2008-2015, the results of these analyses were published in DoDSER reports [13]. Currently, the monitoring of suicide in the American Armed Forces is conducted as part of the STARRS-LS 2016–2020 programme [14]. Effective prevention of suicide in all NATO armies, including the Polish Armed Forces, is reduced by: a limited understanding of the symptoms of increased risk of suicide as visible to other people, misguided beliefs regarding the likelihood of the accomplishment of suicide threats or attempts, avoiding psychological or medical assistance in a suicidal crisis due to the fear of environmental stigmatisation, and sometimes also a limited access to such help. The aim of the STO-HFM-218 report, dedicated to the authorities and leadership of NATO, is to popularise the understanding of the conditions associated with suicidal behaviour in soldiers, to enhance the ability to early diagnose the symptoms of pre-suicidal syndrome, and to promote programmes for effective suicide prevention in the military.

The recommendations presented in the report will be discussed in the next publication.

## Conclusions

- Suicide is one of the leading causes of death among soldiers in NATO armed forces.
- Depressive disorders and disorders associated with the use of alcohol and psychoactive substances are the most common medical risk factors.
- Misguided beliefs about suicide, a limited access to professional assistance, and the fear of environmental stigmatisation are the principal obstacles to effective suicide prevention.
- A coordinated psychological education and systematic, evidence-based monitoring of suicide are the basis of modern suicide prevention.
- The recommendations of the NATO report should be implemented in the Polish armed forces.

**Table 5. Top 3 Psychiatric conditions in military suicides of the compared states**  
**Tabela 5. Trzy najczęstsze rozpoznania psychiatryczne w samobójstwach żołnierzy porównywanych państw**

Country	Year	Diagnosis		
		1.	2.	3.
Australia	2010	F40-48 (-)	F30-39 (-)	F10 (-)
Austria <sup>1</sup>	2013	F43.2 (-)	F30 (-)	F10 (-)
Belgium				
Denmark		-	-	-
Estonia		-	-	-
Finland	2011	F40-F48 (49.7%)	F30-39 (18.6%)	F10 (17.2%)
France	2005-2010	F30-39 (71.3%)	F43-F48 (40.2%)	F09 (4.3%)
Netherlands				
Canada	2002	F30-39 (-) 16%	F40-48 (-) 10%	F10-19 (-) 5%
Lithuania*	2011	F32 (41.9%)	F40-48 (41.9%)	F60-69 (6.9%)
Latvia	-	-	-	-
Poland	2012	F32 (50.0%)	F43.2 (30.4)	F10 (19.6%)
Romania	-	-	-	-
Slovenia	2011	F43.2 (33%)	F32 (22%)	F69 (15%)
Turkey	2013	F43.2 (-) -	F32 (-)	F40-F41 (-)
UK	2013	F43 (-) 11.3%	F32 (6.1%)	F10 (-) 1.6%
USA	2009	F43.1 (9-20%)	F32 (8-15%)	F09 (4-8%)

Explanation of the ICD-10 codes

F00-F09 Organic mental disorders, F09 Unspecified

F10-F19 Disorders due to psychoactive substance use, F10 Disorders due to use of alcohol

F20-F29 Schizophrenia, schizotypal and delusional disorders

\* F10-19: 4.7%; F50-F59: 2.3%; F20-29: 2.3%

F30-F39 Mood (affective) disorders: F32 Depressive episode

F40-F48 Neurotic and stress-related disorders: F43.1 Post-traumatic stress disorder (PTSD); Acute stress reaction;

F43.2 Adjustment disorders

F50-F59 Behavioural syndromes associated with physiological disturbances

F60-F69 Personality disorders

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# FGFR2 gene expression analysis in gastric cancer patients treated with first-line chemotherapy based on fluoropyrimidine

Analiza ekspresji genu *FGFR2* u chorych na raka żołądka leczonych chemioterapią pierwszej linii opartą na fluoropirymidynie

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**Abstract.** The aim of the study was an assessment of the frequency and significance of FGFR2 receptor expression and its gene amplification as a potential prognostic and predictor factor. The presence of FGFR2 gene amplification and FGFR2 receptor expression was assessed in formalin-fixed, paraffin-embedded tissues using, respectively, a FISH assay and an IHC in an advanced gastric cancer cohort. In this pilot study, the clinical data was analysed of 36 patients treated with first-line chemotherapy based on fluoropyrimidine derivatives. One of the 36 patients (3%) exhibited FGFR2 amplification. FGFR2 receptor expression was observed in 11% (4/36) of the patients, and overexpression of this receptor was observed in 6% (2/36) of them. In the univariate analysis, PFS and OS did not differ between the expressed FGFR2 and no-expression groups. Multivariate analysis indicated that FGFR2 expression was not an independent predictor and prognostic factor for PFS and OS, respectively. FGFR 2 expression does not appear to be an independent prognostic and predictor in patients with advanced gastric cancer treated with palliative fluoropyrimidine chemotherapy.

**Key words:** gastric cancer, FGFR2 gene amplification, FGFR2 receptor expression

**Streszczenie.** Cel. Celem badania była ocena częstości i znaczenia ekspresji receptora FGFR2 oraz amplifikacji jego genu jako potencjalnego czynnika prognostycznego i predykcyjnego. Metody. Obecność amplifikacji genu *FGFR2* i ekspresji receptora FGFR2 oceniano w tkankach utrwalonych w formalinie, w bloczkach parafinowych, stosując odpowiednio oznaczenia metodą FISH i immunohistochemiczne w kohorcie zaawansowanego raka żołądka. W pilotażowym badaniu przeanalizowano dane kliniczne 36 chorych poddanych chemioterapii pierwszej linii pochodnymi fluoropirymidyny. Wyniki. Jeden z 36 chorych (3%) wykazał amplifikację genu *FGFR2*. Ekspresję receptora FGFR2 obserwowano u 11% (4/36) chorych, zaś nadekspresję tego receptora u 6% (2/36). W analizie jednoczynnikowej ekspresja receptora FGFR2 nie miała istotnego wpływu na PFS i OS. Analiza wieloczynnikowa wskazała, że ekspresja FGFR2 nie była niezależnym czynnikiem predykcyjnym i prognostycznym odpowiednio dla PFS i OS. Wniosek. Ekspresja FGFR2 nie okazała się niezależnym prognostykiem predykcyjnym u pacjentów z zaawansowanym rakiem żołądka leczonych paliatywną chemioterapią opartą na fluoropirymidynie.

**Słowa kluczowe:** rak żołądka, amplifikacja genu *FGFR2*, ekspresja receptora FGFR2

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## Introduction

Globally, gastric cancer is the fifth most common neoplasm, and the third most frequent cause of death in oncological patients, leading to approximately 723 thousand deaths annually [1]. Over the last four decades, the prevalence of gastric cancer in the population of patients with neoplasms has been reduced by a factor of almost three. Presently, malignant neoplasms of the stomach are found in approximately 5% of men and 3% of women. In 2010, 3400 men and 1900 women were diagnosed with these conditions. The 5-year survival in patients with gastric neoplasms increased slightly in the first decade of the 21st century, from 14.6% to 16.4% in men, and from 18.2% to 19.8% in women [2].

Patients with advanced gastric cancer receive systemic palliative chemotherapy to extend survival, and to improve the quality of life. Presently, the standard first-line chemotherapy is based on fluoropyrimidine and platinum derivatives. At least half of the patients qualify for second-line treatment. Despite the therapy, the prognosis is poor, and overall survival is 10-13 months [3].

FGF play an important role in the pathogenesis of various gastric diseases, including neoplasms. Experiments on cell lines demonstrated that FGF-1 and FGF-2 affect the adhesion, differentiation and infiltration of neoplastic cells. A study on gastric cancer cell lines revealed that Ki23057, an inhibitor of the FGFR2 receptor, may overcome the resistance of neoplastic cells to irinotecan, paclitaxel and etoposide. The main mechanism underlying the synergistic effect of this therapeutic combination is the induction of apoptosis [4].

Immunohistochemical assessment of gastric cancer cells from the primary tumour tissue reveals FGFR2 protein expression in 31-51% of patients. The most important changes observed in the FGFR2 gene include amplification, which are found in approximately 4-7% of patients, and may be an adverse prognostic factor [5].

The aim of the study was to analyse the frequency of FGFR2 protein expression and amplification of the FGFR2 gene, together with selected clinicopathological parameters in patients with advanced gastric cancer treated with first-line chemotherapy based on fluoropyrimidine.

## Material and methods

The retrospective analysis comprised a cohort of subsequent patients with locally advanced or metastatic gastric cancer, treated at the Department of Oncology, Military Institute of Medicine, in the years 2010-2015. The inclusion criteria comprised:

- histopathological confirmation of gastric cancer,
- presence of locally advanced (non-resectable) or metastatic gastric cancer,
- disease stage confirmed by an objective radiological examination (computed tomography of the chest, abdominal cavity and pelvis),
- starting the first-line fluoropyrimidine-based palliative chemotherapy in the period from 01/01/2010 to

31/12/2015,

- completion of at least one full cycle of first-line fluoropyrimidine-based palliative chemotherapy,
- absence of other malignant neoplasms, except for cutaneous basal cell carcinoma or cervical intraepithelial neoplasia (CIN).

The exclusion criteria comprised:

- starting the first-line palliative chemotherapy with the use of cytostatics other than fluoropyrimidine,
- starting the first-line palliative chemotherapy before 01/01/2010 or after 31/12/2015,
- completion of adjuvant chemotherapy within 6 months from starting the first-line fluoropyrimidine-based palliative chemotherapy,
- completion of the first cycle of the first-line fluoropyrimidine-based palliative chemotherapy at a centre other than the Department of Oncology of the Military Institute of Medicine in Warsaw.

The neoplastic tumour tissue from the first study cohort, i.e. 36 patients, available in the form of paraffin blocks in the Pathomorphology Division of the Military Institute of Medicine, was sliced and placed on silanised slides. When the preparations were ready, the FGFR2 gene was analysed using the FISH method. Signals in 50 cells were assessed, including the FGFR2 signals (red) and CEN10p signals (green). The result was the calculated FGFR2/ CEN10p ratio.

Simultaneously, the material was stained for FGFR2 expression, using a commercial antibody in a dilution of 1:500 (Abcam ab 10647).

## Methodology of immunohistochemical assays

The immunohistochemical assessment involved the intensity of staining, percentage of the stained neoplastic cells, and location of staining. The preparations were initially assessed in the Celon Pharma S.A. Research and Development Laboratory, and then by two independent pathomorphologists (SC and AM).

The assessment methodology was developed, and two scores for the determination of FGFR2 expression in the gastric cancer cells were proposed: HercepTEST and H-Score.

### HercepTEST score

A four-point score (0-3+) was used to assess the immunohistochemical preparations:

- 0 – no staining, non-specific staining or individual, few cells (<10%),
- 1+ – weak cytoplasmic staining, staining of moderate intensity involving  $\geq 10\%$  of the neoplastic cells (note: groups/clusters of stained neoplastic cells must be present),
- 2+ – membrane staining of moderate intensity (2+) involving  $> 10\%$  of the neoplastic cells,
- 3+ – membrane staining of high intensity (3+) involving  $\geq 10\%$  of the neoplastic cells.

**H-Score**

This score assessed both the intensity of staining, and the percentage of the stained cells in the entire component of cancer infiltration, including both the intensity of immunohistochemical reaction on a scale of 0 to 3, and the area of the mentioned 4 types of reaction, expressed as the percentage of the structure of the infiltrating tumour. Using the formula:

$HS = 1 \times Pi \text{ (weak)} + 2 \times Pi \text{ (moderate)} + 3 \times Pi \text{ (strong)}$ , the immunohistochemical expression index was derived for the reactions. The Pi value signified the percentage of the surface area of the invasive component demonstrating a proper reaction intensity.

**Statistical analysis**

The statistical analysis in this study used descriptive statistics. The Kaplan-Meier estimator was used to assess the survival function, median and 95% confidence interval for the progression-free survival (PFS), and the overall survival (OS). The log-rank test was used to compare the effect of expression of the studied proteins on the above parameters. Univariate analysis was followed by the Cox proportional hazard multivariate test to create a model of independent predictive and prognostic factors. Non-parametric statistical tests, such as Mann-Whitney test or chi-square test, were used to assess the effect of FGFR2 expression and the amplification of its gene on the clinical response parameters. The factors that were statistically significant ( $p < 0.05$ ) were considered to demonstrate an independent effect on PFS and OS. The statistical analysis was conducted with Statistica Statsoft version 12.0.

**Results****Characteristics of the study group**

The pilot study involved 36 subsequent patients with advanced or metastatic gastric cancer treated in the Department of Oncology of the Military Institute of Medicine, who received first-line palliative chemotherapy based on fluoropyrimidine, and whose tissue material from the primary gastric tumour was available from the Pathomorphology Division of the Military Institute of Medicine. Among 36 patients, 50% (18/36) were men and 50% (18/36) were women. The median age was 65.8 years (range of 29-84 years). The tumour grade in 25% (9/36) of the patients was G2, in 61% (22/36) it was G3, and in 14%

(5/36) the tumour grade was not assessed. The primary disease stage was assessed as T1 in 3% (1/36), T2 in 11% (4/36), T3 in 25% (9/26), and T4 in 61% (22/36) of patients. The lymph nodes were invaded in 61% (22/36) of patients. Table 1 presents detailed characteristics of the study group.

**Assessment of expression and amplification of *FGFR2* gene in gastric cancer cells**

In the analysed group the expression of the fibroblast growth factor receptor (FGFR2) was assessed. Positive expression was found in 11% (4/36) of patients. According to the HercepTEST score, overexpression was observed in 6% (2/36) of the patients. Amplification of the FGFR2 gene was found in one patient, i.e. 3% of the study group. In the neoplastic tissue of this patient also a high membrane expression of FGFR2 was detected, with the H-score of 300. The data are presented in Table 2.

**Univariate analysis for PFS**

Table 3 presents the effects of the analysed clinicopathological parameters on the progression-free survival, using the Cox proportional hazard model. A predictive value for location of metastatic lesions in the lungs and ovaries, as well as for the number of invaded areas was observed in the study group. The analysed variables did not reveal any significant predictive value for FGFR2 expression (Fig. 1), age, sex, grade (G), tumour size, presence of metastasis to the lymph nodes, gastrectomy, ascites, general performance or the presence of metastases in peritoneum, distant lymph nodes, bones, liver or pancreas.

The multivariate analysis using the Cox proportional hazards model included all the factors detected in the univariate analysis that demonstrated a statistically significant effect on progression-free survival (i.e. presence of metastases to the lungs or ovaries, and the number of areas invaded by the metastases), and expression of FGFR2 protein. Based on the multivariate analysis, two variables: metastases in the lungs and ovaries were independent adverse predictive factors for progression-free survival (HR, hazard ratio was 4.49 [95% CI: 1.49-16.09]  $p = 0.0090$  and 10.31 [95% CI: 2.83-37.58]  $p = 0.0004$ , respectively) (Tab. 4).

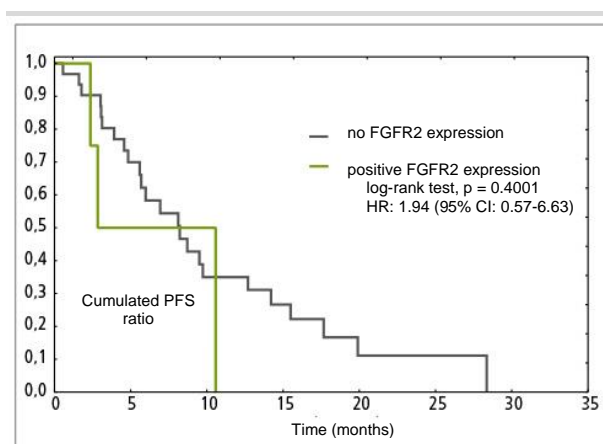
**Table 1. Examined group description (N = 36)**  
**Tabela 1. Charakterystyka badanej grupy (N = 36)**

Parameter	N	%
<b>Sex</b>		
Female	18	50
Male	18	50
<b>Age (median, range)</b>		
	65.8	29-84
<b>Histological grade G</b>		
1	0	0
2	9	25
3	22	61
Absent	5	14
<b>Tumour size (T)</b>		
1	1	3
2	4	11
3	9	25
4	22	61
<b>Feature N</b>		
0	10	28
1	5	14
2	6	17
3	11	31
Absent	4	11
<b>Gastrectomy</b>		
No	11	31
Yes	25	69
<b>Ascites</b>		
No	32	89
Yes	4	11
<b>ECOG</b>		
0	16	44
1	18	50
2	2	6
<b>Local relapse</b>		
No	29	81
Yes	7	19
<b>Pulmonary metastases</b>		
No	32	89
Yes	4	11
<b>Lymph node metastases</b>		
No	15	42
Yes	21	58
<b>Peritoneal metastases</b>		
No	27	75
Yes	9	25
<b>Hepatic metastases</b>		
No	26	72
Yes	10	28
<b>Pancreatic metastases</b>		
No	34	94
Yes	2	6
<b>Bone metastases</b>		
No	34	94
Yes	2	6

**Table 1. Examined group description (N = 36)**  
**Tabela 1. Charakterystyka badanej grupy (N = 36)**

<b>Ovarian metastases</b>		
No	32	89
Yes	4	11
<b>Metastases to other sites</b>		
No	30	83
Yes	6	16
<b>Number of areas invaded by neoplastic metastases</b>		
1	15	42
2	11	31
3	4	11
4	4	11
5	1	3
6	1	3

HR - hazard ratio, ECOG - Eastern Cooperative Oncology Group performance score



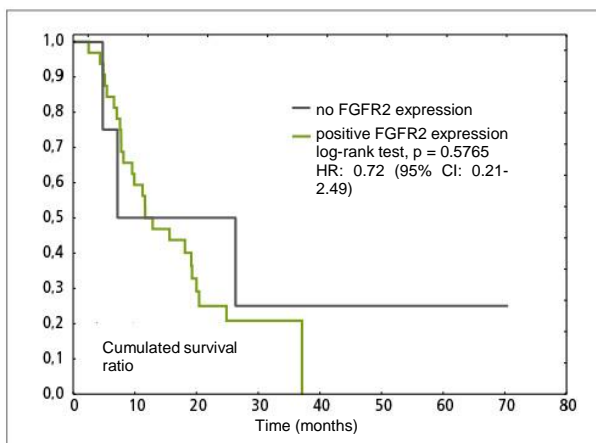
**Figure 1.** FGFR2 gene expression influence on progression-free survival using the log-rank test with Kaplan-Meier estimator  
**Rycina 1.** Wpływ ekspresji FGFR2 na czas przeżycia wolnego od progresji choroby przy zastosowaniu testu log-rank w estymatorze Kapla-na-Meiera

Based on the univariate analysis of the variables with reference to the overall survival in the studied group, worse general performance and the presence of pulmonary metastases were associated with a shorter OS. The other analysed variables, such as *FGFR2* expression (Fig. 2), age, sex, histological grade (G), tumour size, regional lymph node metastases, gastrectomy, ascites, or the presence of metastases in the peritoneum, distant lymph nodes, ovaries, bones, liver and pancreas were not prognostic factors, as none of them demonstrated statistical significance.

## ORIGINAL WORKS

**Table 2. FGFR2 gene expression and amplification analysis**  
**Tabela 2. Ocena ekspresji i amplifikacji genu FGFR2**

Parameter	N	%
FGFR 2 expression acc. to <i>H</i> -score		
0	32	89
20	1	3
30	1	3
90	1	3
300	1	3
FGFR 2 overexpression acc. to HerceptEST		
Absent	34	94
Overexpression	2	6
FGFR2 amplification		
No	35	97
Yes	1	3



**Figure 2.** FGFR2 gene expression influence on overall survival using the log-rank test with Kaplan-Meier estimator

**Rycina 2.** Wpływ ekspresji *FGFR2* na czas przeżycia całkowitego przy zastosowaniu testu log-rank w estymatorze Kaplana-Meiera

The results of the univariate analysis are presented in Table 5.

The multivariate analysis included the variables that in the univariate analysis demonstrated a statistically significant effect on overall survival: general performance according to ECOG, presence of pulmonary metastases, and FGFR2 expression, due to the character of the study. Based on the multivariate analysis using the Cox proportional hazards model, the independent adverse prognostic factors in the studied population ( $p < 0.05$ ) were the following: lower performance status (ECOG 2) (HR = 22.06 [95% CI: 3.74-130.20]) and presence of pulmonary metastases (HR = 7.36 [2.18-24.85]).

**Table 3. Cox regression (proportional hazards) model for each of the analysed factors**

**Tabela 3. Model proporcjonalnego hazardu Coxa dla każdego z analizowanych czynników**

Parameter	HR	95% CI	+ 95% CI	P
Sex				
Female	1			
Male	0.763953	0.351342	1.661130	0.496893
Age				
<65	1			
>65	1.001769	0.454284	2.209063	0.9965
Histological grade				
G				
1-2	1			
3, unspecified	1.304444	0.545443	3.1196218	0.550229
Tumour size (T)				
1-2	1			
3-4	1.002178	0.342243	2.934638	0.996834
Regional lymph nodes				
free	1			
Positive, no data	0.668972	0.296202	1.510874	0.333481
Gastrectomy				
No	1			
Yes	0.732862	0.317005	1.694257	0.467308
Ascites				
No	1			
Yes	2.265073	0.486817	10.53899	0.297289
ECOG				
0	1			
1	1			
2	3.659460	0.457144	29.29417	0.221563
Local relapse				
Yes	1			
Yes	0.602946	0.224250	1.621158	0.316081
Pulmonary metastases				
No	1			
Yes	7.387843	2.163083	25.23262	0.001419
Distant lymph node metastases				
No	1			
Yes	1.045108	0.480259	2.274298	0.911447
Peritoneal metastases				
No	1			
Yes	1.817696	0.778363	4.244830	0.167309
Hepatic metastases				
No	1			
Yes	1.01658	0.253839	4.0712	0.981466
Pancreatic metastases				
No	1			
Yes	1.81113	0.230693	14.2188	0.572121

## ORIGINAL WORKS

**Table 3. Cox regression (proportional hazards) model for each of the analysed factors**  
**Tabela 3. Model proporcjonalnego hazardu Coxa dla każdego z analizowanych czynników**

Parameter	HR	95% CI	+ 95% CI	P
Bone metastases				
No	1			
Yes	0.34097	0.026499	4.3874	0.409112
Ovarian metastases				
No	1			
Yes	3.370239	1.087386	10.44571	0.035289
Metastases to other sites				
No	1			
Yes	0.61239	0.136805	2.7413	0.521346
Number of invaded areas				
More	1.378731	1.006191	1.889203	0.045685
FGFR2 (IHC)				
No	1			
Positive	1.937339	0.566026	6.630934	0.292159

ECOG - Eastern Cooperative Oncology Group performance status score, FGFR2 - fibroblast growth factor receptor 2, HR - hazard ratio, IHC - immunohistochemistry

The results of the multivariate analysis are presented in Table 6.

## Discussion

The pilot study involved a cohort of 36 patients and demonstrated that the expression of the FGFR2 protein at 11% in the studied population. The studied amplification of the FGFR2 gene is a rare phenomenon, and in our group it was found in 3% of patients.

Fibroblast growth factors (FGF) and their receptors fibroblast growth factor receptors, FGFR) play an important role in numerous cellular processes. They regulate the proliferation, differentiation, survival and migration of cells. Disturbed FGF/FGFR signalling pathways may lead to many pathological conditions, including neoplasms. Abnormal expression of FGFR receptors and their ligands, as well as mutations in their coding genes, were demonstrated, including in prostate cancer, urinary bladder cancer, pulmonary and gastric cancer [6].

**Table 4. Multivariate analysis model**  
**Tabela 4. Model analizy wieloczynnikowej**

Parameter	HR	95% CI	+ 95% CI	P
Ovarian metastases				
No				
Yes	4.89298	1.487543	16.09451	0.008962
Pulmonary metastases				
No				
Yes	10.31126	2.829067	37.58206	0.000407
Number of areas				
1				
More	s.i.	s.i.	s.i.	s.i.
FGFR2 (IHC)				
No				
Positive	s.i.	s.i.	s.i.	s.i.

FGFR2 - fibroblast growth factor receptor 2, HR - hazard ratio, IHC - immunohistochemistry

Ahn et al. [7] found rare occurrence of FGFR2 gene amplification, similarly to our study, at approximately 3% in a group of 1974 patients with gastric cancer. The authors observed a high correlation between the expression of the FGFR receptor assessed in immunohistochemical tests, and the amplification of the FGFR2 gene at a level of 92%. The amplification of the FGFR2 gene was present in 100% patients with a 2+ or 3+ immunohistochemical expression of the FGFR2b receptor (60 cases), and in 54% of 13 patients with 1+ expression. The authors of this study observed a considerable adverse effect of a high FGFR2b expression on the survival of patients.

A slightly higher amplification of the FGFR2 gene than in our study, i.e. 4.9% (16/327), was observed by Seo S. et al. [8] in a group of gastric cancer patients receiving chemotherapy based on platinum derivatives and fluoropyrimidine. The univariate analysis did not reveal any effect of FGFR2 gene amplification on the PFS, while a statistically significantly shorter survival was observed in this group of patients. In the multivariate analysis the FGFR2 gene amplification was not an independent prognostic factor.

Matsuoto et al. [9] obtained similar results to ours regarding FGFR2 amplification, which they found in 4% (11 out of 267) of patients with gastric cancer. The authors observed a tendency for a shorter survival in this subgroup of patients, but the difference was not statistically significant.

**ORIGINAL WORKS**

**Table 5. Cox regression (proportional hazards) model for each of analysed factors**

**Tabela 5. Model proporcjonalnego hazardu Coxa dla każdego z analizowanych czynników**

Parameter	HR	95% CI	+ 95% CI	P
Sex				
Female				
Male	0.623931	0.280482	1.387930	0.247541
Age				
<65				
>65	0.749853	0.339260	1.657371	0.476833
Histological grade G				
1-2				
3,				
Unspecified	0.972215	0.393418	2.402537	0.951322
Tumour size				
(T)				
1-2				
3-4	0.703709	0.225927	2.191892	0.544401
Regional lymph nodes free				
Positive,				
no data	0.733647	0.320595	1.678876	0.463388
Gastrectomy				
No				
Yes	0.745982	0.330936	1.681561	0.479769
Ascites				
No				
Yes	2.45617	0.813927	7.41194	0.110809
ECOG				
0				
1				
2	14.38268	2.522808	81.99659	0.002685
Local relapse				
No				
Yes	0.420490	0.144092	1.227070	0.112869
Pulmonary metastases				
No				
Yes	5.684488	1.755419	18.40780	0.003751
Distant lymph node metastases				
No				
Yes	1.409005	0.652739	3.041483	0.382458
Peritoneal metastases				
No				
Yes	1.370333	0.598436	3.137866	0.456081
Hepatic metastases				
No				
Yes	1.330363	0.554315	3.19289	0.522793

**Table 5. Cox regression (proportional hazards) model for each of analysed factors**

**Tabela 5. Model proporcjonalnego hazardu Coxa dla każdego z analizowanych czynników**

Parameter	HR	95% CI	+ 95% CI	P
Pancreatic metastases				
No				
Yes	0.553316	0.038671	7.91710	0.662887
Bone metastases				
No				
Yes	3.250017	0.204260	51.71161	0.403791
Ovarian metastases				
No				
Yes	1.142805	0.338340	3.860031	0.829813
Metastases to other sites				
No				
Yes	0.931619	0.347920	2.494581	0.887912
Number of areas invaded by metastases				
1				
More		0.657113	3.176799	0.359982
1.444824				
FGFR2 (IHC)				
No				
Positive	0.724827	0.210707	2.493386	0.609673

ECOG - Eastern Cooperative Oncology Group performance status score, FGFR2 - fibroblast growth factor receptor 2, HR - hazard ratio, IHC - immunohistochemistry

In evaluating the receptor expression for FGFR1-4, Murase et al. [10] observed in a group of 222 gastric cancer patients that individual proteins strongly correlated with others. The authors of the study found a considerably higher expression of the FGFR2 gene than that observed in our study (51% vs 11%, respectively). The study revealed that overexpression of FGFR1, FGFR2 or FGFR4 was significantly associated with higher tumour malignancy, including the depth of infiltration, metastases to lymph nodes, tumour stage and presence of distant metastases. The patients who demonstrated overexpression of FGFR1, FGFR2 or FGFR4 also showed a significantly shorter disease-specific survival (DSS), which was an independent adverse prognostic factor.

The optional uses for the FGFR2 gene amplification in the treatment on the gastric cancer cell lines SNU-16 and KATO III with FGFR2 gene amplification were presented by Xie et al. [11].

**Table 6. Multivariate analysis model for overall survival**  
**Tabela 6. Model analizy wieloczynnikowej dla przeżycia całkowitego**

Parameter	HR	95% CI	+ 95% CI	P
ECOG	22.05702	3.736502	130.2053	0.000638
Pulmonary metastases				
No				
Yes	7.36084	2.180118	24.8528	0.001304
FGFR2 (IHC)				
No				
Positive	s.i.	s.i.	s.i.	s.i.

ECOG - Eastern Cooperative Oncology Group performance status score, FGFR2 - fibroblast growth factor receptor 2, HR - hazard ratio, IHC - immunohistochemistry

They discovered *in vivo* growth inhibition of the cell lines exposed to the specific AZD4547 inhibitor, with GI50 levels of 3 and 5 nmol/l, respectively. AZD4547 effectively inhibited phosphorylation of FGFR2 and the subsequent proteins in the signalling pathway, as well as induced apoptosis in the SNU-16 cells. Moreover, blocking of the FGFR2 receptor by AZD4547 resulted in a significant dose-dependent inhibition of the tumour growth in the experimental murine xenograft models with implanted gastric cancer cells with FGFR2 (SNU-16) and PDGFX (SGC083) gene amplification; however, this effect was not observed in the models with tumours containing cells without FGFR2 amplification. Blocking of FGFR2 by shRNA also inhibited the tumour growth, both *in vitro*, and *in vivo*. In addition, compared to monotherapy with AZD4547, an enhanced antineoplastic effectiveness was demonstrated in combination with cytostatics *in vivo*.

## Conclusions

In this pilot study involving patients with advanced or metastatic gastric cancer treated at the Department of Oncology of the Military Institute of Medicine who received first-line fluoropyrimidine-based palliative chemotherapy a positive expression of the FGFR2 receptor was found in 11% (4/36) of patients, while overexpression of this receptor was observed in 6% (2/36) of patients. Amplification of the FGFR2 gene was found in only one

patient (3% of the study group). In the neoplastic tissue of this patient also a high membrane expression of FGFR2 was detected, with an H-score of 300. A positive expression of FGFR2 in the study group did not demonstrate a significant effect on the progression-free survival or on the overall survival. Based on the multivariate analysis two clinicopathological variables were found to be independent adverse predictive factors for the progression-free survival: the presence of metastases in the lungs and ovaries. Poorer performance status and the presence of pulmonary metastases were associated with shorter overall survival.

The study was conducted as part of the STRATEGMED2/266776/17/NCBR/2015 programme, financed by the National Centre for Research and Development.

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# Outpatient cardiac care in the assessment of patients with decompensated heart failure - own experience

Ambulatoryjna opieka kardiologiczna w ocenie chorych z zaostrzeniem niewydolności serca - doświadczenia własne

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**Abstract.** Properly managed outpatient health care should minimise costs and improve the prognosis for patients with heart failure (HF). The aim of the study was to analyse the availability of outpatient health cardiac care and to satisfy the patients' needs, according to the opinions of patients hospitalized with decompensated heart failure. A prospective study was performed in a group of 131 patients with previously diagnosed HF, hospitalized with decompensated heart failure. In the study group (mean age  $73.2 \pm 10.8$  years) males were dominant ( $n=99$ , 75.6%). The majority of the patients presented chronic heart failure, lasting more than 10 years ( $n=61$ , 46.6%). One in three declared that they had not been admitted to an outpatient clinic during the last year. Most patients visited a cardiologist once ( $n=33$ , 25.2%) or twice a year ( $n=33$ , 25.2%). While grading the level of cardiac care, 53 patients (40.6%) assessed it as insufficient and 20 (16%) as poor. In comparison by age group, insignificant statistical differences were reported in respect of the numbers of visits to a cardiologist during the last year. Younger patients used outpatient care slightly more often. HF patients are mostly dissatisfied with the services of the outpatient health cardiac care system, and they make use of it less often than they need.

**Key words:** chronic heart failure, outpatient health care, rehospitalisation

**Streszczenie.** Wstęp. Prawidłowo zorganizowana opieka ambulatoryjna warunkuje ograniczenie kosztów oraz poprawę rokowania u chorych z niewydolnością serca (NS). Celem pracy była analiza dostępności ambulatoryjnej opieki kardiologicznej oraz zaspokojenia potrzeb pacjentów w opinii chorych hospitalizowanych z powodu zaostrzenia niewydolności serca. Metody. Badanie prospektywne wykonano w grupie 131 osób z wcześniej rozpoznaną NS, hospitalizowanych z powodu jej zaostrzenia. Wyniki. W badanej grupie (średni wiek  $73,2 \pm 10,8$  roku) przeważali mężczyźni ( $n=99$ , 75,6%). Większość chorych charakteryzowała się ponad 10-letnim wywiadem NS ( $n=61$ , 46,6%). Co trzecia osoba deklarowała, że ani razu w ciągu ostatniego roku nie była z wizytą u kardiologa w przychodni publicznej. Pacjenci korzystali najczęściej z opieki ambulatoryjnej raz ( $n=33$ , 25,2%) lub dwa razy w roku ( $n=33$ , 25,2%). W ocenie poziomu opieki kardiologicznej 53 pacjentów (40,6%) uznało go za niewystarczający, a 20 (16%) za zły. W porównaniu według kategorii wiekowej odnotowano nieistotne statystycznie różnice w zakresie liczby wizyt u kardiologa w ostatnim roku - pacjenci młodszy nieznacznie częściej korzystali z opieki ambulatoryjnej. Wnioski. Pacjenci z NS są w większości niezadowolony z funkcjonowania publicznego systemu ambulatoryjnej opieki kardiologicznej i korzystają z niego zbyt rzadko w stosunku do potrzeb.

**Słowa kluczowe:** przewlekła niewydolność serca, opieka ambulatoryjna, rehospitalizacja

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## Introduction

Heart failure (HF) is an important epidemiological and socioeconomic problem, posing a great challenge for healthcare systems. The prevalence of HF in the European population is 0.4 - 2%, and the condition is found in approximately 10 million Europeans [1].

In Poland, approximately 1 million patients suffer from HF, and 60 thousand die each year due to its decompensation [2-5]. Despite the constant development in medicine and implementation of new technologies, prognosis in HF is poor, and the mean 5-year survival is around 50% [4, 6]. The economic and social costs of HF are very high, and in the past years they have demonstrated a tendency to rise. Heart failure is the cause of 11% of all hospitalisations in Poland. It is the most frequent cause of hospitalisation in patients over 65 years old. Rehospitalisations are the greatest problem, and as many as 25% of patients need them within a month of a hospital discharge [5]. Properly organised outpatient care decreases the frequency or rehospitalisations, and improves the prognosis for HF patients [7], thus reducing the costs of care and treatment.

The analysis conducted as part of the POLCARD programme demonstrated that the average annual cost of hospitalisation of a patient with HF is 15 times higher than the cost of outpatient care [8].

The data regarding actual problems with the availability of specialist cardiac care are limited and inconclusive. The assessment of the real scale of this issue may provide an objective argument supporting the urgent need to improve the functioning of the healthcare system and the prognosis for patients with HF.

## Aim of the study

The aim of the study was to analyse the availability of outpatient cardiac care, and how the needs of patients are met, according to those hospitalised due to exacerbated heart failure.

## Material and methods. Study group.

The prospective study involved 131 patients of the Department of Cardiology and Internal Diseases of the Military Institute of Medicine, previously diagnosed with heart failure, and hospitalised due to its decompensation in the years 2014-2015. The study subjects were volunteers who gave their consent. The exclusion criteria were: either a lack of consent to participate in the study or

significant intellectual or cognitive limitations that could prevent providing conscious answers to the questions in the survey questionnaire.

## Questionnaire

The study subjects were given questionnaires regarding their opinion about cardiac care, with single-choice questions (Fig. 1). The respondents were informed about the aim of the survey. It was emphasised that the questions refer to public healthcare, and that the answers should not pertain to private healthcare services, as some of the patients also used them. The survey was conducted on the day of discharge from the Department of Cardiology and Internal Diseases of the Military Institute of Medicine.

## Statistical analysis

The statistical analysis was performed using MS Office Excel 2013 and Statistica 7.0 (StatSoft Inc.). The results were expressed as the percentage of different answers to individual survey questions.

Separate analyses were conducted in the women and men subgroups, as well as for patients aged <75 years old and >75 years old (the division was based on the median age in the studied group).

Statistical significance was set at  $p < 0.05$ .

## Results

Men dominated in the studied group ( $n=99$ , 75.6%), and the mean age was  $73.2 \pm 10.8$  years. The population comprised mostly patients with a long history of HF: 61 patients (46.6%) had suffered from the disease for more than 10 years (Fig. 2). In the previous year, 97 patients, i.e. 74% of the study population, had at least one appointment with a cardiologist.

The patients typically received specialist outpatient care once ( $n=33$ , 25.2%) or twice a year ( $n=33$ , 25.2%). However, one in three subjects declared that within the past year they did not have any appointments with a cardiologist within the public healthcare framework.

As many as 53 patients (40.6%) assessed the level of outpatient cardiac care as unsatisfactory. Twenty patients (16%) strongly criticised the outpatient healthcare system in Poland. Over half of the study population expressed dissatisfaction with the current healthcare system and lack of safety.

The comparative analysis based on the sex criterion, a longer period of chronic HF was revealed in the group of women (>10 years:  $n=52.5\%$  vs  $28.1\%$ ,  $p=0.016$  [Tab. 1]).

## SURVEY

**How long have you suffered from heart failure?**

- a) 1-2 years
- b) 3-5 years
- c) 6-10 years
- d) over 10 years

**How many times in the last year did you visit a cardiologist (at a public National Healthcare Fund clinic, not as part of private healthcare services)?**

- a) Once
- b) Twice
- c) Three times
- d) Four times
- e) Five or more times
- no answer

**When was the last time you visited a cardiologist (in a public National Healthcare Fund clinic, not as part of private healthcare services)?**

- a) Within a month
- b) 1-3 months ago
- c) 4-6 months ago
- d) Over 6 months ago
- e) Not in the past year

**Do you think the level of cardiac care for patients with heart failure in public clinics (National Health Fund) is satisfactory?**

- a) Definitely YES
- b) Rather YES
- c) Rather NO
- d) Definitely NO

**Do you feel safe in the present system of public (National Health Fund) cardiac care?**

- a) Definitely YES
- b) Rather YES
- c) Rather NO
- d) Definitely NO

**Figure 1.** Specimen of the patient satisfaction survey  
**Rycina 1.** Wzór ankiety dla pacjentów.

No statistically significant differences were found regarding the frequency of visits to a cardiologist within the last year. In the group of women there was a trend towards lower satisfaction with healthcare, but the difference was not statistically significant. No significant differences were found between men and women in the assessment of the feeling of safety.

**Table 1. Comparison of response by sex**  
**Tabela 1. Porównanie odpowiedzi badanych według płci**

	Males (%)	Females (%)	P
<b>How long have you suffered from heart failure?</b>			
a) 1-2 years	31.3	18.2	s.i.
b) 3-5 years	31.3	14.1	0.031
c) 6-10 years	9.4	15.2	s.i.
d) over 10 years	28.1	52.5	0.016
<b>How many times in the last year did you visit a cardiologist (in a public National Healthcare Fund clinic, not as part of private healthcare services)?</b>			
a) Once	34.4	22.2	s.i.
b) Twice	15.6	28.3	s.i.
c) Three times	9.4	9.1	s.i.
d) Four times	15.6	7.1	s.i.
e) Five or more times	3.1	6.1	s.i.
No answer	20.6	27.2	s.i.
<b>When was the last time you visited a cardiologist (in a public National Healthcare Fund clinic, not as part of private healthcare services)?</b>			
a) Within a month	18.8	27.3	s.i.
b) 1-3 months ago	18.8	19.2	s.i.
c) 4-6 months ago	21.9	10.1	s.i.
d) Over 6 months ago	9.4	11.1	s.i.
e) Not in the past year	31.3	32.3	s.i.
<b>Do you think the level of cardiac care for patients with heart failure in public clinics (National Health Fund) is satisfactory?</b>			
a) Definitely YES	15.6	7.1	s.i.
b) Rather YES	25.0	38.4	s.i.
c) Rather NO	50.0	36.4	s.i.
d) Definitely NO	9.4	18.2	s.i.
<b>Do you feel safe in the present system of public (National Health Fund) cardiac care?</b>			
a) Definitely YES	9.4	4.0	s.i.
b) Rather YES	34.4	38.4	s.i.
c) Rather NO	34.4	37.4	s.i.
d) Definitely NO	21.9	20.2	s.i.

The comparison according to the age criterion (Tab. 2) statistically insignificant differences regarding the number of visits to a cardiologist within the last year were observed: younger patients received outpatient care slightly more often. The differences in the assessment of the level of cardiac care also were insignificant.

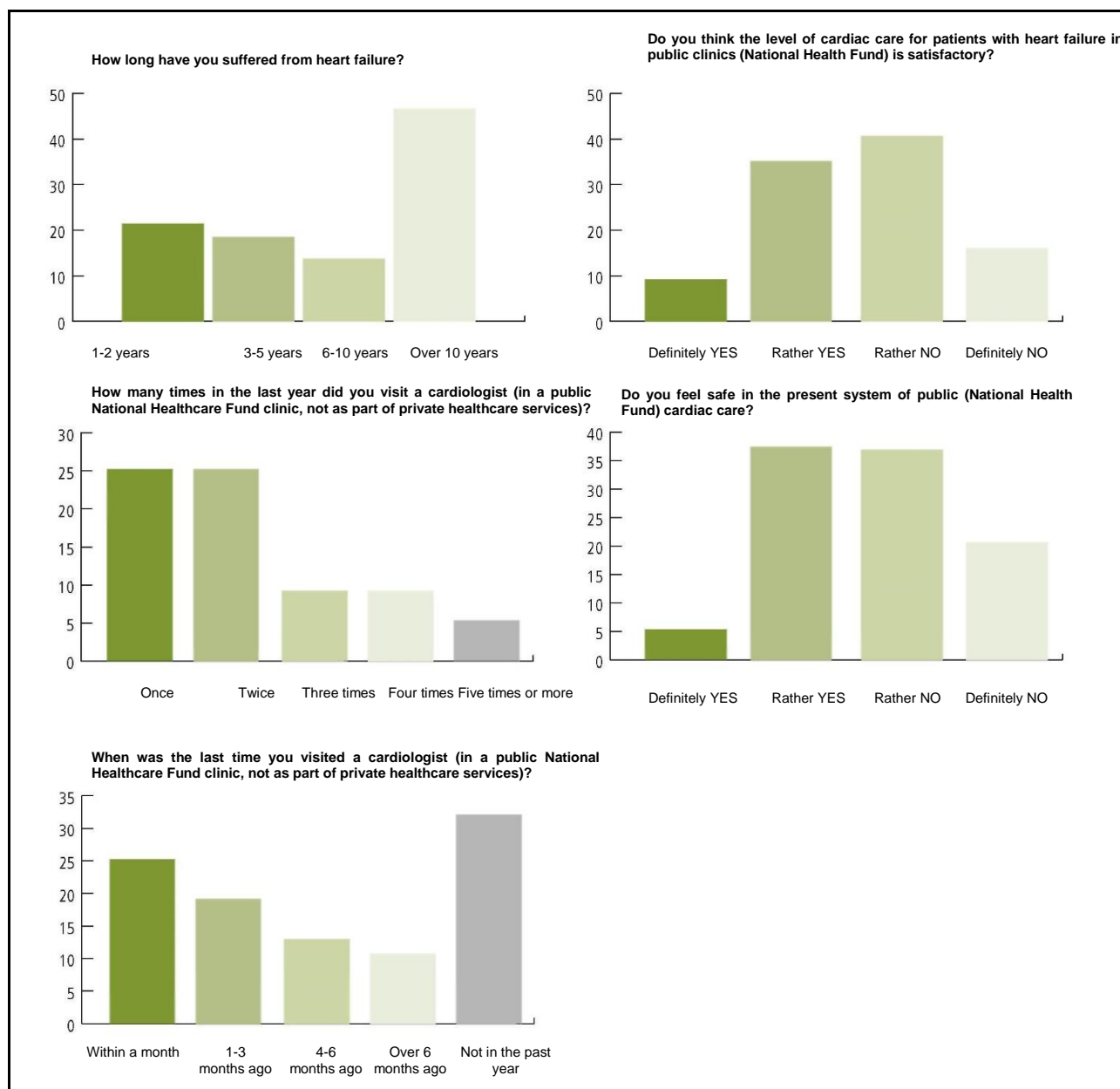


Figure 2. Percentage of different answers to survey questions

Rycina 2. Udział procentowy różnych wariantów odpowiedzi na poszczególne pytania ankietowe

## Discussion

The study revealed that patients with exacerbated HF rarely use publicly financed outpatient cardiac care. Simultaneously, they consider the level of care unsatisfactory. Although it is not directly stated in the answers to the survey questions, we may assume that the

low number of visits to a cardiologist results from the limited availability of this service. It seems to be particularly important in the context of the cause of admission of the study subjects, i.e. exacerbation of heart failure. The ineffectiveness of the chronic outpatient care, with limited access to specialists being a major problem, is considered one of the main reason behind rehospitalisations of patients with HF [9-11].

## ORIGINAL WORKS

**Table 2. Comparison of response by age**  
**Tabela 2. Porównanie odpowiedzi badanych według kategorii wiekowej**

	age <75 years (%)	age >75 old (%)	P
<b>How long have you suffered from heart failure?</b>			
a) 1-2 years	24.6	18.2	s.i.
b) 3-5 years	18.5	18.2	s.i.
c) 6-10 years	9.2	18.2	s.i.
d) Over 10 years	47.7	45.5	s.i.
<b>How many times in the last year did you visit a cardiologist (in a public National Healthcare Fund clinic, not as part of private healthcare services)?</b>			
a) Once	29.2	21.2	s.i.
b) Twice	20.0	30.3	s.i.
c) Three times	4.6	13.6	s.i.
d) Four times	10.8	7.6	s.i.
e) Five or more times	7.7	3.0	s.i.
no answer	35.4	24.3	s.i.
<b>When was the last time you visited a cardiologist (in a public National Healthcare Fund clinic, not as part of private healthcare services)?</b>			
a) Within a month	29.2	21.2	s.i.
b) 1-3 months ago	18.5	19.7	s.i.
c) 4-6 months ago	7.7	18.2	s.i.
d) Over 6 months ago	7.7	13.6	s.i.
e) Not in the past year	36.9	27.3	s.i.
<b>Do you think the level of cardiac care for patients with heart failure in public clinics (National Health Fund) is satisfactory?</b>			
a) Definitely YES	9.2	9.1	s.i.
b) Rather YES	33.8	36.4	s.i.
c) Rather NO	35.4	43.9	s.i.
d) Definitely NO	21.5	10.6	s.i.
<b>Do you feel safe in the present system of public (National Health Fund) cardiac care?</b>			
a) Definitely YES	7.7	3.0	s.i.
b) Rather YES	33.8	40.9	s.i.
c) Rather NO	33.8	39.4	s.i.
d) Definitely NO	24.6	16.7	s.i.

Outpatient specialist care should be a continuation of hospital care [12]. Patients who do not receive the required chronic care are usually suboptimally treated. It has been demonstrated that only 34% of patients discharged from a hospital after an episode of decompensated HF take the

medications according to the instructions provided at the discharge summary [13]. In the current HF registers the lack of compliance is ranked as the second most common cause of exacerbation of chronic HF, and it leads to one in three such hospitalisations [14]. The limited access to qualified personnel is associated not only with suboptimal treatment, but also with a lack of proper education - the key element behind self-care. Michalsen et al. underline the lack of dietary compliance, identified in 41.9% of cases, as the most common cause of rehospitalisation, whereas the lack of adherence to pharmacological instructions was observed in 23.5% of patients [15]. Understanding of the nature of the disease and the ability to control its symptoms on one's own improves the cooperation between the physician and the patient, helps to decrease the number of hospitalisations due to the exacerbation of HF, and contributes to reducing the costs of medical care [9, 10, 16, 17]. Regular contact with qualified personnel, and a suitable level of education increase patients' engagement in the therapeutic process, which additionally enhances the effects of modern drugs [9]. A study by Rywik et al, conducted among primary healthcare physicians, demonstrated that self-care and compliance to current treatment guidelines reduce the frequency of hospitalisations due to HF decompensation [18].

Wierchowicki et al. emphasise that a number of problems of patients with heart failure results from the lack of an integrated healthcare system, including intensive follow up in the post-hospitalisation period, and from the limited access of general practitioners to the necessary diagnostic tests [2]. It is recognised that many hospital admissions could be avoided if an outpatient visit, detailed analysis of the clinical status and modification of the outpatient treatment preceded the occurrence of symptoms of HF exacerbation [19], as the first symptoms of cardiovascular destabilisation may be observed 8-12 days before a decompensation that requires hospitalisation.

Previous scientific reports clearly indicate the benefits associated with an improved quality of outpatient care. Based on the research conducted in the United States in the years 2006-2008, optimal outpatient healthcare was found to improve long-term prognosis, and contribute to a reduced number of hospitalisations due to HF [20]. A study by Jackiewicz et al., assessing the effect of a multidisciplinary outpatient healthcare programme on the prognosis in HF patients, demonstrated that its implementation is associated with a significantly lower number of hospitalisations within 90 days following the hospital discharge [21].

Therefore, the benefits of increased access to specialist care appear to be evident. The situation of patients with HF can be improved by solutions that may be universally implemented despite the limited public resources.

The authors of this study believe that organisational changes should be combined with the introduction of new technologies in outpatient care, particularly telemedicine. Using advanced tools for the assessment of vital parameters in cardiac patients, with the support of remote specialist supervision, may offer a compromise between the needs of patients and the healthcare system's ability to satisfy them.

## Study limitations

The study is limited by the fact that the questionnaire allowed the verification of only the declared, and not the actual degree of using the specialist outpatient healthcare services financed from public resources. In addition, the collected data do not provide evidence for a causative relationship between the outpatient care before a hospital admission, and the occurrence of HF exacerbation; however, the association between these facts may not be random.

## Conclusions

Patients with decompensated heart failure use the public specialist healthcare system less frequently than required. Simultaneously, in most cases they are not satisfied with the system, and do not have the sense of health-related safety.

As an enhanced level of outpatient care has beneficial effect on the prognosis in this group of patients, the functioning of the present system should be improved, e.g. by finding new diagnostic solutions, including telemedicine.

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# Evaluation of the level of knowledge before surgery among patients with lung cancer

Ocena poziomu wiedzy pacjentów z rakiem płuca przed zabiegiem operacyjnym

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**Abstract.** Patient education is an important part of therapy before a surgical procedure. A high level of reliable knowledge has a positive effect during the period of convalescence. The study included 60 patients with lung cancer treated at the Department. The research tool was a questionnaire filled in by respondents themselves. Among the patients, 98% felt adequately informed about the planned surgical procedure. However, it should be noted that the level of knowledge about neoplastic disease is much worse, because 40% of the patients believed that they knew little and 8% claimed they knew nothing about it. 46 patients (77%) indicated an attending physician as the main source of knowledge about cancer. The vast majority (92%) were aware of the dangers of tobacco smoke and identified it as the main cause of lung cancer. About half of the respondents rated their knowledge as unsatisfactory, but the vast majority considered surgery an important stage in their treatment. The quality of patients' knowledge should be verified and expanded, as it positively influences the peritherapeutic process. The family should also be encouraged to support the patient, because it is an important psychological element.

**Key words:** lung cancer, patients knowledge

**Streszczenie.** Edukacja pacjenta stanowi ważny element terapeutyczny przed zabiegiem operacyjnym. Wysoki poziom rzetelnej wiedzy ma pozytywny wpływ w okresie rekonwalescencji. Badaniem objęto 60 chorych z rakiem płuca hospitalizowanych w klinice. Narzędziem badawczym była ankieta wypełniana samodzielnie przez badanych. 98% przebadanych czuło się należycie poinformowanych o planowanym zabiegu operacyjnym. Należy jednak podkreślić, że stan wiedzy o samej chorobie nowotworowej był znacznie gorszy, gdyż aż 40% chorych uważało, że wie na jej temat niewiele, a 8% twierdziło, że nie wie o niej nic. 46 chorych (77%) wskazało lekarza prowadzącego jako główne źródło wiedzy na temat choroby nowotworowej. Znaczna większość (92%) była świadoma szkodliwości dymu tytoniowego i wskazała go jako główną przyczynę zachorowania na raka płuca. Wykazano, że około połowa badanych uznaje swój stan wiedzy za niezadowalający, jednak zdecydowana większość uważa leczenie chirurgiczne za ważny etap terapii. Należy weryfikować jakość wiedzy chorych i poszerzać ją, gdyż ma to pozytywny wpływ na proces okołoterapeutyczny. Warto również zachęcać rodzinę do wsparcia chorego, ponieważ stanowi to ważny element psychologiczny.

**Słowa kluczowe:** rak płuca, wiedza pacjentów

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## Introduction

Lung cancer is the second most common neoplasm, and it contributes significantly to the mortality rates in Poland. In 2013, 21,556 people were diagnosed with malignant pulmonary neoplasms (14,631 men and 6,925 women). The risk of developing lung cancer is approximately 3 times higher in men than

in women. The majority of affected patients are over 50 years old, and approximately half of them are over 65 years old. The therapeutic process, usually complex and comprising numerous stages, may be exhausting for the patient, both physically and mentally. Therefore, a good psychological status should be maintained, and patients should be provided with reliable knowledge [1]. Patient

education is an important element of therapy before a surgical procedure. A high level of understanding has a beneficial effect on the convalescence, and positively affects the psychological status of an oncological patient, as well as eliminates the modifiable risk factors for complications [2-4].

## Material and methods

The study involved 60 patients diagnosed with a lung neoplasm, treated in the Department of Thoracic, General and Oncological Surgery of the Military Medical University Clinical Hospital. Its aim was to assess the understanding and awareness of these patients prior to resection of the lung neoplasm, and to determine the methods of gaining this knowledge. The study material consisted of an original questionnaire, comprising 30 questions with a choice of several answers available (closed questions). The study subjects completed the questionnaire independently before the surgical procedure.

The study group consisted of 31 males (51%) and 29 females (49%). The vast majority of subjects (92% - 55 patients) were over 50 years old, which correlated with the statistical data regarding the incidence of lung neoplasms in Poland collected by the Polish National Cancer Registry [1]. Most patients involved in the study had vocational education (49%) or secondary education (18%). Only 8 (13%) patients had a positive family history of the disease, which suggests that external factors were dominant.

## Conclusions

The vast majority of subjects (98% - 59 patients) felt that they were properly informed and their questions were answered to their satisfaction. Only one person considered the information insufficient. Most patients deemed their understanding of neoplastic disease of the lungs as moderate. The study revealed the presence of two, comparable groups of patients with extensive (39%) or limited (40%) knowledge. A total of 13% of the subjects believed they had extensive understanding of pulmonary neoplasms, whereas 8% declared that they knew nothing or almost nothing about them (Fig. 1, Tab. 1). To verify objectively how much the subjects know, the questionnaire contained questions about several facts related to pulmonary neoplasm (the most common causes, and methods of treatment [Fig. 2-4, Tab. 2-4]).

**Table 1. Subjective assessment of patients' knowledge of the disease**

**Tabela 1. Subiektywna ocena stanu wiedzy pacjentów na temat choroby**

How do you assess your understanding of the disease	Number	Percentage (%)
I know a lot about it	8	13
I know quite a lot about it	23	38
I know little about it	24	40
I know nothing or almost nothing about it	5	8
Total	60	



**Figure 1. Assessment of patients' knowledge about lung cancer**  
**Rycina 1. Ocena wiedzy chorych na temat choroby nowotworowej płuc**

In most cases the patients offered correct answers to the questions.

The greatest number of subjects (92%) indicated their attending physician as the principal source of information about the course and treatment of neoplastic disease. Despite the common access to the Internet, only 3% of subjects derived information from "Dr Google". It demonstrates that patients trust physicians, especially attending ones, and consider them as reliable sources of information (Fig. 5, Tab. 5). 92% of patients were aware that smoking tobacco is the principal cause of lung neoplasms, 88% realised that the disease poses a serious danger for health and is life-threatening. However, 42% of subjects did not quit smoking, and declared active nicotine use at the time of the survey.

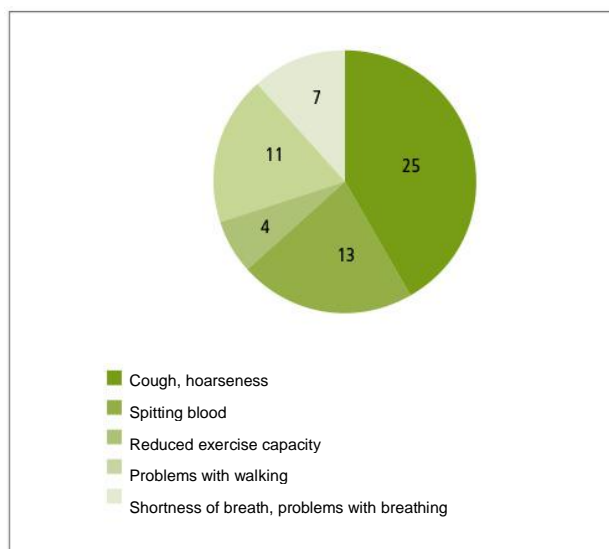
Unexpectedly, the study revealed that despite dealing with a pulmonary neoplasm, patients assess their level of knowledge as good (37%), or very good (18%) (Fig. 6, Tab. 6).

## ORIGINAL WORKS

**Table 2. The most common signs of cancer indicated by patients**

**Tabela 2. Najczęstsze objawy choroby nowotworowej wskazywane przez pacjentów**

What are the symptoms of lung cancer in your opinion?	Number	Percentage (%)
Cough, hoarseness	25	42
Spitting blood	13	22
Reduced exercise capacity	4	7
Problems with walking	0	0
Shortness of breath, problems with breathing	11	18
Memory disorders	0	0
Chest pains	7	12
Total	60	



**Figure 2. What are the symptoms of lung cancer in your opinion?**  
**Rycina 2. Jakie według Pana/Pani są objawy raka płuca?**

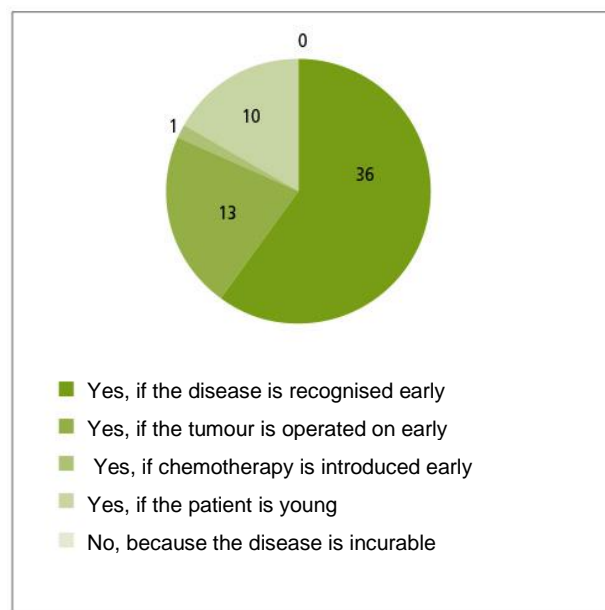
Regardless of specialisation, hospital acclaim or scientific titles, patient support is a very important element of the entire therapeutic process. Over 70% of subjects received support, but there was a large (30%) group of patients who were coping with the disease alone.

The most important element for patients was "family support", while conversation with a physician or psychologist was ranked second and third (Fig. 7, Tab. 7). There was a large group of subjects (77%) who wanted to talk about the disease and receive the help of a psychologist.

**Table 3. Assessment of patients' knowledge on the treatment of lung cancer**

**Tabela 3. Ocena wiedzy pacjentów na temat leczenia choroby nowotworowej płuc**

Is it possible to cure a lung neoplasm?	Number	Percentage (%)
Yes, if the disease is recognised early	36	60
Yes, if the tumour is operated on early	13	22
Yes, if chemotherapy is introduced early	1	2
Yes, if the patient is young	10	17
No, because the disease is incurable	0	0
Total	60	



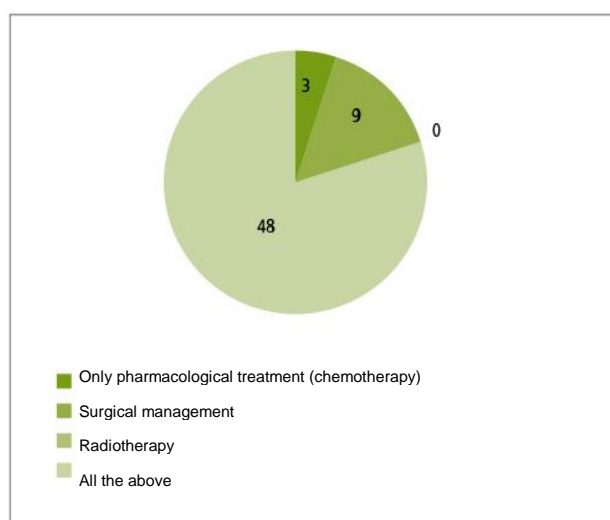
**Figure 3. Is there a possibility of curing neoplastic lung disease?**  
**Rycina 3. Czy jest możliwe wyleczenie choroby nowotworowej płuc?**

## Discussion

According to the authors of this study, the patients' knowledge should be constantly verified and expanded, especially in the time of broad access to the Internet, offering a lot of unverified information, advice and unconventional treatment methods. Establishing a Ministry of Health unit dealing with the "certification" of websites might be worth considering. Providing access to reliable medical portals should be a "gold standard" in improving patients' quality of health and life [5, 6].

**Table 4. Assessment of patients' knowledge about the methods of treatment of lung cancer**  
**Tabela 4. Ocena wiedzy pacjentów na temat metod leczenia choroby nowotworowej płuc**

What are the main methods of treatment in lung neoplasms?	Number	Percentage (%)
Only pharmacological treatment (chemotherapy)	3	5
Surgical management	9	15
Radiotherapy	0	0
All the above	48	80
Total	60	



**Figure 4.** What is the main method of treatment in neoplastic lung disease?

**Rycina 4.** W leczeniu nowotworów płuc stosuje się głównie?

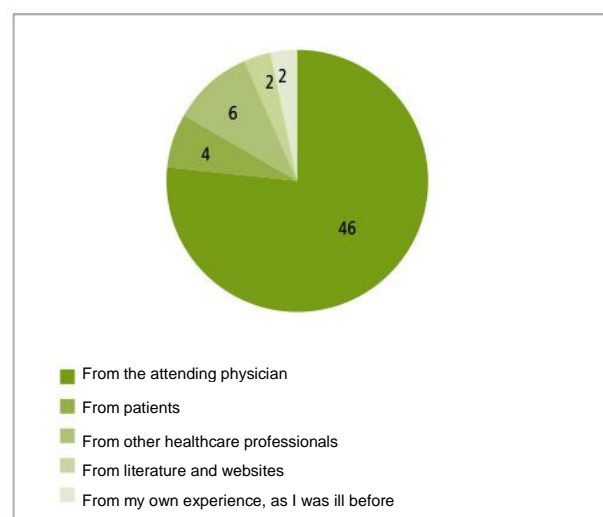
People viewing a "certified" website, marked with a special logo, would know that the information is reliable and in compliance with evidence based medicine. Moreover, the patients could be certain that the page was not created for commercial purposes by advertisers, as well as being free of phishing or malware content [7].

Access to verified information can strengthen the patient's position and enforce the constant professional training of doctors in order to provide them with strong arguments to verify opinions or erroneous interpretations of the facts presented by patients, resulting from a lack of medical education and experience [5, 7].

Some subjects considered their understanding of the disease unsatisfactory (moderate), so it is necessary to organise prophylactic projects and screening tests in high-risk groups.

**Table 5. Sources of information about the disease**  
**Tabela 5. Źródła czerpania informacji na temat choroby**

Where did you find most information about your disease?	Number	Percentage (%)
From the attending physician	46	77
From patients	4	7
From other healthcare professionals	6	10
From literature and websites	2	3
From my own experience, as I was ill before	2	3
Total	60	



**Figure 5.** From what kind of sources have you obtained the most information about your disease?

**Rycina 5.** Z jakich źródeł uzyskał Pan/Pani najwięcej informacji o swojej chorobie?

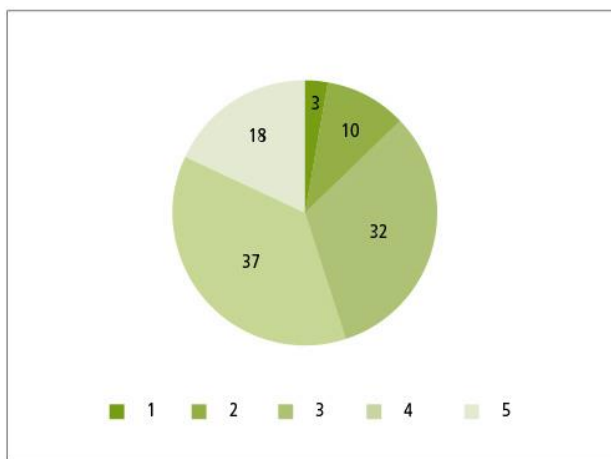
One of the interesting ideas is the distribution of information leaflets, developed and designed for readers without professional medical knowledge, in thoracic surgical / surgical departments. Studies demonstrate that properly developed leaflets better prepare patients for thoracic surgeries. Moreover, they motivate patients to introduce lifestyle changes after the procedure, and to avoid harmful factors, as well as to improve the awareness of the need to care about one's health [2, 8, 9].

Studies reveal that drastic illustrations of anatomical preparations and pictograms with warnings placed on cigarette packages effectively increase the need to skip a cigarette, as well as to give up smoking in general [10].

**Table 6. Subjective assessment of patient's health using a numerical scale**

**Tabela 6. Subiektywna ocena stanu zdrowia pacjenta z zastosowaniem skali liczbowej**

How do you assess your health meaning status, with 1 meaning "very bad", and 5 "very good"?	Number	Percentage (%)
1	2	3
2	6	10
3	19	32
4	22	37
5	11	18
Total	60	



**Figure 6.** Subjective assessment of patient's health using a numerical scale

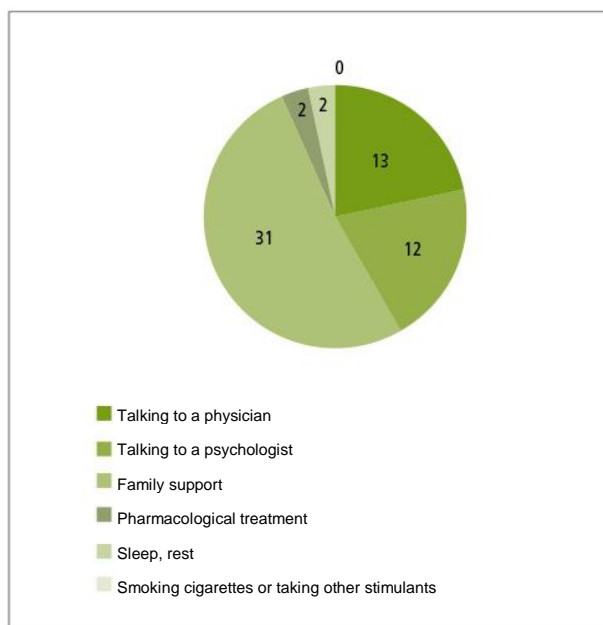
**Rycina 6.** Subiektywna ocena stanu zdrowia pacjenta z zastosowaniem skali liczbowej

Numerous publications indicate that, compared to other types of neoplasms, the needs of patients with a lung neoplasm are particularly often ignored. Constant progress in diagnostics and treatment gives rise to potentially avoidable and complex needs, especially psychological (anxiety, depression, fear of disease recurrence, and death), as well as physical. According to the authors of this article, patients should have broad access to psychological care. Unfortunately, in the Polish reality, this is a rare privilege. Engaging a psychologist in the therapeutic process would enable faster acceptance of the neoplastic disease by patients. It would also allow doctors to transfer the emotional care of the patient to someone experienced and properly prepared, especially regarding work with oncological patients.

**Table 7. What helps patients in an emotional disease-related crisis?**

**Tabela 7. Co pomaga pacjentom w stanie kryzysu emocjonalnego związanego z chorobą?**

What helps patients in an emotional disease-related crisis?	Number	Percentage (%)
Talking to a physician	13	22
Talking to a psychologist	12	20
Family support	31	52
Pharmacological treatment	2	3
Sleep, rest	2	3
Smoking cigarettes or taking other stimulants	0	0
Total	60	



**Figure 7.** What helps patients in an emotional disease-related crisis?

**Rycina 7.** Co pomaga pacjentom w stanie kryzysu emocjonalnego związanego z chorobą?

This, in turn, could give physicians more time for strictly medical tasks associated with the preparation for the surgery and with pharmacotherapy. A study by ME Giuliani revealed that the most frequently unsatisfied need of patients with lung neoplasms was the ability to discuss their health with a hospital employee / healthcare professional. If psychological consultation is not available, the families of the patients should be constantly encouraged (by a physician/personnel) to support and care for their relatives [2, 3].

The level and quality of the patients' understanding of diseases are presently generally unsatisfactory, especially among those with lower education and among the elderly. The following aspects affect the quality of knowledge:

constant medical care, access to education and lifestyle [13].

Patients with a pulmonary neoplasm, qualified for a surgical procedure, must face numerous psychological problems. These result from the significant load associated with the need to adapt to the new situation, which requires a full mobilisation in many aspects of life. A neoplastic disease is a complex process, involving not only the somatic sphere, but also the mental, social and spiritual dimensions, so it is highly individualised [14]. Patients admitted to the surgical department are at different stages of the perception of their disease process. This may apply to their understanding of the disease itself, for example, or the planned diagnostic or therapeutic procedures, expected outcomes etc.

Obtaining information about a disease results in the individualised formation of its image, based on a number of factors, including: attitude to the disease, previous experience with illness – one's own, or that of close ones, the perception of pro-health behaviour formed by the social environment, the ability to adapt to the role of a patient, the functioning style in problematic situations, competence regarding reception of information, determined by the social status and level of education, history of comorbidities, as well as the ability to receive, process and acquire medical information (functioning in the cognitive and emotional sphere).

Certainly the situation is the most difficult for those patients who were never hospitalised or did not have contact with healthcare as first-line patients. For them, functioning in the peri-operative period may be a traumatic episode, where emotional imbalance combined with a lack of previous experience in being ill may result in difficulties with adapting to the new situation and in increased anxiety. The level of understanding in this group of patients may be considerably lower than in those hospitalised previously. When surgical treatment of a neoplasm is necessary, the patient's ability to receive and process medical information may be limited, due to the emotional crisis associated with the disease. Sometimes patients acquire information selectively, as they are concentrated on the fear related to the threat to health and life, or on other factors, such as complicated family situation, obligations or impaired functioning in everyday life, resulting from the surgery and hospitalisation. The attitude to a disease is determined by the level of understanding, as well as by the means of obtaining information about it. Patients who perceive the disease as:

- an opportunity to overcome obstacles will be willing to find medical information about procedures and outcomes of treatment, as well as the course of convalescence;
- a punishment or insurmountable obstacle will avoid information due to excessive focus on their feelings, or relatively higher degree of fear and lack of belief in the effectiveness of the therapy;
- a relief and a method to receive more engagement and interest from the people around them will demonstrate a superficial engagement, and information about the disease will not be important for

them in the therapeutic process,

- an opportunity to omit and avoid obstacles will not seek reliable information but transfer the responsibility for their health and treatment onto the medical personnel, presenting a passive model of coping with illness [15].

The quality of knowledge about the disease certainly affects the relationships with the personnel in the peri-operative period, as well as the ability to adapt to the role of a patient at the surgical ward. Patients for whom the disease and surgery are new may obtain information from the personnel and other people who had a similar procedure [16].

Previous experience with the disease (continuation of treatment, previous surgical procedures, taking care of people with a similar condition) may also affect the quality of information about the disease and functioning in the role of a patient. Another factor affecting the quality of information about the disease is the perception of health and illness in the context of pro-health behaviour. It is formed in the process of socialisation and upbringing, results from beliefs, values, attitudes and acceptance for the presented reactions from the environment in which the patient functions. In the context of pro-health behaviour, important factors include dealing with emotional stress, perception of one's health and appearance, and understanding of desirable actions. Patients with lung cancer are often addicted to nicotine, which frequently triggers the development of the disease, and determines the method of dealing with the crisis situation [17]. They may present the style of dealing with difficulties based on avoiding information; therefore, their main goal may be not adapting to the role of a patient, but looking for substitute activities reducing the emotional tension, as well as using defence mechanisms, which impedes a realistic assessment of their situation. Their understanding of the disease may be incomplete, they may also avoid discussing with their doctor those subjects related to procedures. Another important factor is the style of functioning in problematic situations, corresponding to personality traits. Patients who attempt to control their environment will concentrate on finding information about procedures and on the doctor's instructions, duties and benefits of a patient. Patients who avoid connections in social encounters will rarely build relationships, which may complicate the assessment of the level of their understanding of the disease, as well as their competence to receive knowledge [18]. The ability to receive information may determine its quality, which is particularly visible in patients with dementia syndromes. Deterioration of the cognitive function adversely affects the understanding of a disease, as the messages provided by the personnel before the surgery may be unclear or quickly forgotten by the patient. Due to concentration disorders patients may remember information only partially, or find it difficult to concentrate on important facts. The inability to perform an assessment and the lack of the patient's competence to receive information may increase anxiety reactions or isolation.

It appears that the patients' understanding of the disease and its treatment may be very important in reaching the

therapeutic goals, both during preparation for the surgery, and in the period of convalescence and further treatment. The study results indicate the need for increased patient education in the area of lung diseases, as well as the ability to deal with the difficulties associated with the new crisis situation [19].

## Conclusions

It was demonstrated that approximately half of the subjects assess their knowledge as insufficient, while the majority of them consider surgical treatment an important stage in the therapy. The quality of the patients' knowledge should be verified, and their understanding of the disease should be extended, as it demonstrates positive effects on their emotional status in the therapeutic window period. Families should also be encouraged to support patients, as an important psychological factor.

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# Increased vagal tone in soldiers with above average physical fitness serving in the special forces

Cechy hiperwagotonii wśród żołnierzy o ponadprzeciętnej wydolności fizycznej służących w jednostkach specjalnych

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**Abstract.** Intense physical activity changes the sympathovagal balance and influences the cardiovascular function by increasing vagal tone. The aim of the study was to investigate which changes in rhythm and sympathovagal balance can be observed in soldiers serving in the special forces (SF) in comparison with those serving in regular units (RU). A total of 194 soldiers (124 SF and 70 RU) received an electrocardiographic assessment based on 24-h Holter recordings, with physical capacity objectified by ergospirometry. The SF group was characterized by lower 24-hour mean HR ( $63 \pm 8$  bpm vs  $68 \pm 8$  bpm,  $p < 0.0005$ ), minimal HR ( $45 \pm 5$  bpm vs  $42 \pm 8$  bpm,  $p < 0.0005$ ) and maximal HR ( $111 \pm 19$  bpm vs  $119 \pm 17$  bpm). They also more frequently presented features of increased vagal tone: bradycardia  $< 50$  bpm (98% vs 83%) and pauses exceeding 2 sec (22% vs 9%,  $p = 0.018$ ). Soldiers serving in the special forces present above average physical fitness. As a consequence the rhythm and conjunction changes typical for heart phenomena typical for an athlete could be observed in this population. In some cases it may be advisable to perform exercise test and/or 24-hour electrocardiographic monitoring to exclude abnormalities other than those related to increased vagal tone.

**Key words:** bradycardia, cardiovascular system, physical fitness, soldiers, vagal tone

**Streszczenie.** Intensywny wysiłek fizyczny zmienia równowagę współczulno-przywspółczulną oraz wpływa na funkcjonowanie układu sercowo-naczyniowego poprzez zwiększenie aktywności wagalnej. Celem było zbadanie, które zaburzenia rytmu serca i równowagi współczulno-przywspółczulnej można zaobserwować wśród żołnierzy jednostek specjalnych (grupa SF) w porównaniu z żołnierzami zwykłych jednostek (grupa RU). W grupie 194 żołnierzy (124 SF i 70 RU) przeprowadzono 24-godzinne monitorowanie elektrokardiogramu metodą Holtera oraz ergospirometrię. Grupa SF charakteryzowała się mniejszą 24-godzinną średnią HR ( $63 \pm 8$  bpm vs  $68 \pm 8$  bpm,  $p < 0,0005$ ), minimalną HR ( $45 \pm 5$  bpm vs  $42 \pm 8$  bpm,  $p < 0,0005$ ) i maksymalną HR ( $111 \pm 19$  bpm vs  $119 \pm 17$  bpm). Częściej prezentowali cechy zwiększonego napięcia nerwu błędnego: bradykardię  $< 50$  bpm (98% vs 83%) i pauzy dłuższe niż 2 s (22% vs 9%,  $p = 0,018$ ). Żołnierze SF prezentują ponadprzeciętną wydolność fizyczną. W tej grupie można zaobserwować zmiany rytmu i przewodzenia typowe dla serca sportowca. W niektórych przypadkach należy rozważyć przeprowadzenie testu wysiłkowego i/lub 24-godzinnego monitorowania metodą Holtera w celu wykluczenia nieprawidłowości niezwiązanych z hiperwagotonią.

**Słowa kluczowe:** bradykardia, układ sercowo-naczyniowy, wydolność fizyczna, żołnierze, wagotonia

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## Introduction

High-intensity training is often related to morphological changes in the heart and its function, commonly referred to as an athlete's heart. Depending on the type of physical training, especially endurance or strength exercise, two kinds of structural remodelling of the heart have been suggested: eccentric and concentric left ventricular

hypertrophy [1, 2]. This classification, however, is not an absolute, but rather a relative concept since there are no pure pressure or pure volume load exercises [1].

Regular intense physical activity changes not only the structure of the heart but also influences its function by altering the sympatho-vagal balance of the autonomic nervous system [3]. The more intense

and long lasting the exercise, the greater is the dominance of parasympathetic or vagal tone, which leads to specific rhythm disturbances. These include: sinus bradycardia, sinus arrhythmia (mostly related to respiration), sinus pauses and wandering atrial pacemaker. Typical conjunction disturbances are first degree atrio-ventricular block, Mobitz type I second degree atrio-ventricular block, and atrioventricular dissociation [3-6]. These disturbances seem to be benign and disappear during exercise or even while changing position from supine to sitting or standing. Most studies on rhythm and conjunction disturbances in athletes are based on changes registered in 12-lead electrocardiograms [7-9].

### Aims

The aim of the present study was to investigate which changes in rhythm and the sympatho-vagal balance can be observed in soldiers serving under high psychosomatic stress in comparison to soldiers serving in regular units. We hypothesized that those soldiers with above-average training may present similar cardiovascular pheno-type as athletes. Therefore, some electrocardiographic features should not be interpreted as abnormalities but as a reflection of increased vagal tone. We based our assessment on 24-h Holter electrocardiographic recording in two groups of soldiers: those serving in the special forces and those in regular military units. Their physical capacity was objectified by ergospirometry.

### Materials and methods

The SF group comprised 124 young to middle-aged males (25-45 years old) serving for at least 12 months in the special forces, who were exposed to specific psychophysical burdens associated with the nature of military service, i.e. operations related to regular military conflicts, at altitudes >2000 m above sea level, in very dry or humid climates. The nature of their duties demanded regular and long-term training. It was assumed that they were individuals of above average physical fitness. The RU groups consisted of 70 healthy, young to middle-aged males (25-45 years old), of average physical fitness, serving in regular units.

All participants were volunteers and signed written informed consents. Exclusion criteria comprised: (1) known cardiovascular disease before enrolment (such as coronary artery disease, heart failure, hypertension of the second degree, significant arrhythmias); (2) symptoms suggestive of these illnesses; (3) known skeleto-muscular issues; (4) pulmonary diseases; and (5) disabilities

that did not allow the following of the study protocol. The study protocol was approved by the local ethics committee of the Military Institute of Medicine.

### Diagnostics

The study protocol comprised 2 days of testing, during which each participant underwent a physical examination with special attention focused on the risk factors for cardiovascular diseases. Office systolic and diastolic blood pressure (SBP and DBP) were measured in a sitting position after 5 minutes of rest, by a qualified nurse. The cut-off value for hypertension was >140/90mmHg according to the European Society of Cardiology Guidelines [10].

The 24-hour Holter electrocardiographic monitoring was conducted with the use of three-channel recorders. Recordings were started at about 10:00 hours ( $\pm 2$  hours) on the first day and finished at about 10:00 hours ( $\pm 2$  hours) on the next day. The subjects were directed to go to bed around 10 pm and rise around 6 am. They were advised to maintain a normal daily routine, excluding strenuous physical exercise and the consumption of alcoholic beverages. All recordings were analysed with the use of a commercial analyser. The final analysis focused on mean, minimal and maximal heart rate (HR), presence of bradycardia <50 beats/min and <40 beats/min, pauses >2 sec, supraventricular and ventricular extrasystoles, and conjunction disturbances such as atrio-ventricular blocks or sinus block. Increased vagal tone was defined as the presence of at least one of the following: bradycardia <40 beats/min, pauses >2 sec, atrio-ventricular blocks or sinus block. Due to the poor quality of the 24-hour Holter monitoring records from 4 subjects, they were excluded from the final analysis (3 in the SF group and 1 in the RU group).

In order to objectively assess the physical fitness of the participants, an ergospirometry (cardio-pulmonary exercise test - CPET) was conducted with a ramp protocol with the use of the ZAN 680 system (ZAN Messgerate GmbH; Germany). The following parameters were taken into consideration as characterizing the subject's physical fitness: percentage of predicted load (% pred. load) and percentage of predicted peak oxygen uptake (% pred. peak  $VO_2$ ).

### Statistical analysis

The statistical analysis was performed using Statistica 10.0 software (StatSoft Inc., Tulsa, USA). The distribution and normality of data were assessed by visual inspection and the Kolmogorov-Smirnov test. Continuous variables were presented

as means  $\pm$ standard deviations (SD), and categorical variables as absolute and relative frequencies (percentages). The analysis of the differences between absolute values of the variables was performed with the use of the t-test for normally distributed data and the Mann-Whitney U-test for non-normally distributed data. The assessment of the relation between variables was performed based on Pearson and Spearman correlation coefficients.

## Results

### General characteristics

The general characteristics of the study and control groups are presented in table 1. The SF group was older than the RU group and had a higher body mass index. The SF group also presented lower HR and lower SBP. There was no statistical difference in DBP, although there was a trend toward lower values in the SF group.

### Physical fitness

Results of ergospirometry revealed that the SF group, as anticipated, was characterized with a higher % pred. peak load (SF versus RU: 115% versus 89%,  $p < 0.0005$ ) and a higher % pred. peak  $VO_2$  (116% versus 106%,  $p = 0.002$ ).

### 24-hour Holter electrocardiographic monitoring

The SF group was characterized by a lower mean 24-hour HR (SF versus RU:  $63 \pm 8$  bpm versus  $68 \pm 8$  bpm,  $p < 0.0005$ ), minimal 24-hour HR ( $45 \pm 5$  bpm versus  $42 \pm 8$  bpm,  $p < 0.0005$ ) and maximal 24-hour HR ( $111 \pm 19$  bpm versus  $119 \pm 17$  bpm,  $p < 0.0005$ ). Bradycardia  $< 50$  bpm and increased vagal tone were also more common in the SF group (SF versus RU: 98% versus 83%,  $p < 0.0005$  and 97% versus 23%,  $p = 0.001$ ; respectively). Pauses exceeding 2 seconds were recorded in 22% of subjects in the SF group, whereas only in 9% in the RU group ( $p = 0.018$ ). There was no statistical difference in the prevalence of atrio-ventricular blocks or sinus blocks (Table 2).

## Discussion

The presence of the athlete's heart phenomenon, with its structural and functional changes to the cardiovascular and autonomic nervous systems, forced international medical societies dealing with sports medicine to create separate criteria for the electrocardiogram assessment of athletes [8-9].

**Table 1. General characteristics of the SF group and the RU group**

**Tabela 1. Ogólna charakterystyka grupy badanej i grupy kontrolnej**

	SF group (n=124)	RU group (n=70)	P
Age (years), mean $\pm$ SD	37 $\pm$ 4	26 $\pm$ 4	<0.0005
HR (bpm), mean $\pm$ SD	60 $\pm$ 9	72 $\pm$ 15	<0.0005
SBP (mm Hg), mean $\pm$ SD	120 $\pm$ 10	131 $\pm$ 12	<0.0005
DBP (mm Hg), mean $\pm$ SD	75 $\pm$ 7	77 $\pm$ 7	0.057
Body weight (kg), mean $\pm$ SD	83 $\pm$ 8	78 $\pm$ 10	0.0001
Height (cm), mean $\pm$ SD	179 $\pm$ 6	178 $\pm$ 6	0.42
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	26.1 $\pm$ 1.9	24.2 $\pm$ 2.5	0.001
Current smokers, n (%)	4 (3%)	36 (51%)	<0.0005
Smokers in the past, n (%)	25 (20%)	6 (9%)	0.03

BMI - body mass index, HR - heart rate, SBP - office systolic blood pressure, DBP - office diastolic blood pressure

**Table 2. Results of 24-hour Holter recordings**

**Tabela 2. Wyniki 24-godzinnego monitorowania metodą Holtera**

	SF group (n=121)	RU group (n=69)	P
Mean heart rate (bpm), mean $\pm$ SD	63 $\pm$ 8	68 $\pm$ 8	<0.0005
Minimal heart rate (bpm), mean $\pm$ SD	45 $\pm$ 5	42 $\pm$ 8	<0.0005
Maximal heart rate (bpm), mean $\pm$ SD	111 $\pm$ 19	119 $\pm$ 17	<0.0005
Bradycardia $< 50$ bpm/min, n (%)	118 (98%)	57 (83%)	0.007
Bradycardia $< 40$ bpm/min, n (%)	71 (59%)	34 (49%)	0.234
First degree atrioventricular block, n (%)	1 (0.8%)	2 (3%)	0.267
Second degree atrioventricular block Mobitz I type, n (%)	9 (7%)	4 (6%)	0.677
Second degree atrioventricular block Mobitz II type, n (%)	2 (1.7%)	0 (0%)	0.285
Advanced atrio-ventricular block, n (%)	2 (1.7%)	0 (0%)	0.285
Pauses $> 2$ sec, n (%)	27 (22%)	6 (9%)	0.018
Increased vagal tone, n (%)	117 (97%)	57 (23%)	<0.0005

These criteria have been used in the cardiovascular screening of athletes before competitions in order to catch those who are at risk of serious cardiac diseases or sudden cardiac death, without causing unnecessary disqualifications. In the present study we showed that similar rhythm and conjunction disturbances, probably as a result of increased vagal tone, could be observed in the 24-hour Holter electrocardiographic recording in soldiers who underwent heavy physical training as a regular part of their service. The results of the ergospirometry showed that these soldiers had above average exercise capacity, expressed by high peak load and peak  $\text{VO}_2$ , which suggested the benign character of these features.

The physical examination revealed typical findings connected with higher levels of physical fitness: the lower HR and lower BR 24-hour Holter recordings showed that the SF group had lower mean, minimal and maximal HR, more often presented bradycardia <50 bpm, pauses exceeding 2 seconds and increased vagal tone. We did not find any difference in the prevalence of conjunction disturbances, though first and second degree Mobitz type I atrio-ventricular blocks were observed in both groups. Similarly to our study, Vitasalo et al. compared 24-hour Holter recordings of 35-highly trained athletes with 35 matched controls, in which they showed that athletes had lower mean and minimal heart rates, more often presented bradycardia and pauses exceeding 2 seconds [11]. However, they also observed a higher prevalence of first and second degree atrio-ventricular blocks in athletes, which was not noted in our SF group. This may be due to the fact that these soldiers do not undergo a typical athletic competition regimen but instead perform individual training without following a strict protocol. On the other hand, among the RU group were individuals with high levels of fitness. The difference in age (older SF subjects) also mattered.

The possibility of the presence of electrocardiographic indicators of increased vagal tone in soldiers with above-average training should be considered during periodic examinations. Most of them are just a sign of good fitness and should not be interpreted as a pathology. Carefully completed anamnesis itself may reveal the cause of the electrocardiographic increased vagal tone. In some cases further diagnostics may be helpful to exclude clinically relevant pathologies: ergospirometry provides an objective assessment of exercise capacity, while the 24-hour Holter monitoring helps to identify advanced conjunction disturbances. Special attention should be attached to subjects presenting symptoms (i.e. syncope, dizziness) and/or an inadequate chronotropic response to exercise [12].

## Limitations

The main limitation of our study was the small number of participants in each group. Moreover, the average age in the SF group was higher than in the RU group, because only the most experienced and the best soldiers are qualified to serve in special units, contrary to the regular units, where the soldiers are at the first step of their career. This may underestimate the differences. Another limitation was that the soldiers do not undergo a typical controlled athletic training regimen but train individually, without following a strict training protocol. Even though the changes in rhythm and conjunction in the study group seem to be typical for increased vagal tone, further research into the electrocardiographic and echocardiographic changes is needed in order to fully assess the presence of the athlete's heart phenomenon in the special forces.

## Conclusion

The soldiers serving in the special forces have above average physical fitness. As a consequence, rhythm and conjunction changes typical for an athlete's heart phenomenon can be observed in this population. In some cases it may be advisable to perform an exercise test and/or 24-hour electrocardiographic monitoring to exclude abnormalities other than those related to increased vagal tone.

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# The purpose of life for chronically ill people

## Poczucie sensu własnego życia pacjentów przewlekle chorych

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**Abstract.** The spiritual dimension constitutes the fourth dimension of human existence, supplementing the other three: the physical, the psychological and the social. It can both be conducive to health by the giving or rather continuous discovering of the purpose to life, suffering or dying, and it can have a negative impact through idle devotion to a Supreme Being, involving passive waiting for an intervention or religious interpretation of the causes of illness leading to experiencing it in a sense of guilt, injustice or harm. The feeling of meaningfulness is expressed by an individual's motivation to act, while at the same time it is the degree to which a person experiences their existence both in the cognitive and emotional dimensions, reaching the final conclusion that their life makes sense. The present research aims to examine whether and to what extent healthy people feel different from chronically ill people in the intensity of the feeling of purpose in their own life, and whether individual groups of the chronically ill differ in expectations about the future and assessment of their relations with relatives.

**Key words:** chronic diseases, evaluation of own existence, purpose in life, relations with relatives

**Streszczenie.** Wymiar duchowy stanowi czwarty wymiar ludzkiego istnienia, uzupełniając trzy pozostałe: fizyczny, psychiczny i społeczny. Może on zarówno sprzyjać zdrowiu - poprzez nadawanie czy raczej nieustanne odkrywanie sensu życia, cierpienia i umierania, jak i wpływać negatywnie - biernie oddanie się Istocie Najwyższej, wiążące się z becznym oczekiwaniem na interwencję, czy religijne interpretowanie przyczyn choroby prowadzące do przeżywania jej w poczuciu winy, niesprawiedliwości, krzywdy. Poczucie sensowności wyraża się motywacją jednostki do działania, jest to równocześnie stopień, w jakim człowiek przeżywa swoje istnienie zarówno w wymiarze poznawczym, jak i emocjonalnym, dochodząc do ostatecznej konkluzji, że jego życie ma sens. Prezentowane badanie ma na celu sprawdzenie, czy i w jakim stopniu osoby zdrowe różnią się w nasileniu poczucia sensu własnego życia od osób przewlekle chorych oraz czy poszczególne grupy osób przewlekle chorych różnią się oczekiwaniami wobec przyszłości i pod względem oceny swoich relacji z bliskimi.

**Słowa kluczowe:** choroby przewlekle, poczucie sensu życia, ocena własnego istnienia, relacje z bliskimi

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## Introduction

The spiritual dimension has recently been perceived as a type of psychological resource, as a new subject of interest to the humane sciences. However, the dimension itself is not entirely new. Philosophy and theology have explored it for centuries. Logotherapy [1, 2] clearly referred to this dimension. Victor Frankl, the author of the concept, was the first person to attempt to convince doctors and

psychologists to expand their perception of man as a psychophysical and spiritual unity.\*

According to Heszen-Niejodek [3], the essence of spirituality is transcendence, which is going beyond the presently experienced "I". "The direction of transcendence is determined by the values cherished by the person with regard to the immaterial sphere". Transcendence may take place both within a person (self-actualisation, self-improvement, personal development), and outside a

\* According to Heszen-Niejodek the spiritual dimension of man is related not only to Frankl's concept of "noogenic", but also Maslow's self-actualisation, Antonovsky's coherence or Kozielski's transgression. Moreover, she discusses the relationship between spirituality and religious

devotion, adapting a moderate position: next to a shared scope of content, there are also areas individual for either concept (see literature: 3, pp. 35-36)

person (towards a higher being, energy).

It may also be directed towards the well-being of another person, which is then placed above one's own. As with other features and dimensions, spirituality varies between individuals in intensity, quality and content. It is a latent variable, so it may but does not need to present itself. It is a disposition, a potential [3]. Life situations, especially difficult experiences associated with dangerous, chronic diseases, may contribute to a manifestation or development of spirituality.

Spirituality is the fourth dimension of health, complementing the other three: physical, mental and social ones [4, 3]. Although the spiritual dimension shares content with the mental (positive emotions associated with transcendence) and social spheres (the well-being of another person as a superior value), there is no relationship between the physical and spiritual dimension. However, this approach may be controversial. This dichotomy seems to resemble the assumed until recently separation of the "psyche" and the "soma" in the narrow understanding of psychosomatics. A question may be asked: is there no content shared between the condition of the spirit and that of the body? After all, "spirituality is assumed to have a positive, beneficial effect on the somatic health. This may result from: stress management and prevention of its negative influence on the health, the correlation between spirituality and certain emotional states and behaviours, or the formation of certain relationships with the environment" [5, 4].

The spiritual dimension can have a positive effect on the level of health (it offers meaning for suffering or even death, provides specific coping strategies, favours optimism and hope, stimulates pro-health behaviours), but also a negative one: negative coping strategies (passive trust in God, waiting for his direct intervention) or negative emotions triggered by a religious interpretation of the causes of the disease (regret, feeling of guilt, sense of injustice and being hurt).

The sense of meaningfulness expresses one's motivation to act. It is the degree to which an individual believes in the meaning of life from an emotional perspective, and trusts that at least some of the problems and challenges we experience are worth our effort, devotion and engagement. A person with a high sense of meaningfulness perceives problems as challenges worth dealing with [6-8].

## Research questions

1. Does the intensity of the sense of meaning of life differ between healthy individuals and chronically ill patients? If so, then to what degree?
2. Are the expectations towards the future different between individual groups of chronically ill patients? Do they assess their relationships with friends and relatives differently?

## Material and methods

The study involved two groups: healthy subjects and

chronically ill patients. The first group comprised 80 people who: feel healthy, do not take any long-term medicines, are not in therapy due to any conditions, are not invalids and do not require rehabilitation or care. The second group of 182 chronically ill patients comprised: patients with ischaemic disease following one myocardial infarction (N = 41), patients receiving continuous treatment due to primary arterial hypertension (N = 35), patients receiving treatment due to a malignant neoplasm (N = 36), patients with diabetes (N = 33) and patients with bronchial asthma (N = 37).

The duration of the disease varied between one year and several years (M = 10.37; SD = 8.08). 62 patients were ill for 1-5 years, 52 patients were ill for 6-10 years, and 68 patients were ill for 11 years or more. All the patients were under constant medical care due to the consequences of their conditions.

The healthy subjects were slightly younger (M = 48.02, SD = 6.86) than the chronically ill patients (M = 53.03, SD = 7.97). The number of men and women in both groups was similar: among the healthy subjects were 41 women and 39 men, while the group of patients comprised 95 women and 87 men.

The study was conducted in the years 2011-2015, individually at home, or in a hospital ward. Many patients declared a need for contact outside the study; therefore, meetings were often divided into two or three sessions. The time required to fill in the questionnaires was usually less than an hour.

The sense of meaning of life was measured using the Meaning of Life Score, which involves the aspect of "expecting" (assessment of the current situation and the future), the aspect of "relations" (assessment of the meaning of interpersonal relations), and the general index of meaning, created by the above aspects combined.

The score is based on an existential-humanistic approach. It seems important to assess one's sense of the meaning of life in a disease, or rather despite the disease. This aspect appears to extend beyond the psychosocial dimension, and affect the spiritual sphere,

The purpose in the lives of chronically ill people transcended the limitations and encountered difficulties [2, 4, 9, 10].

A similar method, both with regard to the theoretical premises (Frankl's existential analysis) and the construction of PIL (purpose in life test) developed by Crumbaugh and Maholick [11-13]. However, the aim of the presented study was to connect (1) the problem of the sense of meaning and the assessment of subjective satisfaction with one's life with (2) a measurement of potential changes in expectations towards the future and their relationships with the assessment of one's health status, and with (3) examination of the need to use the support of the social environment. Therefore, the development of a new research tool seems justified.

The preliminary study used a questionnaire containing 17 bipolar statements, together with a seven-point assessment scale, which were initially verified empirically. Based on a factor analysis, ten statements that best differentiated the subjects were selected.

1. *I know exactly what I live for – I don't know what I live*

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for

2. *I can rely on other people's help – I don't know if I can rely completely on anyone*
3. *Other people need me a lot – Nobody needs me*
4. *I have someone to live for – I have no-one to live for*
5. *I am liked – I am not liked*
6. *I live the life I want – I can't live the life I want*
7. *I believe I'll live long – I don't think I'll live long*
8. *I think that I'll be healthy in the next few years – I'm afraid I'll have health problems in the next few years*
9. *My life is good – My life isn't good*
10. *The future will be calm – The future will be full of tension*

The aspect of "expectations towards the future" comprises statements about the assessment of one's life at present, and expresses expectations towards the future, especially regarding the health prognosis and length or quality of life. The aspect of "relations with other people" covers the assessment of the awareness of purpose and one's relationships with other people, both in the context of receiving help, and feeling needed.

The results of statistical operations are presented in Tables 1 and 2.

The value of Cronbach's alpha was 0.88, which was satisfactory. The charges of factors for individual statements were in the range of 0.67 and 0.85.

All internal correlations between the items of the Meaning of Life Score were statistically significant (they all reach a level of 0.001).

**Table 1. Correlations of individual statements with separate factors (N = 262)**  
**Tabela 1. Korelacje poszczególnych twierdzeń z wyodrębnionymi czynnikami (N = 262)**

Statements	Expectations	Relations	General index
Awareness of the purpose of one's life	0.49	0.83	0.72
Chances for support from others	0.30	0.69	0.54
Sense of being needed	0.43	0.84	0.69

Sense of closeness	0.43	0.86	0.70
Sense of being accepted	0.46	0.75	0.67
Acceptance of lifestyle	0.76	0.36	0.67
Belief in a long life	0.74	0.44	0.70
Expected improvement in health	0.80	0.38	0.70
Satisfaction with life	0.74	0.43	0.69
Belief in a calm future	0.80	0.44	0.74

All p < 0.000

**Table 2. Charge of factors (Varimax standardized)**  
**Tabela 2. Ładunki czynników (Varimax znormaliz.)**

Statements	Expectations	Relations
Awareness of the purpose of one's life	0.28	0.76
Chances for support from others	0.14	0.67
Sense of being needed	0.21	0.82
Sense of closeness	0.15	0.85
Sense of being accepted	0.33	0.69
Acceptance of lifestyle	0.75	0.27
Belief in a long life	0.68	0.15
Expected improvement in health	0.77	0.11
Satisfaction with life	0.68	0.33
Belief in a calm future	0.76	0.25

The results were entirely satisfactory, and met the requirements for research tools in humane sciences. The general sense of the meaning of life was within 7-70 points. In the "expectations" aspect, the results were within 5-35 points, as in the "relations" aspect. The higher the score, the greater the sense of meaning of one's life.

**Table 3. Scale of the Meaning of Life: average results and their comparison**  
**Tabela 3. Skala Sensu Życia: wyniki średnie i ich porównanie**

Meaning of Life Score	Meaning of expectations		Meaning of relations with others		General index	
	M	SD	M	SD	M	SD
Health	26.77	4.44	30.92	3.82	57.70	7.20
Coronary artery disease	22.41	6.33	28.78	6.92	51.20	11.99
Hypertension	21.27	6.93	29.45	3.88	50.73	9.79
Neoplastic disease	20.32	7.82	29.29	5.45	49.61	11.82
Diabetes	23.57	6.22	29.67	4.25	53.24	9.22
Asthma	21.90	4.88	29.81	4.68	51.72	9.54

## Results and discussion

The mean results and their comparison for all the study groups are presented in Table 1. The higher the score obtained by subjects for each factor, the higher the sense of meaning of one's life. The maximum score in the assessment of expectations towards the future and relationships with people is 35, and for the "general sense" is 70.

Unambiguously high differences in the sense of the meaning of life, especially in the aspect of expectations and the general sense of meaning, are observed between the groups of healthy subjects and ill patients, except for those patients with diabetes (Tab. 3). Table 4 presents the analysis of the results regarding individual items on the Meaning of Life Score. As for the expectations towards the future, the greatest difference is observed between healthy individuals and patients with neoplasms ( $p < 0.000$ ), arterial hypertension ( $p < 0.000$ ) and asthma ( $p = 0.003$ ), as well as patients with ischaemic disease ( $p = 0.004$ ). The differences between various groups of patients are not statistically significant. Patients do not expect a significant improvement in their health status, and do not believe in a happy future or a long and calm life. They do not consider their life as good, as it is not what they want to see or what they expected.

In the assessment of contacts with people healthy individuals and patients differ in their awareness of being needed and the general awareness of the purpose in life. The results are not negative, but they demonstrate a statistically significant difference between patients and healthy individuals.

Based on clinical observations and direct relations with the study subjects, it is worth emphasising that the sense of loneliness increases with time. In the first phase of hospitalisation patients are willing to discuss their relationships with friends and relatives; however, after a few weeks their sense of support from those important to them becomes increasingly insufficient. The awareness that this support is reduced often contributes to a decreased sense of the meaning of life, both regarding the past, and the expectations for the following years.

**Table 4. Statements of the Meaning of Life Scale: average results and their comparison**  
**Tabela 4. Twierdzenia Skali Sensu Życia: wyniki średnie i ich porównanie**

Statements	Healthy volunteers (N=80)		Patients (N=182)		T
	M	SD	M	SD	
Awareness of the purpose of one's life	6.18	1.06	5.78	1.47	2.14
Chances for support from others	5.89	1.28	5.91	1.30	0.10
Sense of being needed	6.40	0.96	5.81	1.33	3.58
Sense of closeness	6.56	0.88	6.34	1.24	1.47
Sense of being accepted	5.90	0.99	5.54	1.20	2.33
Acceptance of lifestyle	5.15	1.51	4.94	1.72	0.96
Belief in a long life	4.89	1.51	4.19	1.72	3.12
Expected improvement in health	5.98	0.86	3.78	1.74	10.68
Satisfaction with life	5.70	1.13	4.74	1.81	4.34
Belief in a calm future	5.06	1.41	4.30	1.87	3.24

## Conclusions

- Certain groups of chronically ill patients differ significantly from healthy individuals in the general index of the sense of meaning of life. The greatest differences are observed in patients with neoplastic diseases ( $p < 0.01$ ). The difference is statistically significant also for patients with arterial hypertension ( $p < 0.05$ ) and coronary disease ( $p < 0.05$ ).
- No significant differences are found between individual groups of chronically ill patients in the sense of meaning of life, both regarding the assessment of expectations, and satisfaction with interpersonal relations.
- The duration of disease, despite a span of several years, does not result in changes in the general sense of meaning of life ( $F = 0.03$ ;  $p = 0.97$ ).

The age ( $F = 0.83$ ;  $p = 0.80$ ) of the studied chronically ill subjects did not affect the sense of meaning of life either.

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# Angioblastoma in the cervical segment of the spinal cord – a case report

Naczyniak płodowy odcinka szyjnego rdzenia kręgowego – opis przypadku

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**Abstract.** Angioblastoma is a rare, slowly growing benign tumour, one which typically develops in the posterior cranial cavity and spinal cord. It is more common in children. Its very slow expansion causes the long-term compensation of neurological deficits. The study presents a description of a 50-year old patient with insidiously aggravating symptoms suggestive of damage to the brachial plexus. As the CT of the cervical segment of the spine was non-contributory and the results of the neurophysiological examinations ambiguous, an MRI of the cervical spine was performed even though the patient had a pacemaker. The examination revealed the presence of a tumour in the cervical segment of the spine. The patient was operated on, while an anatomopathomorphological examination disclosed the presence of angioblastoma. The case shows what a variable array of symptoms intraspinal changes can manifest and how important the role of MRI examination can be in diagnosing patients with a cardiac pacemaker.

**Key words:** angioblastoma, cardiac pacemaker, spinal tumours, von Hippel-Lindau syndrome

**Streszczenie.** Naczyniak płodowy jest rzadkim, wolno rosnącym nowotworem o charakterze łagodnym, lokalizującym się zwykle w tylnej jamie czaszki i rdzeniu kręgowym. Częściej występuje u dzieci. Bardzo powolny rozrost powoduje długotrwałą kompensację deficytów neurologicznych. W pracy przedstawiono opis 50-letniej chorej z podstępnie narastającymi objawami sugerującymi uszkodzenie splotu ramiennego. W związku z niediagnostycznym wynikiem badania TK odcinka szyjnego kręgosłupa oraz niejednoznacznymi wynikami badań neurofizjologicznych wykonano badanie MRI odcinka szyjnego kręgosłupa pomimo posiadania przez chorą rozrusznika serca. Badanie ujawniło obecność guza w obrębie szyjnego odcinka rdzenia kręgowego. Chorą zoperowano, a badanie anatomopatologiczne wykazało naczyniaka płodowego. Prezentowany przypadek demonstruje, jak zmienną symptomatologię mogą prezentować zmiany wewnątrzrdzeniowe oraz jak istotną rolę w diagnostyce odgrywa badanie MRI u chorych ze stymulatorem mięśnia sercowego.

**Słowa kluczowe:** guzy rdzenia kręgowego, naczyniak płodowy, stymulator mięśnia serca, zespół von Hippel i Lindau

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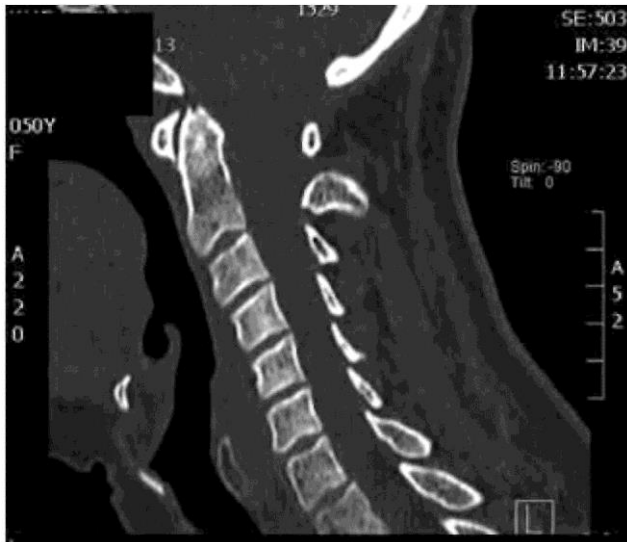
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## Introduction

Hemangioblastoma is a rare, well-vascularised, slowly growing tumour. It is usually located subtentorially, and connected with the meninx, so it was previously classified as an angiomeningioma. The tumour comprises stromal cells and small blood vessels; it may occur sporadically, or as one of a number of hyperplastic lesions in patients with von Hippel-Lindau syndrome (VHL syndrome). Usually it is

located in the spinal cord (50%), cerebellum (40%) or brainstem (10%). It is found rarely in a supratentorial location (<2% of cases). Hemangioblastoma, also known as capillary hemangioblastoma, is a benign tumour (WHO grade 1). In 2000, WHO declared it a tumour of unknown histogenesis. It is found with a similar frequency in men and in women. In patients with VHL syndrome hemangioblastomas may be found at an earlier age than in the sporadic forms.

## CASE REPORTS



**Figure 1.** A CT examination of the patient did not allow the assessment of intraspinal structures

**Rycina 1.** Badanie TK prezentowanej chorej nie pozwoliło ocenić struktur wewnątrzkanatowych



**Figure 2.** A non-contrast MRI revealed the presence of a tumour within the spine

**Rycina 2.** Badanie MRI bez podania kontrastu uwidocznilo obecność guza w obrębie rdzenia

The clinical symptoms of hemangioblastoma are usually associated with impaired circulation of cerebrospinal fluid due to a growing paramural nodule or a pseudosyringomyelia cavity, typically resulting in an increased intracranial pressure and/or hydrocephalus. A total of 75% of the cases of hemangioblastoma in a neuroimaging examination are associated with an enhanced by gadolinium, peripheral paramural nodule, accompanied by a cyst/pseudosyringomyelia cavity.

### Case report

A 50-year-old patient was admitted to the Department of Neurology, Second Faculty of Medicine, Medical University of Warsaw, due to impaired function of the right upper limb, deteriorating for over a year. A physical examination did not demonstrate any abnormalities. A neurological examination revealed the atrophy of the thenar and hypothenar muscles, hypoesthesia of the right neck within the C3-C4 dermatomes, and hypoesthesia in the right upper limb in the C5-C6 root, as well as weakening of the ligamentous reflexes in the right upper limbs.

The patient was treated long term for arterial hypertension and disorders of lipid metabolism. Due to disturbed cardiac rhythm, in 2007 she received a cardiac stimulator implant.

Laboratory tests (complete blood count, electrolytes, coagulogram, renal and hepatic

function parameters, CRP, ESR, general urinalysis, thyroid hormones, vitamin B12 concentration) did not reveal any abnormalities. During her stay in the hospital, the patient received computed tomography (CT) of the cervical spine, which demonstrated a slight spondylosis at C4-C5, without any other abnormalities. The examination of the somatosensory-evoked potentials from the upper limbs indicated lesions in the area of the C6-C8 posterior roots, bilaterally, more pronounced on the right side, as well as lesions within the right cuneate fasciculus.

Due to the inconclusive results of additional tests, i.e. CT of the cervical spine and somatosensory-evoked potentials, combined with the patient's clinical picture, an MRI of the cervical spine was performed (despite the implanted stimulator). The test was conducted following a consultation with a cardiologist, and it revealed a massive, cystic lesion expanding the cervical cord. The lesion was clearly and uniformly enhanced after administration of a contrast medium. It was located at the level of C3/C4 in the dorsal part of the cord, and it was approximately 13 mm in diameter. The patient received neurosurgical treatment. A histopathological examination demonstrated a tumour composed of neoplastic stromal cells, surrounded by a dense net of capillaries. Immunohistochemical staining of both types of stromal cells demonstrated expression of neuron specific enolase (NSE) and S100 protein. The patient was diagnosed with angioblastoma.



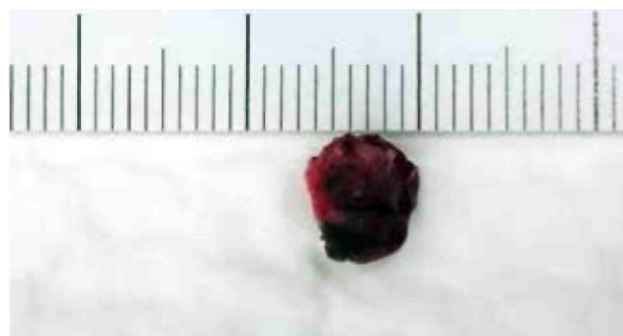
**Figure 3.** Contrast administration allowed the location of the solid part of the tumour, known as a "raspberry tumour"

**Rycina 3.** Podanie kontrastu pozwoliło zlokalizować część twardą guza - tzw. guzek malinowy

## Discussion

Hemangioblastoma is a rare neoplasm, located usually in the posterior cranial cavity, within the cerebellum. Its name is derived from Lindau's hypothesis from 1931, postulating that these tumours are innate lesions, and their microscopic image resembles embryonic cells. Based on original, developmental biological observations conducted by Sabin in 1917, Stein suggested a vascular-mesenchymal origin of the hemangioblastoma cells.

In children proper diagnosis is often preceded by acute hydrocephalus [6]. In adult patients, sporadic hemangioblastoma occurs usually in decades 4-6 of life. It typically invades the posterior cavity structures or the spinal cord. It is composed of a larger, cystic part, resembling a syringomyelia cavity, and a usually small, round, well-enhanced by a contrast medium raspberry nodule. In surgical patients with solid tumours the improvement of the neurological status is worse than in patients with a pseudosyringomyelia cavity [8]. Hemangioblastoma excludes von Hippel-Lindau syndrome. In approximately 30% of cases, hemangioblastoma is associated with innate von Hippel-Lindau disease (VHL), with concurrent malignant renal hyperplastic lesions. Contrary to RCC metastases, the stromal cells of hemangioblastoma are immunonegative for epithelial differentiation markers, i.e. EMA and cytokeratin, but they express NSE and inhibin, which are not expressed by renal cancer cells. Differentiation between hemangioblastoma and clear cell renal cell carcinoma (ccRCC) is significant for prognosis, and appears to pose the greatest challenge.



**Figure 4.** "Raspberry tumour" - post-surgery picture

**Rycina 4.** Guzek malinowy - fotografia pooperacyjna

The differential diagnostics should also consider the similarities between hemangioblastoma and paraganglioma, pilocytic astrocytoma of the cerebellum, certain types of meningioma, and solitary fibrous tumours with a phenotype of pericyte-derived hemangioma. In such a situation, an accurate diagnosis can be made after a histopathological examination of the paramural nodule. In 2017, there were reports concerning an increasing number of hemangioblastoma tumours within the past 12 years in the group of patients over 65 years old [5]. There are case reports of diffused hemangioblastomas of the CNS, occurring many years after a surgical removal of a hemangioblastoma located in the cerebellum [7]. It is believed that the dominant mechanism in the pathogenesis of hemangioblastoma is inactivation of two alleles of the VHL gene (von Hippel-Lindau gene). It appears that other, so far unknown, mechanisms may play an important role; however, they are probably different in the course of von Hippel-Lindau syndrome and in sporadic hemangioblastoma [9].

Due to an increasing availability of imaging tests with the use of electromagnetic fields, MRI examinations are performed more often nowadays. Its specificity makes it essential in the imaging diagnostics of the diseases of the spinal cord and roots. In special clinical situations, as in the presented case, the MRI examination in a patient with cardiac stimulator allows the establishment of an accurate diagnosis. The test is then associated with a minimal risk of complications [10].

The course of the disease in the presented case indicated an injury of the spinal cord, and although the CT study did not reveal any pathologies, the symptoms prompted a MRI examination which demonstrated a pathological lesion. This case shows the importance of finding the right diagnostic method based on the observed clinical symptoms. Due to diagnostic inquisitiveness, a proper diagnosis was made and appropriate treatment was introduced. This allowed the prevention of a potential complication of the disease, i.e. tumour haemorrhage, which could be lethal.

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# Endogenous endophthalmitis in a patient with long-term diabetes with complications

Endogenne zapalenie wnętrza gałki ocznej u chorego z wieloletnią powikłaną cukrzycą

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**Abstract.** Endophthalmitis is a rare, but potentially dangerous condition that can lead to irreversible vision loss. Inflammation develops in particular in immunocompromised patients who suffer from systemic diseases complicated by bacteraemia or candidiasis. In the case described, inflammation developed in a patient with long-term, poorly controlled diabetes, diabetes-related complications, right-sided pneumonia, lower limb skin inflammation and a urinary tract infected with *Streptococcus agalactiae*. *Streptococcus* B group is a common cause of intraocular inflammation, although *Streptococcus agalactiae* infection in adults is very rare. Treatment with systemic corticosteroids and broad-spectrum antibiotics stopped the progression of intraocular inflammation and stabilized the patient's general condition.

**Key words:** endophthalmitis. *Streptococcus agalactiae* infection, diabetes

**Streszczenie.** Zapalenie wnętrza gałki ocznej jest rzadko występującą, ale potencjalnie bardzo niebezpieczną chorobą, która może powodować nieodwracalną utratę widzenia. Zapalenie rozwija się przede wszystkim u pacjentów z osłabioną odpornością immunologiczną, którzy cierpią na choroby ogólnoustrojowe powikłane bakteriami lub kandydiami. W opisywanym przypadku zapalenie rozwinęło się u chorego z wieloletnią źle kontrolowaną i powikłaną cukrzycą, z towarzyszącym prawostronnym zapaleniem płuc, stanem zapalnym w zakresie skóry kończyn dolnych i zakażeniem układu moczowego *Streptococcus agalactiae*. Paciorkowce z grupy B są częstą przyczyną zapalenia wewnątrzgałkowego, chociaż zakażenie *Streptococcus agalactiae* u dorosłych występuje bardzo rzadko. Ogólnoustrojowa steroidoterapia i antybiotykoterapia o szerokim spektrum doprowadziły do zahamowania postępu zapalenia wewnątrzgałkowego i stabilizacji stanu ogólnego pacjenta.

**Słowa kluczowe:** zapalenie wnętrza gałki ocznej, infekcja *Streptococcus agalactiae*, cukrzyca

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## Introduction

Endophthalmitis is a rare disease, but it may cause an irreversible loss of vision. It is usually exogenous, and endogenous forms constitute 2-16% of the described cases [1, 2]. The endogenous (metastatic) endophthalmitis results from the penetration of the blood-eye barrier by an

infectious factor from the blood [3]. The most important factors of the endophthalmitis include HIV infection, AIDS, diabetes, renal failure, intravenous drugs, urinary infections or urinary catheter, organ abscess, previous liver transplantation, malignant neoplasm, infectious endocarditis and gastrointestinal infections [4, 5].

### Aim of the study

The aim of the study was to present a case of a patient who developed diabetic retinopathy and endogenous endophthalmitis in the course of long-term type 2 diabetes.

### A case report

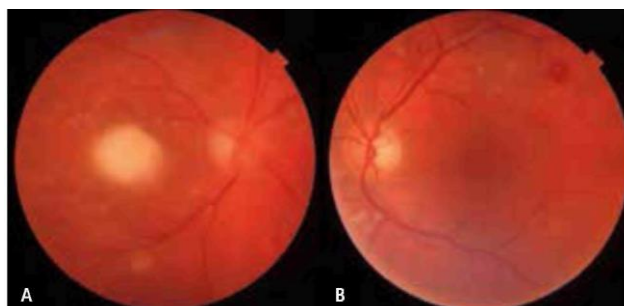
A 37-year-old male attended the Department of Ophthalmology of the Military Institute of Medicine with impaired vision, pain and redness of the right eye (RE), persisting for 3 weeks. The impairment of visual acuity was accompanied by a gradually growing spot with a greyish-blue halo and floaters before the eye. The patient complained about worsening general well-being, weakness, fever up to 38.5°C, reduced effort capacity, dyspnoea, slight chest pain and cough. He had a history of biocular non-proliferative diabetic retinopathy.

Two weeks before the patient was hospitalised in the Department of Endocrinology of the Military Institute of Medicine due to poorly-managed non-insulin dependent diabetes (HbA<sub>1c</sub> was 9.9%, glucose concentration of 230-417 mg/dl), spontaneous arterial hypertension and inflammation of the skin of the lower limbs. The laboratory tests revealed ESR after 1 h - 63 mm (0-8), concentration of acute phase protein (CRP) - 44.5 mg/dl (0-0.8), leukocytosis (WBC) - 13.17 x 10<sup>9</sup>/l (4.0-10.0), and increased activity of aminotransferases: AST - 67 U/l (0-37) and ALT - 75 U/l (0-41). The laboratory test results for the coagulation system were normal. Urinalysis revealed a glucose concentration of >1.0 mg/dl (0-30), ketone bodies concentration of 100 mg/dl (0-5), and urobilinogen concentration of 2.0 mg/dl (0-1).

The abdominal ultrasound examination demonstrated an enlarged liver with signs of steatosis, and enlarged spleen. A neurologist was consulted about the case, who recommended outpatient diagnostics for diabetic neuropathy. During the hospitalisation the patient received intensive insulin therapy, fluid therapy and antibiotic therapy with intravenous ciprofloxacin at 200 mg / 100 ml twice a day. The treatment resulted in reducing the inflammation of the skin of the legs. The follow-up tests demonstrated a gradual normalisation of the inflammation parameters and glycaemia. The patient was discharged, and continued the treatment with ciprofloxacin at a dose of 500 mg twice a day, for 5 days.

The patient's best corrected visual acuity (BCVA), tested on a Snellen chart on admission to the hospital, was right eye (RE) - counting fingers at 10 cm, and the left eye (LE) was 0.7. The intraocular pressure measured with a Goldmann applanation tonometer was 18 mm Hg in the RE, and 19 mm Hg in the LE. No pathological lesions of the protective apparatus of either eye were found. A mixed conjunctival injection was present in the RE. Inflammatory cells were present in the corneal endothelium of the RE. In the vitreous body of the right eye an inflammatory infusion was present. In the RE macula a white retinal infiltration was found with blurred outlines, round, flurry, of 3 DD (disc diameter) (Fig. 1A). In the posterior pole of the right eye numerous microaneurisms, intraretinal petechiae, cotton

wool spots and hard exudates were observed. The anterior section of the left eye did not present any abnormalities. In the posterior pole of the LE, as in the RE, were signs of pre-proliferative diabetic retinopathy (Fig. 1B).

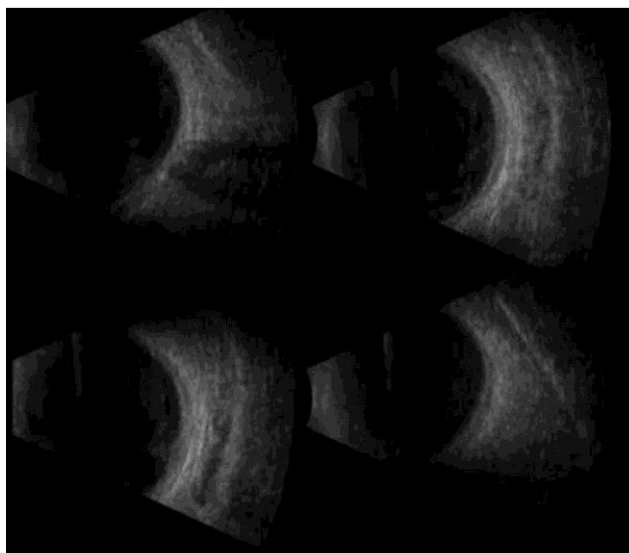


**Figure 1.** On right (A) and left (B) fundus on admission to WIM Ophthalmology Department  
**Rycina 1.** Zdjęcie dna oka prawego (A) i lewego (B) przy przyjęciu do Kliniki Okulistyki WIM

The ultrasound examination of the right eye revealed inflammatory floaters in the vitreous body and hyperechogenic, uniform elevation in the macular projection (Fig. 2).

The optical coherence tomography (OCT) of the RE macula demonstrated a hyperreflective focus with blurred outlines over Bruch's membrane in all the layers of the sensory retina, covering the entire profile of the fovea, with increased light penetration to the choroid, indicating injury of the retinal pigment epithelium. The focus was accompanied by small, intraretinal lesions of high reflexivity in the inner plexiform and nuclear layer, corresponding to hard exudates. Small intraretinal cysts were visible near the nose area (Fig. 3A). OCT of the macula of the LE demonstrated intraretinal cysts and slightly increased foveal thickness (Fig. 3B).

The laboratory test results revealed inflammatory process: ESR after 1 h >120 mm (0-8), CRP - 28.1 mg/dl (0-0.8). IgM antibodies against toxoplasmosis, Lyme disease and mononucleosis did not confirm an active infection, contrary to IgM and IgG antibodies against cytomegalovirus (CMV), which produced a reactive result. Positive hepatitis B antigen or anti-HIV and anti-HCV antibodies were not found. General urinalysis revealed numerous bacterial flora. Urine cultures demonstrated penicillin-sensitive *Streptococcus agalactiae*. No bacteria were grown in blood cultures. A physical examination indicated right-sided pneumonia. A thoracic X-ray revealed atelectatic and inflammatory lesions in the lower lobe of the right lung, with a small amount of fluid in the right pleural cavity. The patient was examined by a specialist in internal medicine, rheumatologist and a specialist in infectious diseases. Based on the assessment of the local and general status, the patient was diagnosed with endogenous endophthalmitis. Empirical intravenous antibiotic therapy was introduced: vancomycin 1.0 g twice a day, and ceftriaxone 1.0 g twice a day. The first addition, intravenous methylprednisolone, was administered in a total dose of 2 g.



**Figure 2.** Right eye ultrasound examination (USG) on admission to the WIM Ophthalmology Department

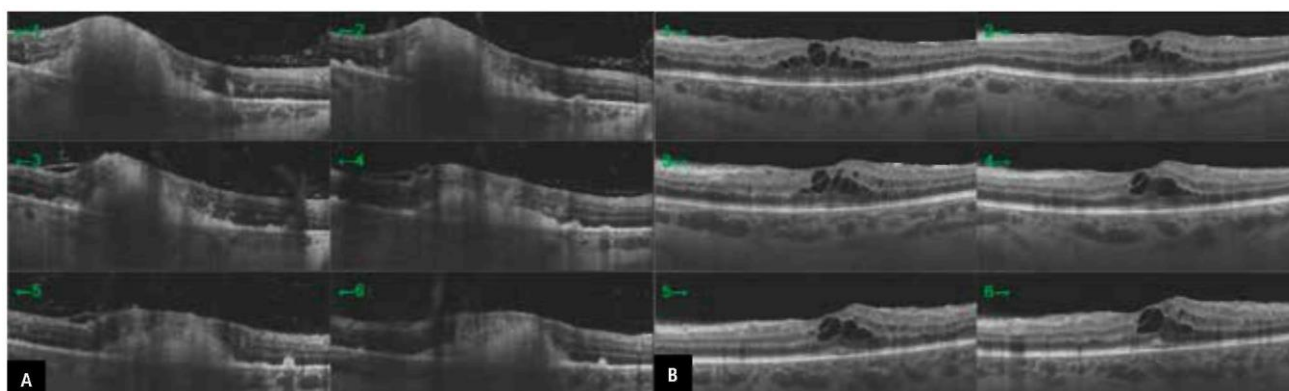
**Rycina 2.** Badanie ultrasonograficzne (USG) oka prawego przy

przyjęciu do Kliniki Okulistyki WIM



**Figure 4.** Post-treatment picture of the right eye fundus

**Rycina 4.** Kontrolne zdjęcie dna oka prawego



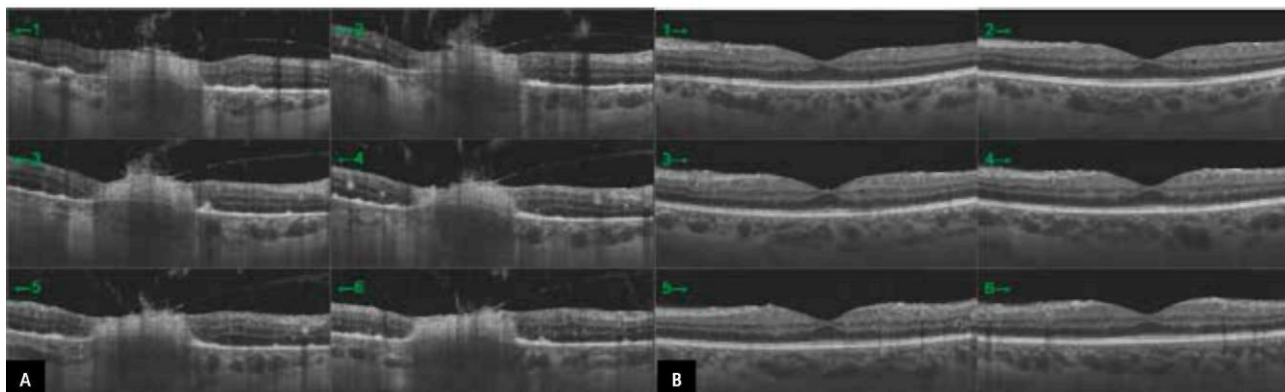
**Figure 3.** Macular OCT of right (A) and left (B) eyes on admission to WIM Ophthalmology Department

**Rycina 3.** OCT plamki oka prawego (A) i lewego (B) przy przyjęciu do Kliniki Okulistyki WIM

Local treatment was recommended: moxifloxacin and dexamethasone to the RE, and periocular methylprednisolone was administered. Due to a high risk of sepsis, the patient was transferred to the Department of Infectious Diseases of the military Institute of Medicine, where the local and intravenous treatment, as well as steroid therapy with methylprednisolone at a dose of 36 mg

were continued. The CMV DNA PCR result did not confirm an active CMV infection. During the hospitalisation the patient was examined by an ophthalmologist every day. His well-being improved, the fever disappeared, and the vision in the RE improved subjectively. A follow-up thoracic X-ray examination revealed regression of the inflammatory lesions.

## CASE REPORT



**Figure 5.** Post-treatment OCT of right (A) and left (B) eyes  
**Rycina 5.** Kontrolne badanie OCT plamki oka prawego (A) i lewego (B)

Considering both the improvement of the patient's general status, and decreasing inflammation markers: ESR after 1 h - 42 mm (0-8), CPR - 1.5 mg/dl (0-0.8), the patient was discharged, and the oral therapy with antibiotics and steroids was continued: amoxicillin (875 mg) with clavulanic acid (125 mg) and methylprednisolone. The initial doses were reduced at suitable intervals until the lowest effective dose was obtained. The patient was under the outpatient supervision of a clinic of infectious diseases and an ophthalmological clinic.

A week after the hospital discharge, during a follow-up ophthalmological visit, the BCVA in the RE did not change, and in the LE it was 0.9. An examination of the RE fundus demonstrated a reduced inflammatory exudate in the vitreous body. In the macula, the outline of the inflammatory lesion became clear, and decreased to 1.5 DD (Fig. 4). A follow-up OCT of the RE revealed a reduction of the thickness of the hyperreflective focus (Fig. 5A). In the LE the outline of the fovea was restored, the thickness of the retina was reduced, and no oedematous cysts were found (Fig. 5B). Fluorescein angiography demonstrated numerous hyperfluorescent foci in the projection of microaneurysms, and hypofluorescent foci in the sites of microhaemorrhages, hard exudates and cotton wool spots in both eyes (Fig. 6). In the RE, in the dye recirculation phase, a diffused hyperfluorescence with clear outlines, corresponding to a post-inflammatory lesion was visible in the macula.

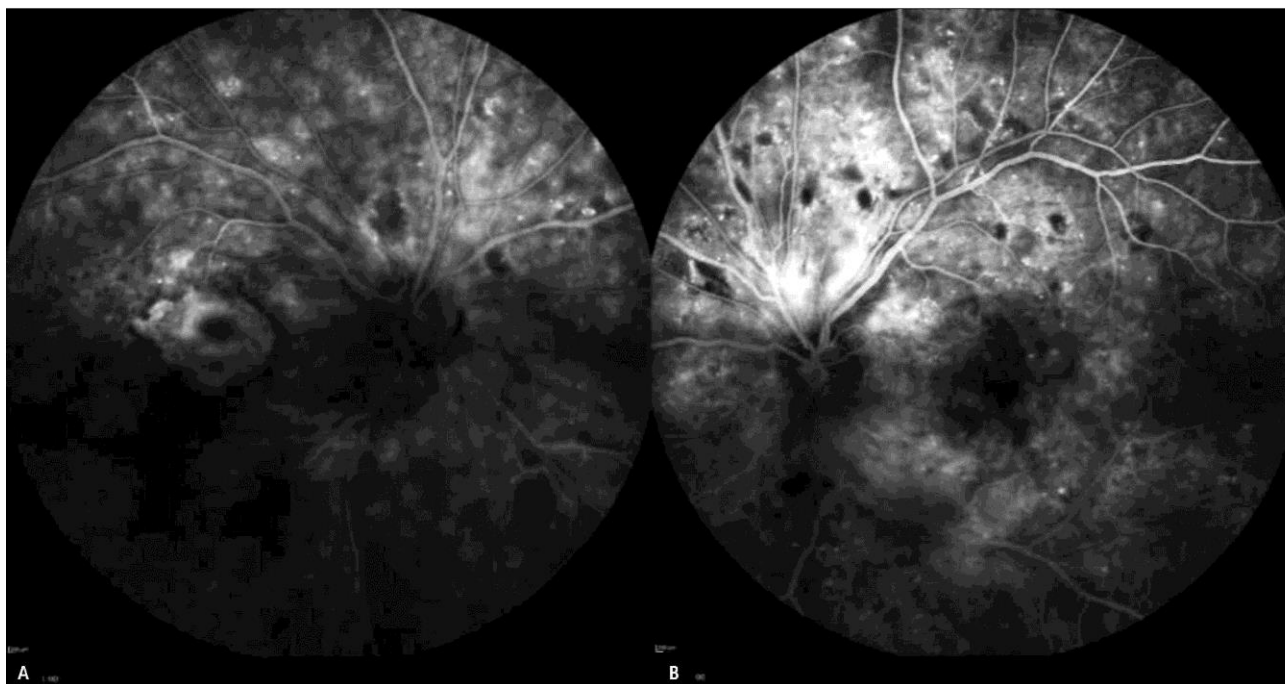
## Discussion

Endogenous inflammation is caused by a diffusion of bacteria and fungi in the blood, due to their penetration through the blood-retina barrier. The inflammation develops especially in patients with reduced immunity, suffering from general systemic diseases complicated with bacteraemia or candidaemia. According to the literature, 0.05% of patients hospitalised due to generalised

infections develop endophthalmitis [4]. The underlying cause of endophthalmitis depends on the primary extraorbital source of the infection, and on the geographical sphere [1]. The most common bacterial factor causing endophthalmitis in Asia are Gram-negative bacteria, whereas in the Western countries these are Gram-positive bacteria [4]. Analysing data from across the world, Jackson et al. found that infections caused by Gram-negative bacteria were the most common [6]. Studies indicate that 55% of cases are due to Gram-negative bacteria, and the most common pathogen is *Klebsiella pneumoniae* (27%). Gram-positive bacteria are responsible for 45% of cases, e.g. *Staphylococcus aureus* for 10%, and *Group B Streptococcus* for 6% [7]. Fungal infections are mostly caused by *Candida*, especially *Candida albicans*, and *Aspergillus species* [8].

The inflammation is focal or diffused, involving the anterior or posterior eye; it may also affect the entire eye ball [9]. Specific symptoms reported by patients with endophthalmitis include pain and eye redness, as well as decreased visual acuity. Apart from the ocular symptoms, patients may experience symptoms of general systemic infection, worsening of the general condition, weakness and fever. These were the symptoms reported by the discussed patient. Ocular symptoms may occur prior to the general ones, or simultaneously. Jackson et al. analysed 342 cases of endogenous bacterial endophthalmitis and demonstrated that fever occurs in 74% of patients, whereas hypopyon is found in 35-40% of cases [6]. In 12% of cases the endophthalmitis affects both eyes [3].

In patients diagnosed with endogenous endophthalmitis it is necessary to look for the general systemic foci of infection. Blood, urine and vitreous body samples need to be collected for cultures and determination of the pathogen responsible for the infection. The pathogen might not be grown, but studies indicate that blood cultures are positive in 72% of cases, and vitreous body cultures are positive in 74% of cases [10]. In the presented case, *Streptococcus agalactiae* were isolated in the urine cultures.



**Figure 6.** Post-treatment fluorescein angiography of right (A) and left (B) eyes  
**Rycina 6.** Kontrolne badanie angiografii fluoresceinowej oka prawego (A) i lewego (B)

Endogenous endophthalmitis is an acute, vision-threatening ophthalmological condition. The prognosis is determined primarily by the time and accuracy of diagnosis, isolation of the underlying pathogen, and immediate implementation of targeted treatment. The analysis of cases conducted in the years 1976-1985 indicates that following endogenous endophthalmitis, 41% of patients had visual acuity in finger counting, 26% experienced loss of light perception, and 30% required enucleation [11].

In the presented case, endogenous endophthalmitis developed in a patient with long-term, ill-managed and complicated diabetes, concurrent right-sided pneumonia, inflammation of the skin of the lower limbs, and urinary infection with *Streptococcus agalactiae*. While *Group B Streptococcus* often causes endophthalmitis, *Streptococcus agalactiae* is very rarely found in adults [12]. In a review of 267 cases of endophthalmitis, *Streptococcus agalactiae* was the responsible pathogen in 5% of patients [13]. Diabetes is the most frequent disease concurrent with bacterial infection. In studies conducted in Atlanta in young adults (18-64 years old) with *Group B Streptococcus* infection, over 40% of patients had diabetes [14]. Infection frequently spreads to the skin and soft tissue, causing connective tissue inflammation, superinfection of bed sores or diabetic foot [15]. Individuals with reduced immunity may develop pneumonia and urinary infections [16]. Some authors suggest that vitreous body cultures are not necessary for the diagnosis, if the focus of inflammation has already been found. Treatment of endogenous endophthalmitis requires the immediate introduction of antibiotic therapy [17]. *Group B*

*Streptococcus* is susceptible to penicillin G, ampicillin, and other semi-synthetic penicillin [18]. However, their resistance to clindamycin and erythromycin is increasing – 15-20% of bacteria may be resistant to these antibiotics [18]. Vancomycin, chloramphenicol and 2nd and 3rd generation cephalosporins are effective alternatives. Aminoglycosides demonstrate a limited activity towards *Group B Streptococcus* in monotherapy, but also a synergistic effect in combination with ampicillin or penicillin G [19]. In the presented case, at the time of admission a significant amount of retinal damage was visible in the OCT. The patient's general status required isolation and hospitalisation at the Department of Infectious Diseases. The prompt introduction of antibiotic therapy enabled stabilisation of the patient's general condition, and inhibition of the intraocular inflammation. Due to the location of the inflammation focus in the macula, the vision in the right eye did not improve.

## Conclusions

Recognition of endogenous endophthalmitis requires detailed diagnostics, both with laboratory, and imaging methods. The aim is to determine the location of the focus of infection, and the underlying pathogen. A close cooperation between the ophthalmologist and specialists in internal diseases, infectious diseases and radiology is recommended. The development of endophthalmitis in a young patient with complicated diabetes indicates the need for careful glycaemic control and treatment of comorbidities. The inflammation caused by *Streptococcus*

## CASE REPORT

*agalactiae* may take a severe course, resulting in a complete loss of vision, or ocular enucleation.

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# Brain abscess – a case report

## Ropień mózgu. Opis przypadku

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**Abstract.** The paper presents the case of a brain abscess with an intraventricular rupture, with an atypical clinical picture without correlation with the radiographic image. Both the clinical course of the disease and the treatment methods are presented. The features of a brain abscess CT and MRI are discussed, including spectroscopy and diffusion weighted imaging.

**Key words:** brain abscess, magnetic resonance, diffusion-weighted imaging, magnetic resonance spectroscopy. *Streptococcus intermedius*

**Streszczenie.** W pracy przedstawiono przypadek ropnia mózgu z przebicciem do układu komorowego o nietypowym obrazie klinicznym, niekorelującym z obrazem radiologicznym. Przedstawiono przebieg choroby i sposoby leczenia. Omówiono cechy ropnia mózgu w obrazach tomografii komputerowej i rezonansu magnetycznego z uwzględnieniem spektroskopii i obrazowania dyfuzyjnego.

**Słowa kluczowe:** ropień mózgu, rezonans magnetyczny, obrazowanie dyfuzyjne, spektroskopia rezonansu magnetycznego. *Streptococcus intermedius*

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## Introduction

The incidence of brain abscesses is approximately 8% of the focal cerebral lesions in developing countries, and 1-2% in highly developed ones [1]. It is a life-threatening condition that requires prompt diagnostics and treatment. Currently, the mortality rate is approximately 15% [2]. In patients with cyanotic heart disease, brain abscess is found 10 times more frequently than in the general population. The most common defect is tetralogy of Fallot. A right-to-left cardiac shunt allows bacteria to penetrate into the cerebral circulation, avoiding the pulmonary bed [1]. Most brain abscesses (approx. 90%) develop as a result of paranasal sinus infection, mastoiditis or otitis media. Other abscesses are haematogenous (mostly in the course of infectious endocarditis). Haematogenous multiple brain abscesses are associated with bacteraemia, and are usually caused by *Staphylococcus* and *Streptococcus* bacteria [1]. *Streptococcus anginosus* is a group comprising *S. intermedius*, *S. anginosus* and *S. constellatus*. They produce proteolytic enzymes leading to tissue necrosis, and contribute to the development of abscesses [3]. *Streptococcus intermedius* is a well-known pathogen causing pyogenic lesions outside the CNS [4]. The role of imaging methods in the diagnostics of brain abscesses is growing. Advanced magnetic resonance

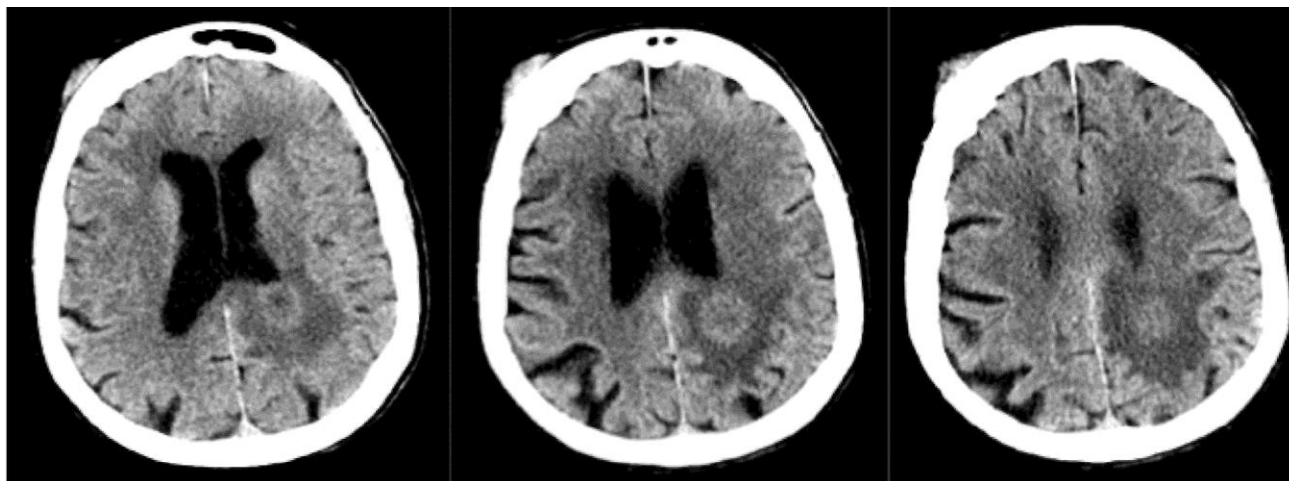
(MR) techniques, i.e. diffusion-weighted imaging and spectroscopy, are used increasingly often, and enable a diagnosis with a high degree of probability. It allows the prompt introduction of broad-spectrum antibiotics, before histopathological confirmation is available.

The present case was associated with significant diagnostic problems. An atypical clinical picture and an ambiguous intraoperative assessment did not correlate with the results of the imaging studies, which delayed proper treatment.

## A case report

An 81-year-old patient was admitted to the Department of Neurology due to a weakness in the right upper limb, persisting for 2 days. The patient did not report headache or any other neurological symptoms. The body temperature was normal, and laboratory tests revealed an increased level of leukocytes ( $20.17 \times 10^3/\mu\text{l}$ ); CRP concentration was normal (0.5). The computed tomography (CT) examination performed on the day of admission demonstrated a round focal lesion in the left parietal lobe, surrounded by oedema, with compression of the left lateral ventricle (Fig. 1). The patient was initially diagnosed with a possibly metastatic tumour.

## CASE REPORT



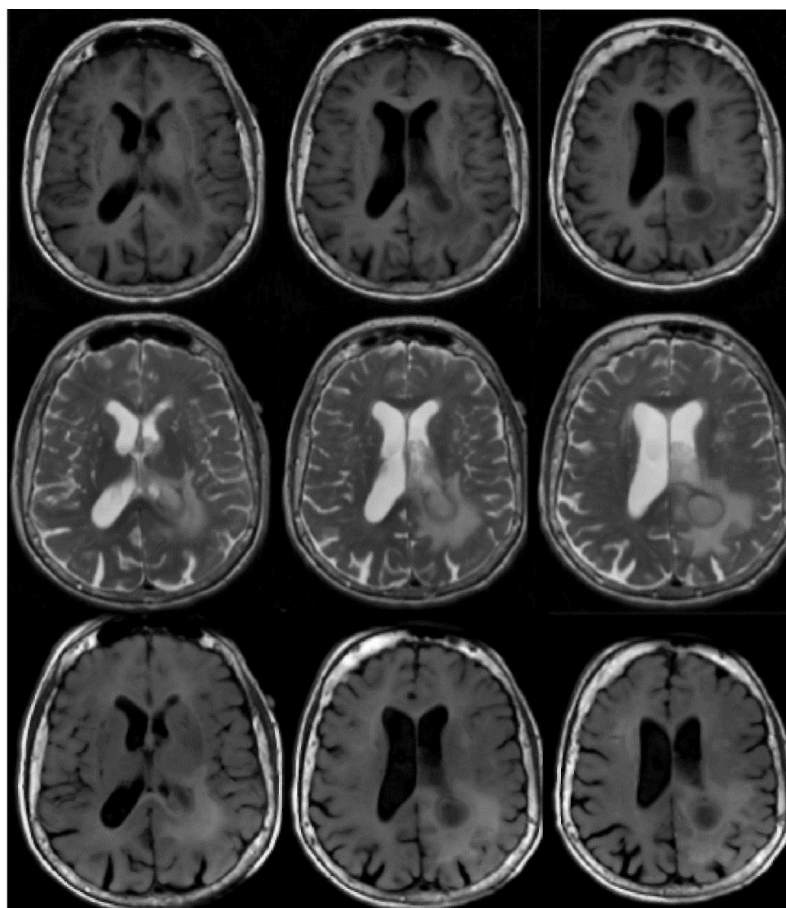
**Figure 1.** Non-enhanced head CT: round lesion in left parietal lobe surrounded by oedema, with compression of the posterior horn of the left lateral ventricle

**Rycina 1.** TK głowy bez środka kontrastującego: okrągła zmiana ogniskowa w lewym płacie ciemieniowym otoczona strefą obrzęku, uciskająca róg tylny lewej komory bocznej

Within the next 5 days the patient's status deteriorated. She developed a fever of 39.2°C, and CRP concentration increased to 3.5. On day 4 of hospitalisation, antibiotic therapy with ciprofloxacin and ceftriaxone was introduced. The patient's condition started to improve. On day 7, a head MR examination was performed (Fig. 2). No contrast-enhancing medium was applied, due to abnormal renal parameters (eGFR reduced from 50 to 16 ml/min). The MR test revealed a thick-walled, well-defined focal lesion in the left parietal lobe, 3 cm in diameter. The lesion demonstrated a low to intermediate signal intensity in T<sub>1</sub>-weighted images, high signal intensity in T<sub>2</sub>-weighted images, and it was surrounded by oedema. The DWI sequence (diffusion weighted imaging) revealed a restricted diffusion both within the lesion, and in the adjacent lateral ventricle (Fig. 3). Based on the MR test results, the radiologist suspected a brain abscess with intraventricular rupture. The diagnosis was difficult to accept by the clinicians, due to the non-specific symptoms, and the quick improvement in the patient's condition. After the next 7 days, when the renal parameters had normalised, another MR examination was performed, this time with contrast-enhancing agent (Fig. 4), followed by MR spectroscopy (MRS). The test revealed a decreasing

restriction of diffusion in the lesion, its communication with the ventricular system, and annular wall enhancement in the focus, and in the posterior horn of the left lateral ventricle. A single-voxel MRS (Fig. 5) demonstrated a lactate peak, typical for abscesses, as well as increased concentrations of amino acids, acetates and succinates. The lesion was qualified for surgical treatment.

A free bone flap craniotomy was performed in the left temporo-parietal area. The appearance of the cerebral surface was normal. A brain incision, extending to the occipital horn of the left lateral ventricle, was made with the use of a surgical microscope. A creamy content resembling purulence was collected from the ventricle for culturing and histopathological examination. According to the surgeons, the lesions were consistent with the masses of a ruptured dermoidal cyst or disintegrated metastasis rather than with the content of an abscess. The pathological masses were sucked and washed out from the ventricle. In the roof of the ventricle they were located in a recess, from which material was collected for histopathological examination. The ventricular system was flushed with a 0.9% solution of NaCl. The surgery was uncomplicated. The antibiotic therapy was continued for the next 7 days.



**Figure 2.** Non-enhanced head MRI (upper row - T<sub>1</sub>-weighted images, middle row - T<sub>2</sub>-weighted images, lower row - FLAIR images): cystic lesion with thick capsule in left occipital lobe, suspected rupture into ventricular system, perilesional oedema

**Rycina 2.** MR głowy bez środka kontrastującego (rzęd górny - obrazy T<sub>1</sub>-zależne, środkowy - obrazy T<sub>2</sub>-zależne, dolny- obrazy FLAIR): plynowa grubościenna zmiana ogniskowa w lewym płacie ciemieniowym z podejrzeniem przebicia do układu komorowego, obrzęk wokół zmiany

The patient, in a moderately severe condition, was transferred to the Department of Rehabilitation of the Military Institute of Medicine with a right-sided hemiparesis, and right ipsilateral hemianopsia. Three weeks after the surgery, the histopathological test result confirmed the diagnosis of abscess. Ceftriaxone-sensitive *Streptococcus intermedius* was grown from the material from the lesion. The patient was transferred to the Department of Neuroinfections of the Hospital of Infectious Diseases for further broad-spectrum antibiotic therapy. After the 4-week antibiotic therapy was completed, the patient was re-transferred to the Department of Rehabilitation of the Military Institute of Medicine. Her condition was moderately severe, and she suffered from a moderate right-sided hemiparesis. A gradual improvement in the patient's neurological status and function was observed. She was discharged in a generally good condition to be taken care of by her family.

## Discussion

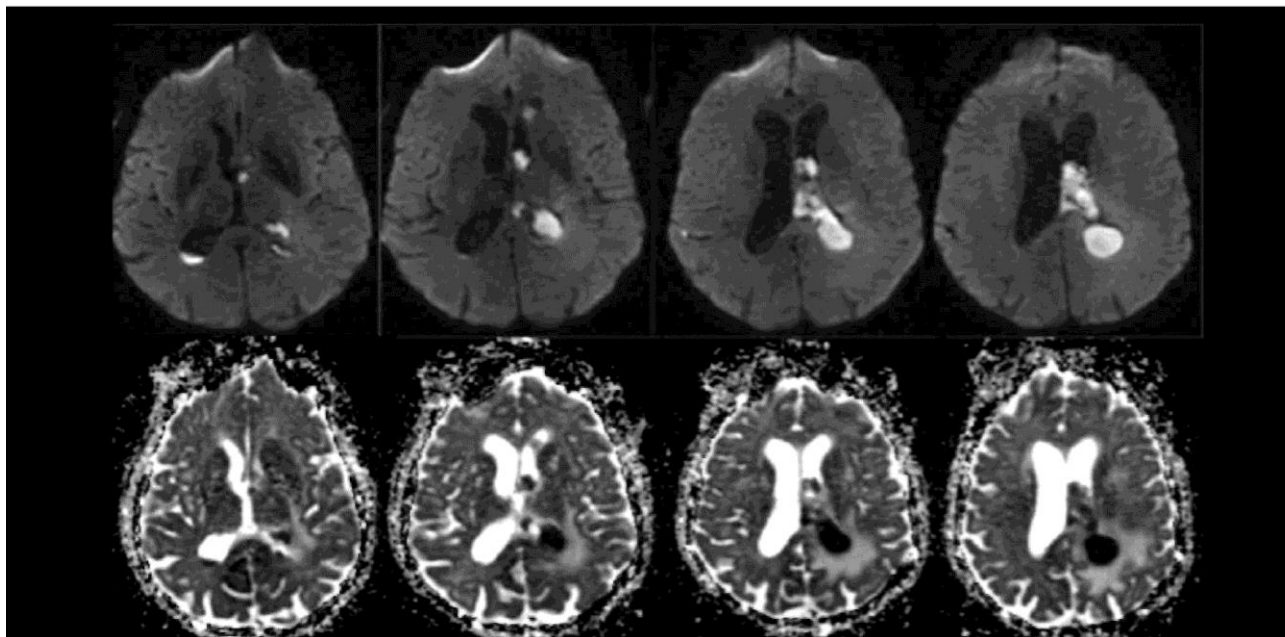
Proper management and effective treatment of a brain abscess is possible with the collaboration of many specialists: a neurosurgeon, neurologist, specialist in infectious diseases and neuroradiologist.

The clinical picture is a consequence of the four major

effects of an abscess in the CNS: a local mass effect, intracranial pressure, destruction of the affected neural tissue, and focal neurological deficits. The most common symptoms include headache, consciousness disorders, nausea and vomiting, and high fever. Convulsions may also occur [1]. However, the symptoms may be atypical, and they do not always indicate an inflammation [3]. In addition, the source of infection sometimes cannot be found [4]. Initially, the disease develops as a focus of brain inflammation, which evolves in a collection of purulence, surrounded by a well-vascularised capsule.

Based on imaging studies, the natural course of a brain abscess may be divided into four phases: early encephalitis (lasting 1-4 days), late encephalitis (4-10 days), early (11-14 days) and late (>14 days) phase of capsule formation [5]. In imaging diagnostics, a MR examination is superior to a CT. In an MR examination the abscess demonstrates a low signal in T<sub>1</sub>-weighted images, with a peripheral enhancement following the administration of a contrast medium. In T<sub>2</sub>-weighted images an intermediate- or high-intensity signal of the lesion is not attenuated in the FLAIR sequence. A mature abscess is surrounded by a capsule of low signal intensity in T<sub>2</sub>-weighted images. The development of MR techniques associated with diffusion-weighted imaging and hydro-spectroscopy allows the use of new sequences to establish the correct diagnosis.

## CASE REPORT



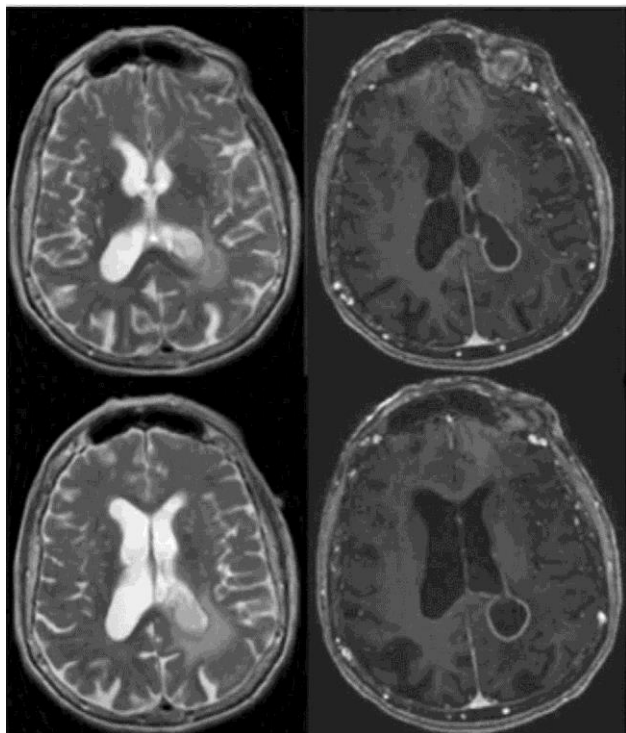
**Figure 3.** Head MRI (upper row-DWI, lower row-ADC): diffusion restriction in the lesion and ventricular system, confirming intraventricular rupture

**Rycina 3.** MR głowy (rzęd górny - obrazy DWI, dolny-obrazy ADC): ograniczenie dyfuzji w obrębie zmiany oraz w układzie komorowym, potwierdzające przebieg do układu komorowego

Abscesses demonstrate a high signal intensity in diffusion weighted images (DWI), and reduced apparent diffusion coefficient (ADC) [6], whereas most necrotic or cystic brain tumours have an intermediate signal in the DWI images, and elevated ADC. The differences result from the composition of the necrotic material in an abscess and in a tumour. The inflammatory cells, proteins, cellular debris and bacteria present in the abscess demonstrate high viscosity, and significantly limit the diffusion of water. Moreover, water molecules are bound by amino acid groups on the surface of macromolecules, which increases the effect of restricted diffusion. Exceptions include abscesses with a fungal aetiology and tuberculous abscesses in which diffusion increases [1]. The necrotic component of tumours contains cellular debris, serous fluid and small quantities of inflammatory cells. This composition contributes to a greater diffusion of water, compared to an abscess. DWI imaging also helps to assess the evolution of the abscess. In the absence of a cavity with restricted diffusion, a persisting inflammation and new collection of the purulent content may be suspected [7]. In the present case the DWI images present the rupture of the abscess into the lateral cavity. MRS reveals primarily a high lactate peak (1.3 ppm of the abscissa) and amino acid (0.9 ppm), acetate (1.92 ppm) and succinate (2.24 ppm) peaks [8, 9]. The lactates, resulting from anaerobic glycolysis, may occur outside the abscess in necrotic areas in tumours, in stroke areas, in an epileptic focus, post-radiation necrosis, and in the last phase of demyelination in the course of multiple sclerosis [6]. If an abscess is suspected, not only lactates, but also products of bacterial metabolism should be sought, i.e. succinates and acetates, which cannot be found in tumours with a necrotic and cystic component [10].

As levels of individual metabolites may, but do not have to, be present in MRS, differentiation between an abscess and other lesions is more accurate if both MRS and DWI are conducted [10, 11]. Restriction of diffusion, typical for abscesses, may also be observed in metastases to the CNS, especially in the adenocarcinoma [12]. Brain abscesses must be differentiated from lesions with annular enhancement, including metastases (primarily of adenocarcinoma), cerebral infarction, demyelination foci, post-radiation necrosis, lymphoma, AIDS, injury and glioblastoma. Prompt identification of the pathogen is of crucial importance for optimal antibiotic therapy. Unfortunately, approximately 20% of cultures from abscesses are sterile. A polymerase chain reaction (PCR) test offers an alternative, fast and precise method of pathogen identification [13].

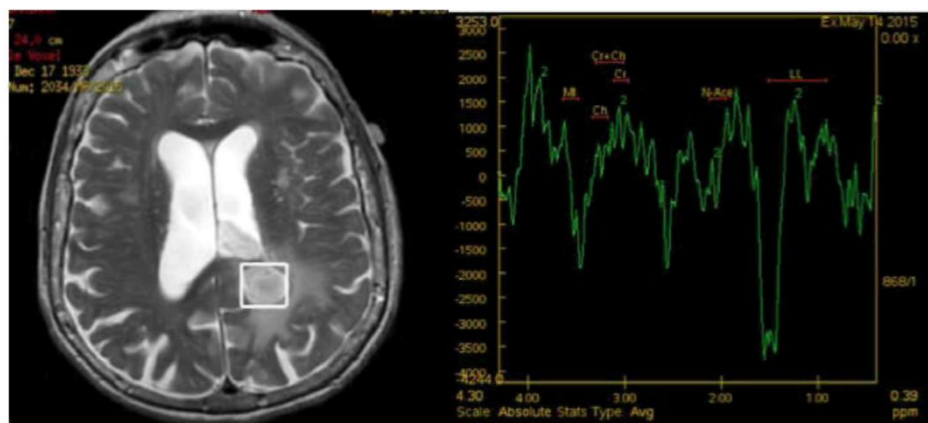
There are no clearly established management procedures in brain abscesses. A combination of surgical methods and antibiotic therapy is preferred. CT-controlled stereotactic aspiration, due to a limited invasiveness, is used frequently instead of a surgical access. In the case of small, individual abscesses, diagnostic aspiration is applied for 6-8 weeks, followed by intravenous antibiotic therapy. If the abscesses are larger than 2.5 cm, drainage and intravenous antibiotic therapy for 6-8 weeks are necessary. The size of the abscess usually decreases after approximately 2 weeks of treatment. Reduction of the annular contrast enhancement, and disappearance of the clearly defined capsule in the T2-weighted images is a sign of effective treatment. Another form of drainage is recommended if the abscess grows after 2 weeks of treatment, or if antibiotic therapy is ineffective after 3-4 weeks [8].



**Figure 4.** Enhanced head MRI (from the left: T<sub>2</sub>-weighted images, T<sub>1</sub>-weighted images after contrast administration): decreased oedema, communication between abscess and left lateral ventricle, enhancement of abscess capsule and ventricle wall (consistent with ventriculitis)

**Rycina 4.** MR głowy z podaniem środka kontrastującego (od lewej -obrazy T<sub>2</sub>-zależne oraz T<sub>1</sub>-zależne po podaniu kontrastu): zmniejszenie obrzęku, łączność ropnia z lewą komorą boczną, wzmocnienie torebki ropnia i ściany komory (odpowiadające zapaleniu wyściółki komór)

The prognosis for patients with a brain abscess is reduced by concurrent immunological disorders, diabetes, liver cirrhosis, and low Glasgow Coma Scale (GCS) score [1]. The location of the abscess in the subcortical nuclei or in the thalamus is also an adverse factor, as it is often associated with a rupture to the ventricular system. In a study by Lee et al., in a group of 62 patients with brain abscesses and intraventricular rupture, 48% of cases were associated with severe neurological deficits, vegetative state or death [14]. The abscess rupture to the ventricular system is a serious complication, adversely affecting the prognosis. More aggressive management may be necessary in these cases. Early craniotomy is recommended, with abscess evacuation, washing out of the ventricular system, ventriculostomy, and a combination of intravenous and intrameningeal antibiotic therapy.



**Figure 5.** MR single voxel spectroscopy: pathological spectrum within the lesion with lactate peak

**Rycina 5.** Spektroskopia MR metodą pojedynczego woksela: patologiczne spektrum w obrębie zmiany z pikiem mleczanów

In the present case no predisposing factors were found. No immunity disorders, sinus or temporal bone infection, recent head injury or surgery were observed, and ECHO examination excluded bacterial endocarditis. The patient did not receive chemotherapy or corticosteroids. A relatively good clinical status was not consistent with the results of imaging studies. The correct diagnosis was established early on the basis of the MR examination; however, it did not correlate with the atypical clinical picture and ambiguous intraoperative assessment. Therefore, the empirical antibiotic therapy started on day 4 of hospitalisation was completed already by day 10. The broad-spectrum targeted antibiotic therapy was reintroduced after the results of the histopathological examination and cultures were obtained. The adverse location of the abscess and complication, intraventricular rupture, led to serious neurological deficits in the form of hemiparesis.

## Conclusions

Unknown focal lesion in the CNS require extensive imaging diagnostics. The best method available, effective in the diagnosis and differentiation of brain abscesses is contrast-enhanced MR examination with DWI assessment and MRS. The absence of the typical clinical symptoms of infection does not exclude an early stage of brain abscess. Early diagnosis and the implementation of suitable treatment is of crucial importance in this condition.

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# Multiple pyogenic liver abscesses, a rare complication of a common disease – a case report

Mnogie ropnie wątroby - rzadkie powikłanie częstej choroby. Opis przypadku

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**Abstract.** Liver abscess is commonly a solitary lesion in the liver and occurs as a consequence of biliary tract infection. Multiple liver abscesses and abscesses of other aetiologies are not frequently reported. Overall mortality for multiple liver abscess is very high, if left with no treatment or not treated early. The paper presents a case of a 62-year-old female with multiple pyogenic liver abscesses of an aetiology diagnosed intraoperatively, who was successfully treated by percutaneous drainage and antibiotic therapy.

**Key words:** multiple liver abscesses, percutaneous drainage

**Streszczenie.** Ropień wątroby to zazwyczaj pojedyncza zmiana w wątrobie będąca konsekwencją infekcji w zakresie dróg żółciowych. Zmiany mnogie i o innej etiologii są rzadko opisywane. Mnogie ropnie wątroby nieleczone lub leczone zbyt późno cechuje bardzo duża śmiertelność. W pracy przedstawiono przypadek 62-letniej chorej z mnogimi ropniami wątroby o etiologii ustalonej śródoperacyjnie, skutecznie leczonej drenażem przezskórnym oraz antybiotykoterapią.

**Słowa kluczowe:** mnogie ropnie wątroby, drenaż przezskórny

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## Introduction

A Pyogenic liver abscess is a restricted space in the hepatic tissue filled with purulence, formed as a result of a bacterial infection or, rarely, amoebiasis. The bacterial infection usually originates in the urinary tract or in the gastrointestinal tract through the portal vein. In rare cases liver abscesses are complications of an injury or fungal infection [2, 3, 11]. They are usually cryptogenic lesions of unknown origin [3, 4].

The factors predisposing for liver abscesses include: diabetes, liver cirrhosis, impaired immunity, use of proton pump inhibitors, status post splenectomy and male sex [2, 3, 5].

This condition poses an interdisciplinary problem, requiring effective pharmacological treatment, as well as, frequently, a surgical intervention. Pyogenic liver abscesses are significant focal lesions of hepatic parenchyma that, if not diagnosed early,

may lead to severe, potentially life-threatening complications [8].

## A case report

A 62-year-old female patient was admitted urgently to the Department of General Surgery of the 5th Military Research Hospital with Polyclinic in Kraków with a suspicion of multiple pyogenic intrahepatic abscesses. The patient complained about pain in the right upper abdomen persisting for approximately 2 weeks, fever up to 39.5°C, general weakness, and one episode of vomiting food content. The patient was treated long-term for arterial hypertension, glaucoma, degenerative lesions of the spine, and spinal disc hernia in the cervical region. Approximately 15 years before she had a panhysterectomy due to uterine myomas.



**Figure 1.** CT of abdomen before treatment: multiple lesions of various shapes in both liver lobes

**Rycina 1.** TK jamy brzusznej przed leczeniem: w obu płatach wątroby widoczne liczne różnokształtne zmiany

On admission the patient was in a generally good condition, logically responsive, with arterial pressure of 130/80 mm Hg, regular cardiac function (approx. 88/min.), the abdominal layers were convex at the level of the thorax, the abdomen was soft, painful in the right upper abdomen upon deep palpation, the peritoneal symptoms were negative, and peristalsis was normal.

Laboratory tests revealed a mild anaemia (HGB 11.3 g/dl) and elevated inflammatory markers: WBC - 19.2 G/l and CRP - 397.1 mg/l; ALT activity was 109 U/l, amylase - 12 U/l, AST - 92 U/l, and GGTP - 187 U/l.

Abdominal ultrasound examination demonstrated a few heterogeneous hypoechogenic lesions of 49 x 46 mm, consistent primarily with pyogenic abscesses. The diagnostics included abdominal CT examination which revealed a heterogeneous liver of maximum size, with poorly defined in the native phase hypodense lesions throughout the organ. In the arterial phase, areas of reduced enhancement appeared, with a sectional edge enhancement and clearly hypodense in the portal venous phase. The lesions had blurred outlines, were of various shapes, and were polycyclic. The largest one measured 65 x 55 x 50 mm and was located in the left lobe, while in the right lobe there were some smaller ones, of up to 50 mm in the right lobe pole (adjacent to the parenchyma of the right kidney).

An ultrasound-controlled puncture of the lesion in the IV hepatic segment was performed with the use of a Pigtail drain.

A sample for bacteriological testing was collected (*Staphylococcus aureus*). A blood sample for culturing was collected; but the result was negative. Antibiotic therapy was introduced (Invaz) and nutritional treatment. High inflammatory parameters and fever persisted for the following days. Due to the lack of improvement after conservative treatment, the patient was qualified for laparoscopic exploration. Intraoperatively numerous

adhesions were found in the small pelvis, the caecum and ileum demonstrated an inflammatory infiltration, descending to the small pelvis on the right side. Moreover, gangrenous lesions were found on the appendix in the post-caecal position, with a large periappendiceal abscess whose wall invaded the caecum and a few loops of the small intestine. The surface of the liver was normal in gross appearance. The patient was qualified for laparotomy, during which an appendectomy was also performed, and the pelvic abscess was evacuated. A sample for microbiological testing was collected, and a culture of *Fusobacterium nucleatum* was grown.

Postoperatively, fluid was found in both pleural cavities. An ultrasound-controlled bilateral puncture of the pleural cavities was performed. Due to reduced morphotic blood parameters, two units of PRBCs were transfused, and 2 units of FFP. The patient's status deteriorated, and dyspnoea increased. An ultrasound of the pleural cavities was performed at the patient's bed, revealing air and fluid in the right pleural cavity. The pneumothorax was relieved percutaneously. The patient was qualified for suction drainage of the right pleural cavity. In addition, the pyogenic liver abscesses were reassessed in an ultrasound examination, and the decision was made to puncture and drain them simultaneously.

The patient was taken to the operating theatre, where the right 900 ml cavity was drained. Approximately 900 ml of serous content with blood was evacuated. With ultrasound, an abscess was located in the right hepatic lobe, and a Pigtail drain was introduced in its cavity. Approximately 40 ml of purulent content was drained. Then, with ultrasound monitoring, an abscess was located in the left hepatic lobe, and a Pigtail drain was introduced in its cavity (approximately 50 ml of purulent content was evacuated). The collected purulence was sent for microbiologic testing. A positive result for *Fusobacterium nucleatum* infection was obtained, consistent with the cultures from the pelvic abscess. After the procedure the patient received mechanical ventilation, and was transferred to the Intensive Therapy Unit for further treatment.

Following 31 days of hospitalisation at the Intensive Therapy Unit, the patient was transferred to the Department of General Surgery for further treatment. During the stay at the hospital the patient received rehabilitation, her diet was gradually expanded, and the wounds were treated locally. The patient was discharged home in a good general condition, with instructions for further outpatient treatment.

## Discussion

Acute appendicitis is the most common acute surgical disease. The diagnosis is usually established based on a clinical examination, but some patients present atypical symptoms, which complicate the diagnostic process [6, 7]. Atypical symptoms of acute appendicitis may be associated with its position. Diagnosing acute appendicitis when the appendix is in the post-caecal position can be difficult, as the symptoms may imitate other pathologies of

the right side or upper abdomen, such as acute cholecystitis, renal colic or irritable bowel syndrome [6]. Delayed or incorrect diagnosis may lead to serious complications, especially in the case of appendiceal perforation. The incidence of complications may be up to 30% [6].

At the beginning of the 20th century, acute appendicitis was the most common cause of liver abscesses [2]. Currently, they are a very rare result of the disease; however, if untreated or treated too late, they may have tragic consequences for the patient, as in 10-40% of cases they are lethal [2, 6, 9]. The main symptoms the patients report include: fever, pain under the right costal arch, and jaundice [1, 12]. Thoracic X-ray images, typically performed on admission, often reveal right-sided elevation of the dome of the diaphragm, and effusion in the right pleural cavity [3, 4].

Approximately 60% of pyogenic liver abscesses are single lesions located in the right hepatic lobe, which is related to the flow of portal blood, supplied to the right lobe by the superior mesenteric vein [11]. It is also important that the right lobe constitutes the largest part of the liver [11]. Multiple abscesses, localised both in the right and left lobe, are found in approximately 20% of cases [11].

The aetiological factors in bacterial liver abscesses are usually *Escherichia coli*, *Klebsiella sp.* and *Streptococcus milleri*, especially in infections spread through the portal vein [1, 3, 4]. *Fusobacterium nucleatum*, isolated in the presented case from the material from the liver abscesses, is a Gram-negative, anaerobic bacillus, a dominant ingredient of a normal bacterial flora of the gums, nasopharynx and appendix [10]. Liver abscesses resulting from infection with this pathogen are very rare [10]. In the case of liver abscesses, the diagnostic standard involves ultrasound examination and computed tomography [1, 11].

In the past, antibiotic therapy combined with surgical drainage was the treatment of choice in this condition [9, 11]. Currently, surgical drainage has been superseded by percutaneous drainage, characterised by a lack of a significant risk of intraabdominal spillage of the purulent content, lower cost, and shorter time of the procedure. It is also well tolerated by patients. Moreover, it avoids potential perioperative complications or complications associated with general anaesthesia [9].

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# Hypersensitivity reactions to food additives – a case report

## Nadwrażliwość na dodatki do żywności - opis przypadku

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**Abstract.** Urticaria is a heterogeneous disease characterized by the formation of itchy bumps as a primary exanthema. An important role in the pathomechanism is played by the secretion of inflammatory mediators such as histamine, leukotrienes and prostaglandins from the mast cells in the subepidermal layers. The aetiology of the lesions varies. The most common causes of acute urticaria are food allergies and medications, but it is often not possible to determine the causative agent for chronic urticaria (spontaneous urticaria). The paper presents the case of a 42-year-old female with recurrent urticaria, which was associated by the patient with consuming some kinds of food, especially spices, cold meat and canned food, which was associated with reactions to food additives. During a double-blind, placebo-controlled food challenge (DBPCFC), sodium benzoate and sodium glutamate intolerance was shown in the patient.

**Key words:** urticaria, sodium benzoate, sodium glutamate, food additives, food challenge

**Streszczenie.** Pokrzywka jest heterogeniczną chorobą charakteryzującą się powstawaniem swędzącego bąbla pokrzywkowego jako wykwitu pierwotnego. W jej patomechanizmie istotną rolę odgrywa uwolnienie w warstwach podnaskórkowych z komórek tucznych mediatorów zapalnych, takich jak histamina, leukotrieny i prostaglandyny. Etiologia powstania zmian jest zróżnicowana. Najczęstszymi przyczynami ostrej pokrzywki są alergię pokarmowe i leki, natomiast często nie udaje się określić czynnika sprawczego w przypadku przewlekłej pokrzywki (pokrzywka spontaniczna). Prezentujemy przypadek 42-letniej kobiety z nawracającą pokrzywką, której występowanie pacjentka wiązała ze spożyciem niektórych pokarmów, zwłaszcza przypraw, wędlin i konserw, co związane było z reakcjami na dodatki do żywności. U pacjentki na podstawie podwójnie ślepej próby kontrolowanej placebo (DBPCFC) potwierdzono nietolerancję na benzoosan i glutaminian sodu.

**Słowa kluczowe:** pokrzywka, benzoosan sodu, glutaminian sodu, dodatki do żywności, próba prowokacyjna

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## Introduction

Urticaria is a heterogeneous disease, quite common (approximately 11% of the Polish population [1], the greatest incidence being observed among 20-40 year olds), characterised by the formation of an itchy urticaria (a pale wheal surrounded by erythema, resembling lesions following contact with nettles) as the primary exanthema. The aetiology of the condition varies. The most frequent causes of acute urticaria are food allergies and medicines, while in chronic urticaria the causative factor often cannot be determined (spontaneous urticaria). A detailed medical history is very important in the diagnostics of this condition. In chronic urticaria it is essential to seek the foci of infection - 37% [2], and autoimmune disease - 24.5% [3, 4]. However, sometimes the cause is exogenous, and can be

determined only after a long observation.

## A case report

A 42-year-old woman was admitted to the hospital due to chronic skin lesions, consistent with urticaria, on the skin of the face and neckline. The lesions occurred approximately a year before, and the patient associated their intensity with the consumption of certain foods, especially spices, cold and tinned meats, and the use of facial creams. The patient provided test results for specific IgE (the panel of food allergens), and for skin prick tests (panel of inhalatory allergens) performed on an outpatient basis. The food panel included egg yolk and white, cow milk, yeast, wheat and rye flour, rice, soy, peanut and hazel nut, almond, apple, kiwi, apricot, tomato, carrot, potato,

celeriac, cod and shrimp - class 0. The inhalatory panel included: grass, rye, alder, hazel, birch, beech, oak, poplar, mugwort, ribwort plantain, *D. pteronyssinus*, *D. farinae*; all the results were negative. A physical examination on admission revealed erythema of the neckline, without urticaria. No lesions of the mucosal membranes were found. Additional tests: complete blood count, ESR, urinalysis, biochemistry, coagulation screen did not reveal any abnormalities; ANA antibodies were negative, anti-HIV antibodies were negative, TSH and fT<sub>4</sub> concentrations were normal.

**Table. Dosage of sodium benzoate and sodium glutamate – DBPCFC**  
**Tabela. Dawkowanie benzoianu sodu i glutaminianu sodu – DBPCFC**

Day	Substance	08:00 hours (mg)	10:00 hours (mg)	12:00 hours (mg)
1	Sodium benzoate	250	Placebo	500
2	Sodium glutamate	Placebo	500	1000

As the patient's skin lesions could have been caused by food additives, DBPCFC with sodium benzoate was performed, based on the pattern proposed in Standards in Allergology (Tab.) [5] - after the first dose of 250 mg facial pruritus and erythematous lesions were observed. 4 mg of *i.v.* Dexaven were administered. DBPCFC with sodium glutamate revealed a positive result after the first dose of 500 mg of sodium glutamate: oedema of the eyelids and watery rhinitis. Auscultation showed no signs of obstruction over the lung fields. The symptoms subsided over a 2 hour period, without the doctor's intervention. The patient was discharged with instructions to follow a diet low in products containing food additives, and to receive 2nd generation antihistamines should the symptoms occur.

## Discussion

Important in the pathomechanism of urticaria is the release of inflammatory mediators, such as histamine, leukotriens and prostaglandins from the mast cells in the subepidermal layers. Mast cells may be activated both by immune and non-immune mechanisms. As a result, the blood vessels are dilated, and their permeability increases [6]. Skin exanthema may be accompanied by angioedema associated with the oedema of the dermis, subdermal tissue, and submucosal membrane. Urticaria may be classified, according to its duration, as acute (the skin lesions occur and disappear within less than 6 weeks) and chronic (the skin lesions persist for over 6 weeks). Therapy for urticaria usually involves using antihistamines, sometimes steroids, and in the most severe, chronic cases, immunosuppressants and anti-IgE are applied.

Sodium benzoate (E211) is a very popular additive used to prevent the growth of numerous microorganisms, e.g. yeasts and moulds. Its use in the food industry is limited to products such as fruit pulps and purees, jams, sauces,

mayonnaise, pickles, pickled herring and mackerel, margarine, olives, beer, carbonated drinks, fruit yoghurts, vegetable preserves and salads. A typical dose of the substance is 0.1% [7]. It is also used in the cosmetics and pharmaceutical industries.

Sodium glutamate (E621) is a sweet-salty aroma (umami), used widely in the food industry. The substance primarily increases the intensity of meat and vegetable broth, plant spices, ready-made food products, cold meats and parmesan [8]. Sodium glutamate is also naturally found in tomatoes. It is commonly used in Far Eastern countries.

Many reactions to food additives probably are not detected; as a result, it is difficult to determine their frequency. Studies estimate their incidence at <1% in adults, and <2% in children [9]. Food hypersensitivity confirmed with a food challenge test is much less frequent than its initial diagnosis based on medical history. Atopy is not a predisposing factor for hypersensitivity to food additives.

The pathomechanism of reactions to many food additives is unknown. It may be of allergic (where IgE-independent mechanism dominates), but also of an immunotoxic or toxic origin [10]. According to Cardinale et al., the reaction to food additives should be suspected in patients who report symptoms after consumption of many unrelated foods, or if the reaction occurs in response to bought or ready-made products, but not to the same dishes prepared at home, especially if an allergy to food proteins was excluded. Allergy to food additives should be considered in the case of idiopathic reaction.

The most common clinical symptoms include chronic urticaria and angioedema. Other possible forms are anaphylaxis, atopic dermatitis, behavioural disorders, bronchial asthma and allergic rhinitis [11]. Local or oral exposure may cause a number of effects in sensitive individuals: from dermatitis, urticaria, facial flushing, hypotension, abdominal pain and diarrhoea to life-threatening anaphylaxis, asthmatic reaction or oral allergy syndrome. The symptoms occur with the following frequency: facial flushing - 57%, pruritus - 35%, nasal discharge - 32%, diarrhoea - 28%, tachycardia - 25%, and gastric or intestinal cramps - 25% [12]. Monosodium glutamate may result in the 'Chinese restaurant syndrome', involving a triad of symptoms: disturbed heart rhythm, general weakness and neck numbness radiating to the upper limbs and the back [10].

As the role of skin prick tests and *in vitro* tests is insignificant in allergy to food additives, an oral challenge test is recommended as conclusive. DBPCFC is the gold standard. The challenge test should be conducted under doctor's supervision, in a well-equipped centre, as serious exacerbations may ensue, including severe attack of bronchial asthma. A food diary kept by the patient, with recording of every adverse reaction, may help in choosing the right substances for the test. The therapy includes elimination of foods and products containing the harmful additives, as well as the use of symptomatic drugs, if the patient cannot follow the diet [11]. Elimination of foods to which the patient is sensitive is facilitated by the regulations introduced in 1994 in Poland according to

## CASE REPORT

which food manufacturers must list food additives on the packaging of products. However, it is important to remember that restrictive diets are associated with the risk of nutritional deficiencies, especially in children.

### Conclusions

Consumption of food additives is rarely the sole cause of chronic conditions. Exposure to additives is associated with numerous symptoms, but the actual causative relation has not yet been demonstrated. However, it should be suspected in patients reporting the occurrence of symptoms or their exacerbation after consumption of many "ready-made" foods. DBPCFC remains the diagnostic standard. Elimination of food additives is difficult, due to their widespread use in the food, pharmaceutical and cosmetics industries.

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# Image diagnostics by field x-ray units as part of the Polish Multinational Brigade in Iraq

Diagnostyka obrazowa polowych gabinetów RTG w rejonie działania żołnierzy Polskiej Brygady Międzynarodowej w Iraku

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**Abstract.** The article describes the image diagnostics carried out by field x-ray units during operation "Iraqi Freedom", as part of the Polish Multinational Brigade in 2003-2004, in terms of assessments and recommendations for the equipment used at different stages of medical evacuation under combat conditions.

**Key words:** military medicine, field radiology

**Streszczenie.** W artykule omówiono diagnostykę obrazową polowych gabinetów RTG podczas operacji „Iracka Wolność” w Polskiej Brygadzie Międzynarodowej w latach 2003-2004 pod kątem oceny i wskazań do jej stosowania na poszczególnych etapach ewakuacji medycznej w warunkach pola walki.

**Słowa kluczowe:** medycyna wojskowa, radiologa polowa

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## Introduction

When a decision was made in May 2003 to create Multinational Division Central South (MND CS) based on a force of 9000 troops, its assigned sector of 65,000 km<sup>2</sup> covered five provinces: Babylon, Karbala, Al Najaf, Al-Qadisiyah and Wasit. The Polish Brigade, with a force of 2300 troops of 1<sup>st</sup> Brigade Combat Troops (1BCT) formed a fundamental core unit of MND CS [1]. The redeployment of the Polish Military Contingent (PMC) was preceded on 14 to 19 June 2003 with a reconnaissance by 26 officers of different military specialities and selected officers from the staff of the units designated to serve in this Iraqi area of responsibility. The transfer of forces and the resources of the first rotation of the PMC was implemented in two stages and using two methods, with the support of multinational combined task forces (Combined Joint Task Force-7 – CJTF-7) with the use of civil ships\* and passenger planes chartered by the US Armed Forces [2,3]. Those assigned to carry out these tasks also included C-

17 Globemaster transport planes of the U.S. Force and CASA C-295M of the Polish Air Force. The first stage was the transfer of the troops with weapons and personal equipment by air to Camp Wolf near the Central Airport in Kuwait. The equipment and ammunition were transported by sea from Szczecin to the Al-Shuaiba port [3]. Stage two included the dislocation of the PMC by wheeled transport from Kuwait to the bases in Iraq.

## Radiological support for the PMC during the transfer in Kuwait and Iraq

Medical support for the troops going through a short acclimatisation period at Camp Coyote and for logistic detachment at Camp Spearhead, with the responsibility for unloading the equipment at the Al Shuaiba port, was provided on the basis of elements of the American healthcare system. Already during the first days of the stay in Kuwait it became necessary to use the full scope of the

\* Ro-Ro MV *Lince*. 2. Ro-Ro *Baltic*. 3. Container ship *Blue Oxygen*. 4. Con - Ro *Strong American*.

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American diagnostic-medical-evacuation route due to a lateral malleolus fracture in a soldier while practicing sport at Camp Spearhead. The lack of an X-ray device in the local outpatient clinic (Level-1) made it necessary to transport the soldier to the 47th Combat Support Hospital (CSH [Level-3]) at Camp Arifjan, where an X-ray image was taken and relevant medical procedures were implemented (Fig. 1).

Treated at the CSH, the soldier was evacuated medically in an American strategic transport to an airbase managed by the U.S. Air Force in Landstuhl (Germany), and then by national transport to Poland [4, 5].

### Radiological support in Iraq

Medical support in the area of operation of particular military contingents at level 1 was implemented on the basis of national medical units forming the MND CS, and their scope was a result of the size of the contingent itself and its equipment (Fig. 2).

Contingents with low staffing only had ambulances at their disposal. The larger ones, such as the Hungarian contingent, with a force of 300 troops, had a field hospital with a room for wound dressing available (Fig. 3), a hospital department (Fig. 4), a laboratory (Fig. 5) and a dental office (Fig. 6), but was lacking any X-ray facilities. The level 1 medical facility of the PMC developed at Camp Alpha (Babylon), based on a Star 660W truck, also did not have an X-ray device. However, it was possible to use the X-ray unit developed at the base by the Forward Surgical Team\* (FST), tasked with providing qualified surgical aid as well as to stabilise the life functions of the injured (level 2) [6]. A mobile X-ray device (DynaRad, Model 1200) (Fig. 7) was located in its own tent, and the problem of radiological protection was solved by creating a protective zone around the tent (Fig. 8). A patient lying on a stretcher was placed for examination on two transport cases, with which the office was furnished (Fig. 7).



**Figure 1.** Philips Bucky TH X-ray unit in a 20 foot container, 47 CSH in Camp Arifjan, Kuwait, 15 Aug 2003 (source: L. Kolarz)  
**Rycina 1.** Aparat RTG Philips Bucky TH w 20-stopowym kontenerze, 47 CSH w Camp Arifjan, Kuwejt, 15 sierpnia 2003 (źródło: L. Kolarz)

A similar mobile X-ray device (also with a fixed anode) was located at Camp Virginia in the area of Kuwait (Fig. 9). The issue of radiological protection was solved there in quite a different manner.

The reception, admission room, dressing room, laboratory, pharmacy, and even the long firearm storage of the medical personnel were isolated from the X-ray unit by means of a 2 m high protective wall built of sapper sandbags and covered on both sides with 10 mm plywood (Fig. 10).

Radiological support of the troops of 1BCT and MND CS at level 2 was provided at Camp Lima near Karbala by the Medical Support Group (MSG), which developed the Polish Field Hospital (PFH) there with a surgical and internal profile as part of shared national responsibility and CJTF-7 [2, 4, 7, 8]. The field X-ray unit was developed in a tent next to the admission room and the triage area [9]. In this case radiological protection was provided by a 20-foot container adapted on-site to perform the function of an X-ray darkroom. It separated the X-ray unit from the tent of the admission room [10]. The image diagnostics of the PFH was meant to be supplemented by a mobile X-ray Luminax-42X24 device with a "C" arm; however, this was damaged during sea transport (Fig. 11). This forced the use of a mobile HF 110CM device manufactured in the USA, not only in the admission room but also in the operating room (Fig. 12).

\* A Forward Surgical Team has no equivalent in the Polish Army. It is composed of 20 members: 1 orthopaedist, 3 surgeons, 2 nurse anaesthetists, ICU nurses, and medical technicians (number determined according to the current needs). The main task is the haemodynamic stabilisation of the injured by means

of surgical procedures, staunching the haemorrhage within the 'golden hour'. It can perform operations in the field of general surgery, orthopaedics, traumatology and, to a limited extent, neurosurgery.



**Figure 2.** Polish Military Contingent - aid station on a truck, Al Hilla 23 Sep 2003 (source: L. Kolarz)

**Rycina 2.** Polski Kontyngent Wojskowy-sala opatrunkowa na samochodzie ciężarowym, Al. Hilla 23.09.2003 r. (źródło: L. Kolarz)



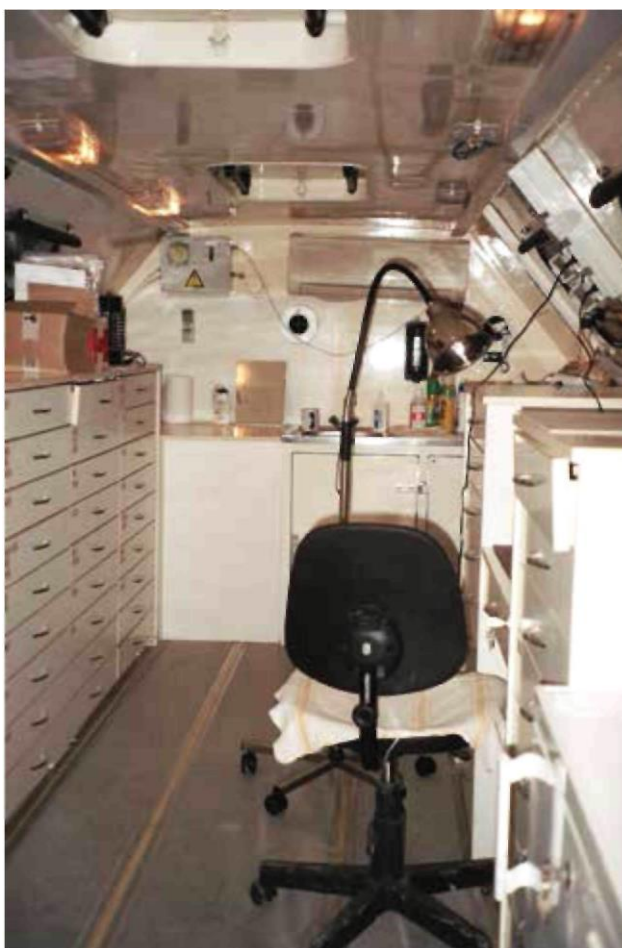
**Figure 4.** Hungarian Field Hospital - hospital ward, Al Hilla 23 Sep 2003 (source: Hilla 23 Sep 2003 (source: L. Kolarz)

**Rycina 4.** Węgierski Polowy Szpital - oddział szpitalny, Al. Hilla 23.09.2003 r. (źródło: L. Kolarz)



**Figure 3.** Hungarian Field Hospital-aid station in a former truck body, Al Hilla 23 Sep 2003 (source: Hilla 23 Sep 2003 (source: L. Kolarz)

**Rycina 3.** Węgierski Polowy Szpital - sala opatrunkowa w zdemontowanej kabinie samochodowej, Al. Hilla 23.09.2003 r. (źródło: L. Kolarz)



**Figure 5.** Hungarian Field Hospital-lab in a former truck body, Al Hilla 23 Sep 2003 (source: L. Kolarz)

**Rycina 5.** Węgierski Polowy Szpital - laboratorium w zdemontowanej kabinie samochodowej, Al Hilla 23.09.2003 (źródło: L. Kolarz)



**Figure 6.** Hungarian Field Hospital-dental office in a former truck body, Al Hilla 23 Sep 2003 (source: L. Kolarz)

**Rycina 6.** Węgierski Polowy Szpital - gabinet stomatologiczny w zdemontowanej kabinie samochodowej, Al Hilla 23.09.2003 (źródło: L. Kolarz)



**Figure 7.** Portable X-ray machine, FST in Camp Alpha (Iraq), 12 Dec 2003 (source: L. Kolarz)

**Rycina 7.** Mobilny aparat RTG, FST w Camp Alpha (Irak), 12.12.2003 (źródło: L. Kolarz)



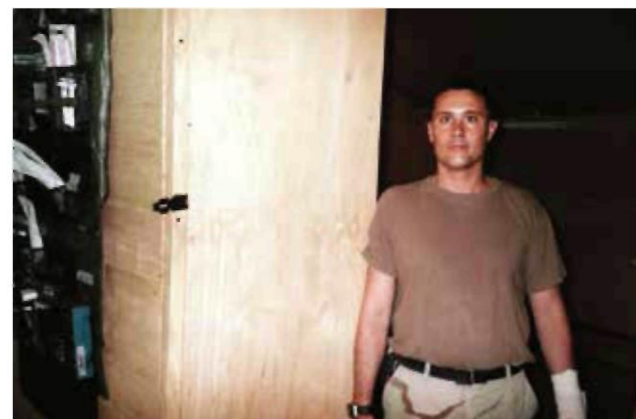
**Figure 8.** X-ray, FST tent in Camp Alpha (Iraq), 12 Dec 2003 (source: L. Kolarz)

**Rycina 8.** Namiot-gabinet RTG, FST w Camp Alpha (Irak), 12.12.2003 (źródło: L. Kolarz)



**Figure 9.** Mobile X-ray device in CSH, Camp Virginia at Al Jahra (Kuwait), Jan 2004 (source: L. Kolarz)

**Rycina 9.** Mobilny aparat RTG w CSH, Camp Virginia w Al Jahra (Kuwejt), styczeń 2004 (źródło: L. Kolarz)



**Figure 10.** X-ray protection wall in CSH, Camp Virginia at Al Jahra (Kuwait), Jan 2004 (source: L. Kolarz)

**Rycina 10.** Ściana ochronna gabinetu RTG w CSH, Camp Virginia w Al Jahra (Kuwejt), styczeń 2004 (źródło: L. Kolarz)



**Figure 11.** Damaged X-ray machine, Luminax-42X24 with a "C" arm, in a container, Aug 2003 (source: L. Kolarz)

**Rycina 11.** Uszkodzony aparat RTG Luminax-42X24 z ramieniem „C” w kontenerze, sierpień 2003 (źródło: L. Kolarz)

The PFH also included a mobile dental ambulance (Fig. 13) equipped with a dental X-ray device and an X-ray device for taking panoramic radiograph images (Fig. 14). During the first rotation the PMC the group of 12 physicians of the MSG represented 12\* medical specialities\* and enabled provision of qualified medical aid (with elements of specialised aid) to a degree greater than just within the scope of internal diseases, general and trauma surgery.

### Medical evacuation and X-ray diagnostics

Medical evacuation from the site of the event (level 1) to the PFH was mainly implemented by means of wheeled transport of the national contingents [2, 11]. Polish and American medical helicopters were used in the case of a necessity to evacuate the heavily injured (HELIMEDEVAC).

\* Medical analysis, anaesthesiology, surgery, internal medicine, dermatology, epidemiology, maritime and tropical medicine, neurology,



**Figure 12.** Mobile X-ray machine, HF 110CM in an operation room, Camp Lima (Iraq) 6 Nov 2003 (source: L. Kolarz)

**Rycina 12.** Mobilny aparat RTG HF 110CM na bloku operacyjnym, Camp Lima (Irak) 06.11.2003 (źródło: L. Kolarz)

The continuation of medical evacuation as a part of CJTF-7 from the level of the 1 BCT tactical formation was 28 CSH (level 3), which on 28 August 2003 was finally moved to the buildings of the Ibn Sina Hospital [12]. This hospital, located in the 'green area' of Baghdad, thanks to the CT scanner and improved staffing in the fields of ophthalmology, neurosurgery and neurology, as dictated by the frequent eye and head injuries of the troops, could conduct highly specialised operations. In practice the hospital achieved level 4, concerning hospitals operating outside the area of war operations. It should be emphasised that at no stage of the medical evacuation, not only in Iraq but also in Kuwait, were there any mobile MRI scanners [13].

ophthalmology, orthopaedics, psychiatry, psychology and radiology.



**Figure 13.** Mobile dental ambulance, Camp Lima (Iraq), Sep 2003 (source: L. Kolarz)

**Rycina 13.** Ruchomy gabinet dentystyczny, Camp Lima (Irak), wrzesień 2003 (źródło: L. Kolarz)



**Figure 14.** Digital pantomograph in a mobile dental ambulance, Camp Lima (Iraq), Sep 2003 (source: L. Kolarz)

**Rycina 14.** Pantomograf cyfrowy w ruchomym gabinecie dentystycznym, Camp Lima (Irak), wrzesień 2003 (źródło: L. Kolarz)

## Discussion

In an assessment of the utility of the equipment available in a field diagnostic imaging lab, it is necessary to emphasise the versatility of uses of a mobile X-ray device. However, in the course of the mission to Iraq there was a noticeable and significant limitation in the capacity and efficiency of the X-ray diagnostics in the case of an increased inflow of the injured, as occurred during periods of intensified fighting in Karbala. These indicated the advisability of redefining the role of the radiologist and that of diagnostic imaging at the level of the admission room and triage area. Diagnostic imaging conducted by a team of technicians and a radiologist, in order for it to be useful, efficient and economically justified, cannot be detached from the scope of aid provided at the stages of medical evacuation. This is partly a result of the specificity of work of this organisational unit and the results expected from it.

Though the tasks of specialists, such as the anaesthesiologist, surgeon, internist, ophthalmologist, dermatologist, and even psychiatrist or psychologist seem clear, the role of a radiologist, who was permanently assigned to the admission room, does not seem to be defined in its full extent. However, diagnostic imaging has much to offer at particular stages of medical evacuation.

- LEVEL 1.** Level 1 covers immediate pre-medical aid provided on the battlefield, which includes actions intended to save life as a part of self-aid or mutual aid (combat lifesaver). Qualified aid (advanced life support – ALS) is provided by paramedics and physicians specialising in emergency medicine. This includes decompression of the pneumothorax, pleural drainage, intubation, IV access, fluid resuscitation, respiratory stabilisation, cricothyrotomy and tracheotomy.

**Conclusions.** A good solution for diagnostic imaging is the equipment introduced by the U.S. Army, the Infrascanner 2000 (Fig. 15), already tested in Iraq in 2008. It enables quick diagnostics for head/brain injuries (traumatic brain injury – TBI). Infrascanner is a mobile, non-invasive device for screening for the presence of intracranial haemorrhages under field conditions, up to depths of 35 mm from the surface of the skin. The examination is based on a comparative analysis of symmetrical areas of the lobes of the brain: frontal, temporal, parietal and occipital lobe up to 48 hours from the occurrence of the bleeding. The sensitivity reaches 88% and the method effectiveness reaches 90%, which allows the detection of subdural and epidural haematomas with a volume as low as 3.5 ml and intracerebral up to depths of 25 mm from the surface of the brain. In terms of usability this puts the Infrascanner at this stage of assessment of trauma and priorities for medical evacuation on an equal level with mCT (mobile computer tomography). The second device in terms of mobility and capability is an ultrasound scanner with a 7.5 MHz linear transducer. It has been proven that a linear transducer with a frequency of 7.5 MHz is more effective in revealing damage to the parenchymatous organs during FAST (focused abdominal sonography for trauma) than a 3.5 MHz phased array transducer [14, 15]. The main objective of FAST is to detect free fluid in the peritoneal cavity in patients with non-penetrating injuries of the abdominal cavity, and then to attempt to determine the source of the haemorrhage. FAST also enables exposure of damage to the parenchymatous organs of the abdominal cavity, such as liver, spleen and kidneys [14]. FAST ultrasound is also useful in fluid diagnostics in the pericardial sac, pleural cavity and pneumothorax diagnostics. FAST has numerous limitations, but the fundamental ‘flaw’ is the requirement of skill and experience in the use of the equipment. FAST, with its standard duration of 2-3 minutes is a very helpful tool in triage, and allows the determination of the necessity, urgency and order of surgical interventions [15].



**Figure 15.** Infrascanner Model 2000 (source: [www.fortune.com/2013/03/29/the-u-s-militarys-miracle-sca](http://www.fortune.com/2013/03/29/the-u-s-militarys-miracle-sca))  
**Rycina 15.** Infrascanner Model 2000 (źródło: [www.fortune.com/2013/03/29/the-u-s-militarys-miracle-sca](http://www.fortune.com/2013/03/29/the-u-s-militarys-miracle-sca))

- LEVEL 2.** The Forward Surgical Team (Level 2) provides ophthalmological, dental, psychiatric care, as well as laboratory and image diagnostics (X-ray/ultrasound). The profile of operations covers resuscitation procedures, saving life within the scope of general surgery, orthopaedics and traumatology, as well as neurosurgery. This is based on the idea of surgical damage control strategy, which covers: treatment of pelvic fractures and temporary stabilisation of the long bones, abbreviated craniotomy, abbreviated thoracotomy, tracheotomy and relaparotomy.
- Conclusions.** It seems that the most rational solution is a quick scan, lasting 13 seconds (in the AP view), of the entire body using a low dosage X-ray, abbreviated as LODOX (Fig. 16). A significant advantage of this device is not only speed, but also the 10 times lower exposure dose than for a conventional examination. The potential/capacity of such diagnostics in the case of mass inflow of the wounded and stricken is proven by the fact that the devices operating on the basis of a similar principle have been broadly used, including for luggage inspection at airports. This method enables assessment of both lung aeration and detection of bullets, shrapnel and trauma and gunshot bone fractures. Even the assessment of the extent of bone trauma enables preliminary assessment of any potential blood loss.



**Figure 16.** LODOX / Statscan (Source: [www.ebdaeng.com/data/products/Lodox/statscan.html](http://www.ebdaeng.com/data/products/Lodox/statscan.html))  
**Rycina 16.** LODOX, Statscan (źródło: [www.ebdaeng.com/data/products/Lodox/statscan.html](http://www.ebdaeng.com/data/products/Lodox/statscan.html))

It is estimated that an adult may lose:

- 1-1.5 l of blood from a damaged lung
- 2 l of blood from a damaged liver,
- 2 l of blood from a damaged spleen,
- 3-5 l of blood in the case of pelvic trauma,
- 1.5-2 l of blood due to a femoral fracture,
- 1 l of blood due to a tibia/fibula fracture,
- 0.8 l of blood due to a humerus fracture,
- 0.4 l of blood due to a forearm fracture [16].

Such information is very useful when planning an effective strategy for operations in an admission room/triage area and implementation of proper fluid therapy, including blood transfusion.

**Abbreviated craniotomy for the purpose of decompression of the intracranial hypertension.** The operation includes the performance of the following procedures: removal of a part of the calvaria, opening of the dura mater, haematoma evacuation, direct removal of the damaged tissues and covering the cavity with a loose transplant of biological membrane.

**Conclusions.** The optimal solution is preliminary assessment using the Infrascanner and a LODOX device. The currently produced LODOX devices also enable scans in lateral views, but this extends the examination to 3-4 minutes. Therefore, in an admission room at level 2 it is only justified to perform a simplified 13-second procedure, and the potential doubts can be dispelled by means of taking targeted images with a mobile X-ray device in the admission room or with an X-ray device with a "C" arm in the operating room.

**Abbreviated laparotomy.** This is aimed at stopping the haemorrhage and preventing contamination of the abdominal cavity. The operation includes the performance of the following procedures: manual pressure on the openly bleeding vessels, removal of a bleeding spleen, haemostatic packing of the liver and the retroperitoneal space, temporary closure of disrupted vessels, temporary closure of an open lumen of the intestine with a purse-string suture, stapler, suture exclusion or partial resection without anastomosis, closure of the layers (often without drainage) and prevention of abdominal compartment

syndrome.

**Conclusions.** In the case of abbreviated laparotomy and thoracotomy in Trauma Room practice it is possible to conduct a 2-3-minute ultrasound examination (focus assessment with sonography for trauma - E-FAST/ BLUE PROTOCOL) before the procedure.

**Abbreviated thoracotomy.** This is meant to stop haemorrhages and major air leaks. The following procedures are conducted during the surgery: haemostatic packing of the pleural cavity, manual pressure, non-anatomic lung resection, treatment of damaged vessels, simple suture of the lung parenchyma, direct closure of the main bronchus, aortic bypass surgery and treatment of heart wounds.

**Tracheotomy** with endotracheal intubation and without intubation.

**Conclusions.** Diagnostics using a mobile X-ray device allow the assessment of lung ventilation and the location of the tube in the trachea, whereas an ultrasound detects the presence of any fluid in the pleural cavity.

The final reconstructive **laparotomy** (final operation) includes the removal of haemostatic packing, final handling of the liver damage, restoring the blood flow to the organs, restoring the continuity of the digestive tract and identification and comprehensive repair of previously unidentified damage. The closing of the abdominal cavity should often be performed with the maintenance of the so-called 'open abdomen', preventing abdominal hypertension and precarious swelling of the intestines.

**Conclusions.** From the point of view of diagnostic imaging the implementation of the aforementioned scope of provided medical aid justifies the possession of the following diagnostic kits at level 2:

- in the admission room: infrascanner, LODOX and a mobile X-ray and ultrasound device,
- in the operating room: a mobile X-ray device with a "C" arm.

The author's experiences (from a period of service during the second rotation of the PMC in Iraq) confirm the major usefulness of a mobile X-ray device, due to the following:

- ease of use,
- 230V power supply for the X-ray device
- the option of establishing an autonomous power supply for the X-ray device by means of a mobile power generator, which enables quick activation of the X-ray unit during the initial phase of development of the hospital.
- low weight of the X-ray device itself, as well as large and wide wheels, facilitating movement of the device, even

on unpaved surfaces between the admission room, operating room and the hospital department,

- X-ray tube with a fixed anode and sealed housing, which enable safe use of the device, even in the case of major amounts of dust in the air (sandstorms); limitations to the use of a fixed anode include lower kV values and exposure times, as well as the necessity of taking longer breaks between the exposures in order to avoid overheating of the lamp (anode).

- **LEVEL 3.** A Level 3 field hospital represents the top tier of medical care developed in the backstage of the theatre of operations. It is used to conduct advanced resuscitation and reanimation, as well as surgical procedures. The profile of operations includes general surgery, orthopaedics, neurosurgery, urology, dentistry and maxillofacial surgery. The injured and sick are covered by specialised care and prepared for evacuation to the prophylactic and therapeutic districts in their home countries or for return to service. The medical personnel comprises general surgeons, traumatologists, neurosurgeons, maxillofacial surgeons, anaesthesiologists, internists, a urologist, a gynaecologist and an otolaryngologist.

- **Conclusions.** The above scope of aid justifies the extension of diagnostic imaging not only with a mobile, but also with a stationary X-ray device, preferably built-up in a container (Figs. 1 and 17). This solution allows the designation of safe zones for use of the X-ray device already during the construction stage, including a graphic layout of the dose strength, not only around the X-ray device, but also the container [8, 10]. A good example is the design of an X-ray unit in a container created on the basis of experiences in Iraq, implemented by the 1st Peacekeeping Operations Hospital in Bydgoszcz. The first trials with a 20-foot container as an X-ray unit were already conducted in 2003 in Camp Lima near Karbala (Fig. 17), but in the end the project was abandoned for the benefit of adapting the container to act as a darkroom, as the PFH only had a 'wet' automatic CURIX 96 film processor [9]. The scope of the conducted operations justifies equipping the operating room with an X-ray device with a "C" arm and mCT (for head examinations), provided that teams are available and ready to conduct operations within the scope of neurosurgery and maxillofacial surgery.

- **LEVEL 4.** A level 4 field hospital (mobile or stationary) was located outside the place of conflict (Kuwait/



**Figure 17.** Darkroom under construction in a 20ft container, built by the radiological team and evaluation of placing an x-ray unit inside the container. Camp Lima, 11 Sep 2003 (source: L. Kolarz)  
**Rycina 17.** Budowa ciemni w 20-stopowym kontenerze przez zespół radiologiczny oraz ocena możliwości budowy gabinetu RTG w kontenerze, Camp Lima, 11.09.2003 r. (źródło: L. Kolarz)

Germany), maintaining constant communication with the theatre of operations. Evacuation of the injured extends to the strategic level. Such a unit offers a full scope of medical and surgical care, as well as the performance of specialised operations within the scope of general surgery, orthopaedics, neurosurgery, urology, dentistry, maxillofacial surgery, gynaecology and obstetrics.

- **LEVEL 5.** This covers: departmental hospitals in the home country and civilian hospitals as a part of the National Crisis Management Plan. Medical care at this stage is available in a full and highly specialised scope [18].

## Conclusions

Armed forces in each country undergo constant processes of modernisation, both within the scope of equipment and the forms of organisation. This is in line with professionalisation of the armies in highly developed states, which involves increasing the specialisation and decreased the staffing combined with the increasing combat value of a single soldier. This is dictated by reasons of a political, economic and demographic nature. Another significant factor is that modern conflicts and expeditionary operations are dominated by low-intensity activities, directed mainly against non-regular and terrorist formations. The scope of conducted diagnostic imaging in the context of providing medical aid at particular stages of medical evaluation should include:



**Figure 18.** Mobile MR Imaging Unit at Bagram Air Base in Afghanistan (source: RNSA News: 2013; 2 [vol. 23]: 2)

**Rycina 18.** Mobilny rezonans magnetyczny na lotnisku bazy wojskowej w Bagram Air Base w Afganistanie (źródło: RNSA News: 2013; 2 [vol. 23]: 2)

- **LEVEL 1** – equipping medical teams with mobile non-invasive infrascanner devices (Fig. 16), which enable quick/screening diagnostics of head/brain trauma aimed at the presence of intracranial haemorrhages reaching up to the depth of 35 mm, i.e. subdural and epidural spaces; the second device in terms of usefulness is a mobile ultrasound device, which, however, requires more skill and experience from the medical personnel;
- **LEVEL 2** – the admission room should be equipped with: infrascanner, LODOX, mobile ultrasound and X-ray device with a “C” arm at the operating room; for the purpose of more effective utilisation of a radiologist and diagnostic imaging it seems more prospective to introduce a low dose X-ray (LODOX) to the list of equipment of an admission room built-up in a container; the advantage of using this type of X-ray diagnostics is that it is quick, lasting only 13 seconds, and a scan of the entire body in the AP view requires no special positioning nor selecting a field for examination, with the exception of putting the injured on the X-ray table, even on a stretcher; at the same time LODOX detects elements of armament (ammunition, grenades), therefore increasing the safety of the personnel;
- **LEVEL 3** – there are grounds for the extension of diagnostic imaging by a stationary X-ray device built-up in a container and mCT (mobile computer tomography) for head examination, provided that neurosurgical or curative treatment within the scope of maxillofacial surgery is available, which is basically conducted at level 4, though this is not the final word on the matter, as indicated by Fig. 18.

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# Health effects of ozone air pollution

## Skutki zdrowotne zanieczyszczenia powietrza ozonem

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The article is based on a lecture presented in the Military Institute of Medicine in Warsaw on 21 April 2017 during the 7<sup>th</sup> Scientific Conference in honour of Brig. Gen. Assoc. Prof. Wojciech Lubiński MD, PhD: The Effect of Air Pollution on Health

**Abstract:** Tropospheric ozone is a main component of "photochemical smog". Most of the Polish population is exposed to it in concentrations exceeding the WHO Air Quality Guidelines, and a substantial part also to levels exceeding the air quality standards legally binding in Poland. Ozone causes the development and exacerbation of respiratory diseases. Epidemiological studies also show an increase in the number of hospital admissions and in mortality on days with increased ozone levels. A growing number and quality of large cohort studies indicate the negative health effects of long-term exposure to ozone, such as an increase in asthma incidence and mortality, including that due to cardiovascular diseases. The health burden of ozone exposure is, according to current assessments, markedly lower than the health effects of fine particulates. However, growing knowledge on the health effects of ozone may, in the near future, enable to significantly increase these estimates, especially since the changes in population exposure are expected to be small.

**Key words:** respiratory diseases, cardiovascular diseases, ozone, mortality, air pollution

**Streszczenie.** Ozon troposferyczny jest głównym składnikiem „smogu fotochemicznego”. Większość ludności w Polsce narażona jest na jego stężenia przekraczające zalecenia WHO, a znaczna jej część również na stężenia przekraczające normy jakości powietrza prawnie obowiązujące w Polsce. Ozon przyczynia się do powstawania i zaostrzenia chorób oddechowych. Badania epidemiologiczne wskazują również na zwiększenie liczby przyjęć do szpitali i umieralności w dniach ze zwiększonymi stężeniami ozonu w powietrzu. Rosnąca liczba i coraz lepsza jakość dużych badań kohortowych wskazuje także na negatywne skutki zdrowotne długookresowego narażenia na ozon, takie jak zwiększenie zapadalności na astmę oraz umieralności, w tym spowodowanej chorobami układu krążenia. Koszty zdrowotne narażenia na ozon są, według aktualnych oszacowań, znacznie mniejsze niż wpływu drobnych pyłów na zdrowie populacji. Powiększająca się wiedza na temat oddziaływania ozonu na zdrowie może jednak w niedalekiej przyszłości spowodować znaczny wzrost tych oszacowań, zwłaszcza przy oczekiwanej niewielkiej zmianie narażenia populacji.

**Słowa kluczowe:** choroby układu krążenia, choroby układu oddechowego, ozon, umieralność, zanieczyszczenia powietrza

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### Introduction

Ozone (O<sub>3</sub>) is the main component of "photochemical smog", observed usually in summer, in windless, sunny weather, in areas of intense road traffic and developed industry. It is a strongly oxidising gas whose the molecules are composed of three atoms of oxygen. In the lower layers of the atmosphere it is formed as a result of photochemical reactions involving nitrogen oxides, volatile organic compounds, methane and carbon oxide [1]. As these gases are relatively stable, and can be transferred in the atmosphere for hundreds or thousands of kilometres, ozone can be found throughout the atmosphere, including locations distant from the sources of the original gases. Due to the increasing use of fossil fuels, the emission of gases from rice fields and animal farms (sources of methane), the concentration of ozone over the oceans and sparsely populated areas have increased from approximately 30 to 75 µg/m<sup>3</sup> in the past 100 years [1].

Stratospheric ozone, providing the earth's surface with essential protection against cosmic ultraviolet radiation, also contributes to a limited extent to the concentration of ozone near the surface of the earth. The rate of ozone formation in the atmosphere depends largely on the intensity of the solar radiation; therefore, ozone concentrations are higher in the low latitude regions, in summer and in the middle of the day, when solar radiation is intense. Ozone quickly reacts with nitrogen oxide (NO), forming nitrogen dioxide (NO<sub>2</sub>). As a result, ozone concentrations in city centres with heavy road traffic, an important source of nitrogen oxides, are usually lower than on the outskirts, in the suburbs or away from urban areas. Ozone penetration into buildings is generally limited by the reactions on the surface of the walls and windows, so ozone exposure is primarily an outdoor phenomenon.

The toxic properties of ozone in the atmosphere are well-studied and described in the literature. Tropospheric ozone has been demonstrated to have adverse effects on plants, reducing agricultural crops and damaging forests. It is also one of short-lived greenhouse gases contributing to the global warming. The World Health Organisation (WHO) guidelines recommend maintaining an 8-hour mean ozone concentration at  $<100 \mu\text{g}/\text{m}^3$  [2]. However, they emphasize that even lower concentrations may adversely affect the health of sensitive individuals. According to the Polish and European standards for air quality, the 8-hour mean ozone concentration should not exceed  $120 \mu\text{g}/\text{m}^3$  for more than 25 days per year. In 2015, in Poland this value was higher in 30 out of 65 sampling points [3]. Concentrations of  $>120 \mu\text{g}/\text{m}^3$  were observed also in all other monitoring points, although for fewer days in 2015.

The aim of this article is to present and summarise the results of recently published literature reviews regarding the health effects of exposure to atmospheric ozone. The conclusions formulated in systemic literature reviews are illustrated or completed with the results of certain studies. Selected results of assessments of the quantitative effect of ozone on the health across the world and in Poland are also presented.

### Pathophysiological mechanisms associated with ozone

Breathing is the major route of exposure to ozone in humans. In normal breathing, approximately 75% of the inhaled ozone is absorbed by the upper respiratory tract and bronchi [2]. As ozone absorption by the upper respiratory tract is lower while breathing through the mouth than through the nose, the penetration of ozone to the lungs is increased during intensive physical effort. The size and surface of the walls of the respiratory tract also affect ozone absorption, making it higher in children and women. The mucus covering the bronchial mucosa prevents direct exposure of the epithelium to ozone; however, the products of oxidation of certain ingredients of the mucus may damage the epithelial cells and lead to inflammation. The degree of ozone absorption can also be affected by the quantity of antioxidants in the mucus, such as vitamin E, related to the nutritional status. Respiratory diseases such as asthma, chronic bronchitis or emphysema result in irregular air flow, and associated uneven exposure of certain parts of the respiratory tract to the inhaled ozone. This increases the susceptibility of those patients to the harmful effects of ozone exposure.

The inhaled gas may adversely affect the organism in many ways [2]. Even short inhalation of ozone leads to the formation of diffused foci of inflammation in the respiratory system, particularly in the nose and bronchi. The inflammation is not limited to the respiratory tract; it increases the hepatic activity, and non-specific immune response. The pulmonary defence systems are activated immediately, and normalise in the case of long-term ( $>3$  days) exposure. Bronchial hyperactivity is observed with the ozone concentrations frequently observed in the ambient air. In repeated exposure the defence reactions of

the respiratory tract are attenuated, but the inflammation, especially in bronchioli, may persist. Prolonged exposure to ozone results in structural lesions in the lungs: mucosal hyperplasia, constriction of the bronchioli, and alveolar fibrosis. These change partially subside after the end of exposure. The sensitivity to adverse effects of ozone is increased by the existing respiratory diseases, advanced age or genetic factors. Although there is evidence for a mutagenic effect of ozone on the cells of the respiratory tract, the carcinogenic properties of the gas have not been confirmed. Certain studies also indicate that ozone has a toxic effect on the nervous system [4].

### Health effects of short-term exposure to ozone

Toxicological, clinical and epidemiological studies on the health effects of short-term (a few hours) exposure to ozone at the concentrations frequently observed in the ambient air were conducted in the 1970s. Extensive literature in this area was regularly analysed and summarised by WHO while developing new guidelines regarding air quality [2]. The newest WHO studies include reports from the REVIHAAP project [5], indicating constant progress in our understanding of the effects of ozone exposure, and from the HRAPIE project [6], which presents recommendations regarding the scope and parameters of a quantitative risk assessment of population exposure to ozone. The results of the latest systematic literature review conducted by the United States Environmental Protection Agency (USE-PA) were published in 2013 [7]. Table 1 summarises the conclusions from this review regarding the causal relationship between exposure to ozone and health effects.

The results of laboratory, clinical and epidemiological studies demonstrate that short-term exposure to ozone is a cause of respiratory diseases. Controlled clinical studies indicate a significant, although transient, reduction in pulmonary ventilatory efficiency, and the occurrence of respiratory symptoms (scratching in the throat, cough, shortness of breath, chest pain with deep inhalation) in young, healthy individuals exposed for a few hours to ozone at concentrations from  $140 \mu\text{g}/\text{m}^3$  [8]. Reduced ventilatory efficiency of the lungs, associated with increased concentrations of ozone, was observed in many panel studies involving healthy children or children with asthma, especially in combination with increased physical effort [7].

Epidemiological studies also revealed the increased incidence of respiratory diseases on days when the ozone concentration in the air was elevated. One of them was an 18-year time series study analysing visits of children under 5 years of age to the emergency rooms of Atlanta hospitals [9]. It reported a significant increase in the number of visits due to upper respiratory tract inflammation and pneumonia on the days following three days of ozone concentrations elevated by 0.7% (95% CI: 0.4-1.1) and 1.4% (95% CI: 0.7-2.3) respectively, with a  $10 \mu\text{g}/\text{m}^3$  increase in ozone concentration, measured as a 3-day average of maximum daily 8-hour means. The risk was higher among children

aged 1-4 years old than in infants. The relationship between the incidence and ozone concentrations was stronger than in the case of other analysed air pollutants (PM<sub>2.5</sub>, molecular carbon, carbon oxide, nitrogen dioxide). A metaanalysis of all 16 available studies on the relationship between pneumonia in children under 18 years of age and short-term exposure to ozone revealed a 0.9% (95% CI: 0.2-1.4) increase in the risk of hospitalisation (or visits to hospital emergency rooms) per 10 µg/m<sup>3</sup> increase in ozone concentration in the air (measured at an 8-hour mean) [10]. A significant correlation with pneumonia was also found for other pollutants: PM<sub>10</sub>, PM<sub>2.5</sub>, SO<sub>2</sub> and NO<sub>2</sub>. Despite a considerable discrepancy between the results of studies, the strength of the relationship was similar for hospitalisations and emergency room admissions among children of various ages (under or above 5 years), and in populations with different incomes.

**Table 1. Evidence on the causality of ozone health effects - USEPA assessment, 2013 [7]**

**Tabela 1. Dowody dotyczące przyczynowości związku zdrowia z narażeniem na ozon wg Oceny USEPA, 2013 [7]**

	Exposure to ozone	
	Short-term	Long-term
Respiratory diseases	+++	++
Cardiovascular diseases	++	+
Effect on the central nervous system	+	+
Perinatal health disorders		+
Neoplasms		-
General mortality	++	+
Mortality due to circulatory causes	++	+
Mortality due to respiratory causes	++	+

+++ - causative relationship, ++ - probably causative relationship, + - suspected relationship, (-) - insufficient evidence of a relationship

All age groups - both children and adults - were included in a large, approximately 3.7 million-case analysis of visits to hospital emergency rooms in California due to various respiratory symptoms [11]. The general number of visits increased by 0.4% (95% CI: 0.3-0.5) per 10 µg/m<sup>3</sup> of the maximum daily 1-hour average on the day of the visit or the day before. A relationship between the number of visits and the ozone concentration on the day of the visit or up to 3 days before was observed also for asthma (1.2%; 95% CI: 0.7-1.6), acute respiratory infections (0.4%; 95% CI: 0.3-0.6), pneumonia (0.2%; 95% CI: 0.1-0.5) and infections of the upper respiratory tract (1.2%; 95% CI: 0.2-2.3). The relationships were stronger in warm periods, compared to the whole year. They were not significantly associated with the exposure to other air pollutants, age, sex or ethnicity of the patients.

A systematic review of studies on the relationship

between the number of visits to hospital emergency rooms or hospitalisations due to asthma and air pollution identified 71 studies published up to 2014 which included ozone exposure [12]. The metaanalysis of all these studies indicated a 0.9% (95% CI: 0.6-1.1) increase in the number of visits per 10 µg/m<sup>3</sup> increase in ozone concentration on the day of the visit or in the preceding days. A slightly stronger correlation between visits and exposure to ozone was observed in women than in men, but no significant difference was found in the intensity of the relationship in various age groups for visits with or without hospitalisation, or with the exposure within two days before the visit or earlier.

The European part of the APHENA study revealed an increase in the number of hospital admissions of patients over 65 years of age due to cardiovascular diseases (ICD-9: 390-429) on those days with elevated ozone concentrations or one day after [13]. The frequency of hospitalisations increased by 0.64% (95% CI: 0.36-0.91) per 10 µg/m<sup>3</sup> increase in the maximum daily 1-hour mean ozone concentration. The study analysed the data regarding hospitalisation from eight European countries. However, this correlation was not observed in the hospitalisation data of all US citizens over >65 years of age or Canadian citizens, also included in the APHENA study. In the study of hospital admissions in 14 large cities in China, including over 80 thousand hospitalisations due to a recent myocardial infarction (ICD-10: 121-122), a significant increase in their frequency was observed four days after a day of elevated ozone exposure [14]. This relationship was also visible after consideration of the effect of other air pollutants, although it was not significant for different time intervals between the day of increased exposure to ozone and hospitalization, and on the day following the exposure a reduced risk of hospitalisation was reported.

Considering the ambiguity of the results of epidemiological studies, the probability of a relationship between cardiovascular diseases and ozone exposure in the USEPA report [7] was based primarily on the studies on animals. They indicate changes in the autonomic nervous system, associated with exposure to ozone, and development and persistence of oxidative stress, as well as inflammation in the respiratory system and in other organs. Some controlled clinical studies in humans are consistent with the results of studies on animals, which indicate changes in inflammatory [15, 16] and oxidative stress [17] biomarkers due to exposure to air ozone, and suggest a susceptibility to thrombus formation [15]. These observations also provide a biological justification for the results of epidemiological studies on the effect of ozone air pollution on mortality.

The relationship between the daily number of deaths and air concentrations of ozone was studied in many populations, using time series analysis. A collective analysis of long-term data from 135 American, Canadian and European cities performed within the APHENA project [13] was the basis for relative risk coefficients developed by WHO [6] for the European assessments of the effects of exposure to ozone. According to this analysis, the daily number of deaths due to all natural causes increased by

0.29% (95% CI: 0.14-0.43) per 10  $\mu\text{g}/\text{m}^3$  increase in ozone concentration, measured as a maximum daily 8-hour mean. The analysis also indicates that the mortality due to cardiovascular causes increased by 0.49% (95% CI: 0.13-0.85), and due to respiratory diseases by 0.29% (95% CI: -0.11-0.70, i.e. statistically insignificantly) per 10  $\mu\text{g}/\text{m}^3$  increase in ozone concentration. For the total of deaths and cardiovascular diseases higher risk coefficients were observed for people under 75 years old than for older individuals. Very similar risk ratios were estimated in a recently published analysis of data from 272 Chinese cities, including 290 million citizens [18]. According to the authors of this study, the daily number of deaths due to natural causes increases by 0.24% (95% CI: 0.13-0.35), and due to cardiovascular diseases by 0.27% (95% CI: 0.10-0.44) per 10  $\mu\text{g}/\text{m}^3$  increase in 8-hour mean ozone concentration. For deaths due to respiratory causes, the risk factors were not statistically significant, similarly to the APHENA study.

Toxicological studies suggest that short-term exposure to ozone may affect the central nervous system [7]. They revealed deterioration in the short-term and long-term memory in rats after 15 days of exposure to ozone at a concentration of 500  $\mu\text{g}/\text{m}^3$  [19]. This is probably associated with damage to the hippocampus due to oxidative processes triggered by ozone [19, 20]. The damage associated with oxidation was also observed in other parts of rat brains [21, 22].

### Health effects of long-term exposure to ozone

The results of epidemiological studies conducted within the past several years, supported by the results of toxicological studies, allow the conclusion that long-term (over one month) exposure to ozone probably contributes to the occurrence and development of respiratory diseases, especially asthma [7]. An important source of information in this area is a cohort study involving children (aged 9-16 years old at the beginning of the observation) conducted in South California [23]. In a 5-year long observation period the incidence of asthma among all the children living in an urban area with elevated ozone concentration (a 4-year average of maximum daily 1-hour means was 150  $\mu\text{g}/\text{m}^3$ ) was not higher than in children from the areas with lower ozone concentrations (100  $\mu\text{g}/\text{m}^3$ ). However, in the areas with increased ozone concentrations the incidence of asthma was 3.3 times higher (95% CI: 1.9-5.8) among the children practising three or more sports compared to those who did not do any sports. This correlation was not found among the population of the area with lower levels of ozone pollution. Later studies by the same researcher indicate that in children living in the area with lower ozone concentrations, the occurrence of certain genetic variants (*HMOX-1*, *GSTP1*, *ARG1*) that demonstrate antioxidative or anti-inflammatory properties is associated with a lower incidence of asthma [24]. The absence of this relationship in those children exposed to higher levels of pollution is interpreted as a sign of "maximum saturation" of the

protective effect of these genes at high doses of oxidative substances.

The relationship between the incidence of asthma and exposure to ozone is illustrated by a cohort study involving over 1.2 million children in the state of New York in the years 1995-1999, observed until the end of 2000 [25]. The risk of the first (in life) hospital admission due to asthma was significantly increased along with a long-term mean ozone concentration at the place of child's residence. In New York City, the probability of hospitalisation of a third of the children with the highest ozone exposure was 69% (95% CI: 52-80) higher than in the third of children with the lowest exposure. For children from other areas of New York state, this increase in the risk was 106% (95% CI: 87-127). Long-term mean ozone concentrations calculated on the basis of 8-hour means during the daily elevation of ozone levels (between 10:00 and 18:00) were in the range 62-110  $\mu\text{g}/\text{m}^3$ . A relatively high increase in the risk due to a long-term exposure may indicate that it contributes to the growing number of children with asthma. This group may be particularly susceptible to short-term elevations of ozone concentration, resulting in exacerbations of the disease later in life, including hospitalisations [26].

A systematic literature review and metaanalysis of studies on the relationship between mortality and long-term exposure to ozone, covering studies published until September 2015, provided 14 articles presenting analyses of the data from eight cohorts [27]. Most data were from American studies, in particular from the American Cancer Society Cancer Prevention Study (ACS CPS) cohort which was the source of five articles. The metaanalysis of the results from all the available studies did not reveal any statistically significant relationship between all-cause mortality or mortality due to cardiovascular or respiratory diseases and long-term mean ozone concentrations at the place of residence. However, the studies using the data regarding ozone concentrations in the warm seasons or maximum daily ozone concentrations indicated a potentially elevated risk of death, especially due to cardiovascular and respiratory causes, in populations with higher exposure to ozone. The results of one of the studies in the metaanalysis, covering 18 years of data from the observation of the ACS CPS cohort including 448 thousand of adult USA citizens [28], were used by the HRAPIE project to propose a risk coefficient [6]. According to this study, the risk of death due to respiratory causes increased by 1.4% (95% CI: 0.5-2.4) per 10  $\mu\text{g}/\text{m}^3$  increase in long-term exposure to ozone, calculated on the basis of maximum daily 8-hour means in summer.

In the recent years, new outcomes of the studies on the relationship between mortality and long-term exposure to ozone have become available. The ones from the extended ACS CPS, covering the cohort of over 669 thousand adult US citizens, followed from 1982 to 2004 [29], present twice as high mortality than in the previous analysis from the same study [28]. Long-term means of maximum daily 8-hour average ozone concentrations were estimated more precisely for areas of 36 x 36 km (for the majority of the study group, also for the squares of 12 x 12 km). According to the analysis of exposure to small particulate matter and nitrogen dioxide (as well as other

disturbing factors), the risk of death due to all causes increased by 1.0% (95% CI: 0.5-2.0) per 10  $\mu\text{g}/\text{m}^3$  increase in exposure to ozone. The number of deaths due to all cardiovascular causes increased by 1.5% (95% CI: 0.5-2.5), whereas mortality due to cardiac rhythm disorders, cardiac failure or cardiac arrest increased by 7.5% (95% CI: 5.0-10.0) per 10  $\mu\text{g}/\text{m}^3$  increase in ozone concentration. Exposure to ozone was also associated with elevated risk of death due to diabetes (by 8.0%, 95% CI: 3.5-13.0) and respiratory diseases (by 6.0%, 95% CI: 4.0-8.0), including pneumonia and influenza (by 5.0%, 95% CI: 1.5-9.0), as well as chronic non-specific respiratory diseases (CNSRD) (by 7.0%, 95% CI: 4.0-10.5). The risk of death due to ischaemic heart disease, cerebral stroke or lung neoplasms was not associated with exposure to ozone.

A Canadian study analysed the data from a cohort of approximately 2.5 million adult Canadian citizens (over 25 years of age at the beginning of the observation), followed for 16 years [30]. Exposure to ozone was assessed using a pollution model with the 21 x 21 km grid, estimating average daily maximum 8-hour means in the warm season of the years (1 May to 31 August). The study demonstrated a significant correlation between the risk of death due to all natural causes and exposure: the risk increased by 1.1% (95% CI: 0.6-1.6) per 10  $\mu\text{g}/\text{m}^3$  increase in long-term ozone concentration. The analysis included the disturbing effect of a number of demographic and socio-economic variables, as well as exposure to particulate matter and nitrogen dioxide. The risk of death due to cardiovascular diseases associated with exposure to ozone was also increased: by 2.3% (95% CI: 1.5-3.2), and the risk of death due to ischaemic heart disease was increased by 3.8% (95% CI: 2.8-4.9). The risk of death due to diabetes was also increased, by 6.8% (95% CI: 3.9-24.3) per 10  $\mu\text{g}/\text{m}^3$  increase in ozone concentration. The correlation between mortality due to cerebral strokes and exposure was not statistically significant. In addition, no increase in the frequency of deaths due to pulmonary neoplasms or respiratory diseases, including CNSRD, was observed in people exposed to higher ozone concentrations (although mortality due to respiratory causes and CNSRD was correlated with exposure to  $\text{NO}_2$ ). The relationship between mortality due to cardiovascular diseases or diabetes and exposure to ozone was stronger in individuals under 80 years of age than in older patients, especially women [30].

A study on the survival of all the residents of continental United States who were covered by Medicare between 2000 and 2012 included nearly 61 million subjects over 65 years of age [31].

The risk of death due to all causes increased by 0.5% (95% CI: 0.45-0.55) per 10  $\mu\text{g}/\text{m}^3$  increase of ozone concentration at the place of residence in the warm season of the year (1 April - 30 September). To assess the exposure, a pollution model with a 1x 1 km grid was applied, faithfully illustrating daily maximum 8-hour mean ozone concentration measured by a monitoring network. In estimation of the relationship between ozone and mortality the disturbing effect of particulate matter, temperature, humidity, age, sex, ethnicity and socio-

economic status were considered.

No significant change of the relative risk coefficient was found in the subgroups exposed to ozone at concentrations below or above 100  $\mu\text{g}/\text{m}^3$ . The risk coefficient determined with the use of the data about ozone concentration in the nearest (within a 50 km radius) air pollution monitoring station was ten times lower, and it was borderline statistically significant, which confirmed the importance of precise assessment of the exposure.

The above results of analyses based on very large data collections published in the recent years considerably support the scientific evidence, and suggest that the "suspicion" of a relationship between mortality and long-term exposure to ozone, based on the USE-PA evaluation from 2013 [7] is justified. To establish the correlation, an exact determination of exposure appears to be important, and especially a sufficiently precise model resolution and calculations based on the maximum ozone levels during the day. It does not mean that there is a threshold of exposure below which ozone is not associated with mortality, but that may result from blurring of the contrast between populations if the background level and ozone concentration at night, when exposure to ambient ozone is less likely, are considered in calculating the mean value.

### Quantitative assessment of the health effects of exposure to ozone

The results of studies on the correlation between mortality due to respiratory diseases and long-term exposure to ozone, as well as risk factors resulting from early analyses of the ACS CPS cohort [28] are presently the primary grounds for the quantitative assessment of the effects of ozone on health, globally and regionally. Together with the estimated degree of population exposure, and with the data regarding mortality due to respiratory causes in individual countries, they allow the calculation of the number of premature deaths that may be contributed to the exposure. The Global Burden of Disease (GBD) project estimate this value at 254 thousand (in the range 97,000 – 422,000) of premature deaths globally in 2015 [32]. The number is by approximately 23% higher than estimated for 2005, but nearly 20 times lower than the global number of deaths ascribed to the exposure to particulate matter in the ambient air (4.2. million, in the range of 3.6 – 4.8 million). GBD project estimates the health effects of exposure to ozone for all the EU countries at 13,100 premature deaths, and for Poland at 570 premature deaths in 2015 [33]. The estimated mortality attributed to exposure to ozone in 2013, published by the European Environment Agency, is higher: 16,000 for EU and 1,150 for Poland [34]. In EU the number of premature deaths attributed to exposure to ozone is much lower than the estimated effects of exposure to particulate matter (467,000) or to nitrogen dioxide (71,000). Also in Poland the health losses attributed of the exposure to ozone are much lower than the effects of the exposure to particulate matter (48,270 of attributed deaths), but at a similar level to those associated with the exposure to nitrogen dioxide (1,610 deaths).

The results of the new analysis based on the ACS CPS

cohort data [29], more precise models of the spatial distribution of ozone, and less restrictive assumptions regarding the assessment of population exposure result in much bigger expected health effects of the exposure to ozone on a global and regional scale [35]. This analysis indicates that annually 1.04 – 1.23 million premature deaths due to respiratory causes across the world may be attributed to the exposure to ozone, depending on the concentration of ozone below which no health effects are expected. It constitutes 20.3 to 24.0% of all the deaths due to respiratory causes. For Europe, the number of deaths in this analysis is 55,900 – 78,900 per year, i.e. 10.6 to 15.0% of all the deaths due to respiratory causes. It has not been yet established if the relationship between cardiovascular mortality and long-term exposure to ozone is causal; therefore, the number of deaths due to cardiovascular causes, attributed to the exposure to ozone, are not estimated. The above studies did not calculate the number of additional cases of asthma, hospitalisation or episodes of respiratory diseases that may be attributed to the exposure to ozone. If taken into consideration, they would significantly increase the estimated health cost of "photochemical smog", both on a global and a Polish scale.

Trends regarding ozone concentrations in Europe are not homogeneous. Mean values tend to slightly increase in urban areas, and decrease in rural areas. Moreover, the frequency and intensity of short-termed ozone episodes tend to decline in these areas [34]. Reduced emission of ozone precursors from the sources associated with human activity in the EU countries within the past 15 years (volatile organic substances by 25-40%, nitrogen oxides by 8%) did not result in decreased ozone concentrations. This may be caused by the emission of volatile substances from natural sources, as well as the increasing hemispheric ozone background. Therefore, the exposure of population to ozone will probably remain a problem in the next decades. Due to the low ozone penetration indoors, staying inside at noon or in the afternoon on days of high ozone concentrations may considerably reduce the total exposure. Avoiding intensive physical activity at the time of increased ozone concentration also reduces the absorbed dose of ozone, as well as its adverse health effects. These may limit the harmful influence of ozone on the health of children and individuals susceptible to its effects, such as patients with asthma.

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# General Professor Zdzisław Antoni Ambroży Dmochowski (1863-1923) – creator of "Military Physician"

Gen. prof. Zdzisław Antoni Ambroży Dmochowski (1863-1923) – twórca „Lekarza Wojskowego"

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As part of my genealogical interests, while searching for the graves of my ancestors at a historical parish cemetery in Tuchowicz (currently a village parish located in the Lublin Voivodship, Łuków Powiat, Stanin Gmina) in 2015, I found the grave of Prof. Zdzisław Dmochowski, who 97 years ago initiated the founding of the "Military Physician" journal. I knew it was located there, as the family of Zdzisław Dmochowski was distantly related to Kruszewski through his wife, Julia Paulina Sosnowska, who was a granddaughter of Aleksandra Kruszewska and Kajetan Walenty Hipolit Sosnowski.

Back in 2015 the grave of Prof. Zdzisław Dmochowski looked much neglected, especially against the background of other ones in this historical cemetery (Fig. 1), and the markings on the tomb were barely legible (Fig. 2). During my next visit to the Tuchowicz cemetery in 2017, I discovered that the professor's descendants were still taking care of the tomb, and had gone as far as replacing the tomb structure, with a more modern form of commemorating the dead, which guarantees that the memory of this place of rest of General Professor Zdzisław Dmochowski shall remain (Figs. 3 – 4).

This serves as a good opportunity to remind us of the persona of Prof. Zdzisław Dmochowski, not just because he helped to found *Military Physician*, our currently most important journal for military physicians [1] (the journal already has almost 100 years of tradition in publishing, uninterrupted even in the years of the Second World War [2]), but also because as a physician and a scientist he was an eminent person, who deserves to be recognised as a great Polish physician.

General Professor Zdzisław Antoni Ambroży Dmochowski (Fig. 5), son of Stanisław Dmochowski of the Pobóg coat of arms and Julia née Kempieńska, was born on 7 December 1864 on the Kłodnica estate in the Lublin Voivodeship. He came from the Dmochowski family of landed gentry, owners of the Jeleniec estate in the Łuków region, where his father was also born. He graduated from the high school in Siedlce and then from medical studies at the University of Warsaw.

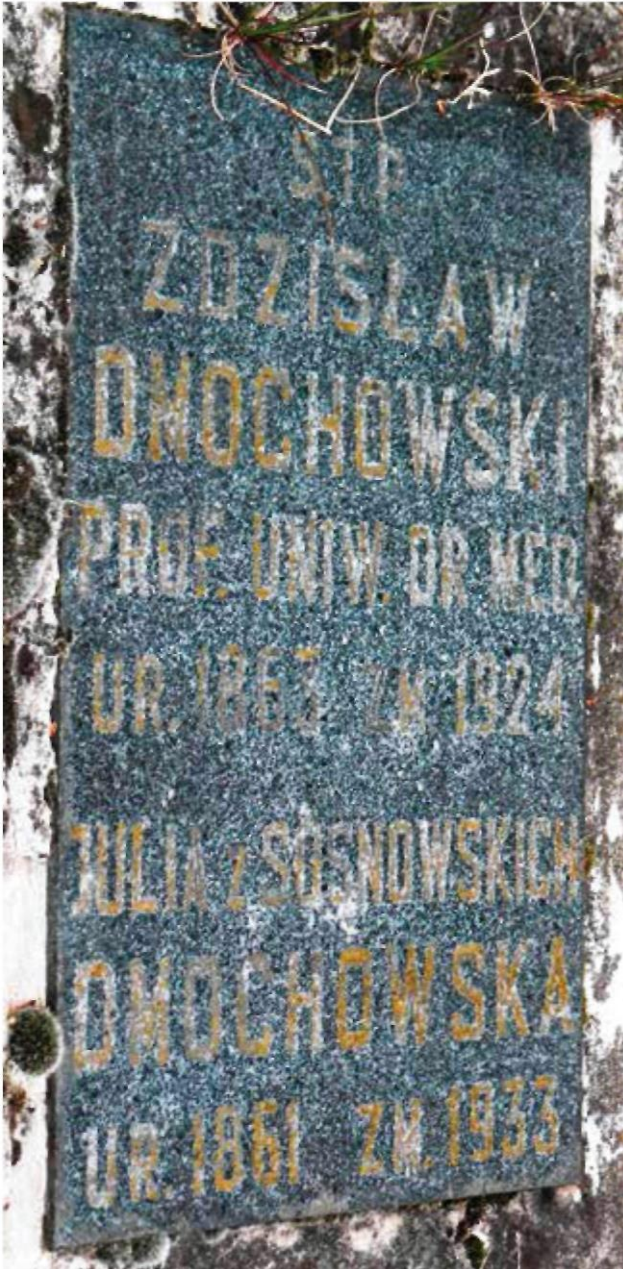
Practically all of his later life as a physician fell during the period of the partitions, with just a little more than four years being left for the time after regaining of independence. During this he donned a military uniform, becoming a military physician.



**Figure 1.** Old tomb of the Dmochowski family at Tuchowicz cemetery (2015)

**Rycina 1.** Stary grobowiec Dmochowskich na cmentarzu w Tuchowiczu (2015 r.)

From the beginning of his medical career, his particular focus of interest was pathological anatomy, although he was also involved in internal diseases and laryngology. He quickly decided to pursue an academic career and in 1889 he became a member of the academic staff at the University of Warsaw, employed at the position of prosector at the Department of Pathological Anatomy. He was strongly associated with the Faculty of Medicine at the University of Warsaw until 1910, being a supervisor for numerous dissertations. At the same time he participated actively in the academic life of Warsaw. In 1907, as a founder member, he organised the Warsaw Scientific Society, while from 1910 to 1912 acted as its vice-president and director of one of the created laboratories [3]. He resigned from these functions in 1912 when he was entrusted with a faculty at the University of Lviv. At the same time, he operated actively in the Warsaw Medical Society. With a PhD in all-medical sciences between 1912 and 1918, first he became an associate professor at Vilnius University [4], and then a full professor and the head of the Department of Pathological Anatomy at the Faculty of Medicine at the University of Lviv [5].



**Figure 2.** Old grave inscription  
**Rycina 2.** Stara tablica nagrobna

In the course of work at these universities he became known as a good organiser and educator. His scientific activities as an anatomist and pathologist were dominated by issues related to the pathology of inflammations and tumours. His greatest achievements included the authorship of the “Diagnostyka anatomopatologiczna” [“Anatomo-pathological diagnostics”] manual (published with the support of the Józef Mianowski Fund), volume I of which was published in 1903, and volume II in 1909.

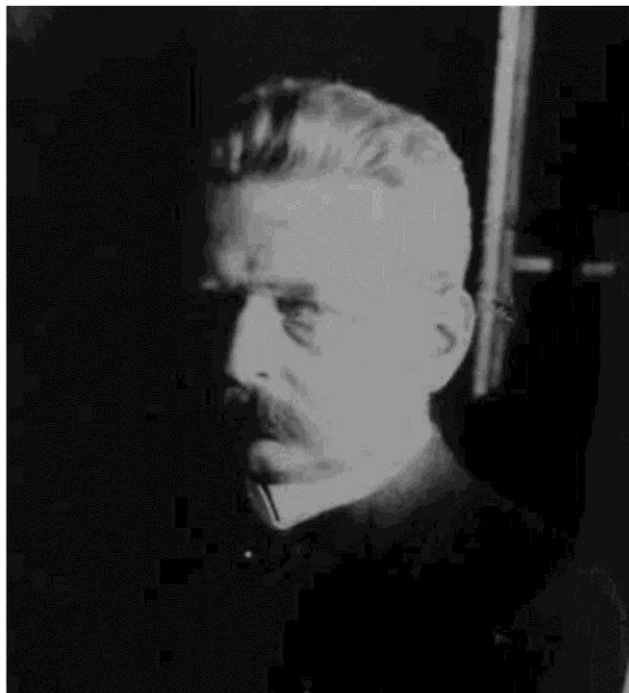


**Figure 3.** Renovated tomb of Dmochowski family at Tuchowicz cemetery (2017)  
**Rycina 3.** Odnowiony grób Dmochowskich na cmentarzu w Tuchowiczu (2017 r.)



**Figure 4.** New grave inscription  
**Rycina 4.** Nowa tablica nagrobna

When Poland regained independence in 1918, Zdzisław Dmochowski was an assistant professor at the University of Lviv, an academic respected in academic circles, not just in Poland but also across Europe. He could boast of academic and organisational achievements, he was an experienced educator, and all of this formed his authority, which attracted active scientists to work with him.



**Figure 5.** General Professor Zdzisław Antoni Ambroży Dmochowski (1863-1923)  
**Rycina 5.** Generał prof. Zdzisław Antoni Ambroży Dmochowski (1863-1923)

These features meant that, at the request of the Head of the Organisational Section of the Sanitary Department, Lt. Col. Prof. Loth, he was offered to join the ranks of the Polish Army [6]. This was associated with the intention to appoint him as the head of the Military Sanitary Council (MSC). He accepted the offer and on 1 January 1919 he was appointed the President of the MSC and given the rank of lieutenant colonel.

This started a short yet fruitful period in his activity for his homeland on an entirely new front. The new position presented a major challenge for Prof. Zdzisław Dmochowski, as he had no prior contact with the army. He had to make a fresh start in new areas: learn about the issues related to the sanitary needs of the Polish Army, the methods used to solve them in other countries and the potential of adapting these solutions to suit the conditions of a reborn Polish state. The previous organisational experience from his work at the university and in scientific associations proved highly useful. Within less than 3 months he had already developed the preliminary principles for the organisation and tasks of the MSC, accepted by means of an order in the Journal of Military Orders of 18 March 1919.

The plan was a very broad one, and covered several dozen tasks. From among them I would like to emphasise the intention to publish a special military and medical journal, which was effectively implemented the following year by founding the "Military Physician" journal, the first issue of which appeared on 3 January 1920. Appropriate candidates to take over the positions of department and

committee heads were found quickly and on 1 April 1919 the MSC initiated its actual activities at the Ujazdowski Hospital in Warsaw. As the president, Lt. Col. Prof. Zdzisław Dmochowski became the head of the Department of Pathological Anatomy of the MSC, and was soon verified as a colonel with seniority from 1 June 1919. At the beginning of 1920 Col. Prof. Zdzisław Dmochowski was selected as the first President of the Warsaw Medical Society. Unfortunately, at the same time he suffered from a bout of severe influenza with complications. The consequences were very serious, he made attempts to return to work, but they were not successful. He never regained full health.

When on 27 August 1921 the MSC was transformed into the Military Sanitary Institute, Col. Zdzisław Dmochowski ended his over 2.5-year-period of presiding the MSC and was appointed the head of the Department of Pathological Anatomy at this institute.

On 2 May 1923 he was decorated with the Commander's Cross of the Order of Polonia Restituta, and after another 6 months, on 31 October 1923, he retired as a titular Brigadier General. His illness inevitably doomed him to home isolation.

Surrounded by his family, bed-ridden by severe disease, he died on 6 January 1924 in Warsaw, bereaving his wife Julia née Sosnowska (whom he married in 1893) and two children: Maria Ludwika (later Maria Chrzanowska) and Zdzisława Włodzimierza, whose descendants continue to live. They organised the renovation of the place of eternal rest of Gen. Prof. Zdzisław Dmochowski, the family tomb of this line of the Dmochowski family, from which he descended. This tomb is also where his parents, wife (who died in 1933) and daughter are buried.

Regardless of the difficult initial years of independence, which overlapped the consequences of the Polish-Soviet War, it should be emphasised how properly eminent merited physicians were commemorated at that time. The minutes of the special session of the Warsaw Medical Society contain the following text (original spelling): "Minutes of 29 January 1924. Session commemorating the late Zdzisław Dmochowski on 29 January 1924. President: Prof. A. Leśniowski. The President welcomed the family of the late Prof. Dmochowski and guests, and emphasised the previous and present significance of the Medical Society in medical life; mentioned that the late Prof. Dmochowski was accepted in the Society as an active member already at the beginning of his medical activities. In the course of his entire life he participated in the works of the Society, by giving lectures that were always well planned or developed in their details, and by sharing his opinions in discussions. As an act of recognition for the work of the late Z. Dmochowski, his character and trust, in 1920 the members of the Society elected him as the President of the Society. This honourable position was held by the deceased in 1920 and 1921, in the most difficult years; however, he managed to maintain the activities of the Society. His state of health did not allow him to undertake further work for the Society and forced him to withdraw from his social and academic work. After a prolonged illness Prof. Dmochowski died on 6 January 1924. All hail to his memory. Those gathered

commemorated him by standing up. Prof. Kryński specified the activities of the late Prof. Z. Dmochowski at the Scientific Society. He undertook much work in the organisational period of the Scientific Society. Owing to his strenuous efforts and endeavours the Scientific Society managed to gain significant funding and purchase a proper building. The late Prof. Z. Dmochowski initiated the formation of research laboratories and was selected to be a Vice-President of the Society. Mr. Z. Sławiński in his speech presented the life of the late Z. Dmochowski, who also tackled intense tasks with indefatigable energy and persistence, devoted to his beloved branch of medical knowledge – pathological anatomy. Prof. Gluziński spoke for the Jan Kazimierz University in Lviv. Prof. Gluziński presented the attitude of the authorities of the University to the late Dmochowski and full recognition for his work. At the end of his speech Prof. Gluziński expressed deep grief and compassion for the remaining family. Mr. L. Paszkiewicz analysed the anatomical and pathological works of the late Z. Dmochowski, mentioning their value, in particular the extensive manual on Pathological Anatomy Diagnostics. Mr. Stefan Rudzki discussed the activities of the late Dmochowski in the PA and presented the vast work that was put into the organisation of the

Sanitary Council and the broad view on sanitary assistance. The President expressed condolences to the remaining family. This ended the session. President: A. Leśniowski. Annual Secretary: W. Kowalski" [7].

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# The murder of Professor Bolesław Jałowcy at the height of the anti-Polish campaign by Ukrainian nationalists against the scientific circle of the Jan Kazimierz University in Lviv

Zabójstwo profesora Bolesława Jałowego jako apogeum antypolskiej akcji ukraińskich nacjonalistów wobec środowiska naukowego Uniwersytetu Jana Kazimierza we Lwowie

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**Abstract.** Lviv as a city was for centuries a great centre of Polish science, culture and art. Most of the inhabitants were Poles who amicably co-existed with representatives of other nations living in the city, such as Jews, Armenians, Ukrainians, Russians. In the interwar period, the city became a centre of activity for Ukrainian nationalist and terrorist organizations, such as the Organization of Ukrainian Nationalists and the Ukrainian Military Organization. The height of extreme Ukrainian nationalist activities took place during the Second World War. The most painful blow that Ukrainian nationalists inflicted on the Polish medical circle was the murder of Professor Bolesław Jałowcy (1906-1943). The murderer has never been punished. The death of this 37-year-old medical scientist caused the intimidation and the first large emigration of Polish lecturers from the Faculty of Medicine at the Jan Kazimierz University in Lviv, who left their beloved city forever.

**Key words:** Lviv, Medical Faculty, Jan Kazimierz University, Ukrainian nationalism, terror, Bolesław Jałowcy

**Streszczenie.** Lwów to miasto, które przez stulecia było wielkim ośrodkiem polskiej nauki, kultury i sztuki. Większość mieszkańców stanowili Polacy, którzy w przyjazny sposób koegzystowali z przedstawicielami innych narodowości żyjącymi w mieście: Żydami, Ormianami, Ukraińcami, Rosjanami i innymi. W okresie międzywojennym miasto stało się również centrum działalności ukraińskich organizacji nacjonalistycznych i terrorystycznych, takich jak Organizacja Ukraińskich Nacjonalistów i Ukraińska Organizacja Wojskowa. Apogeum działalności skrajnych nacjonalistów ukraińskich nastąpiło podczas II wojny światowej. Najbardziej bolesnym ciosem, jaki ukraińscy nacjonałiści zadali polskiemu środowisku medycznemu, było zamordowanie profesora Bolesława Jałowego (1906-1943). Morderca nigdy nie poniósł kary. Śmierć 37-letniego naukowca przyczyniła się do zastraszenia i pierwszej dużej fali emigracji polskich wykładowców Wydziału Lekarskiego Uniwersytetu Jana Kazimierza we Lwowie, którzy na zawsze opuścili swoje ukochane miasto.

**Słowa kluczowe:** Lwów, Wydział Lekarski, Uniwersytet Jana Kazimierza, nacjonalizm ukraiński, terror, Bolesław Jałowcy

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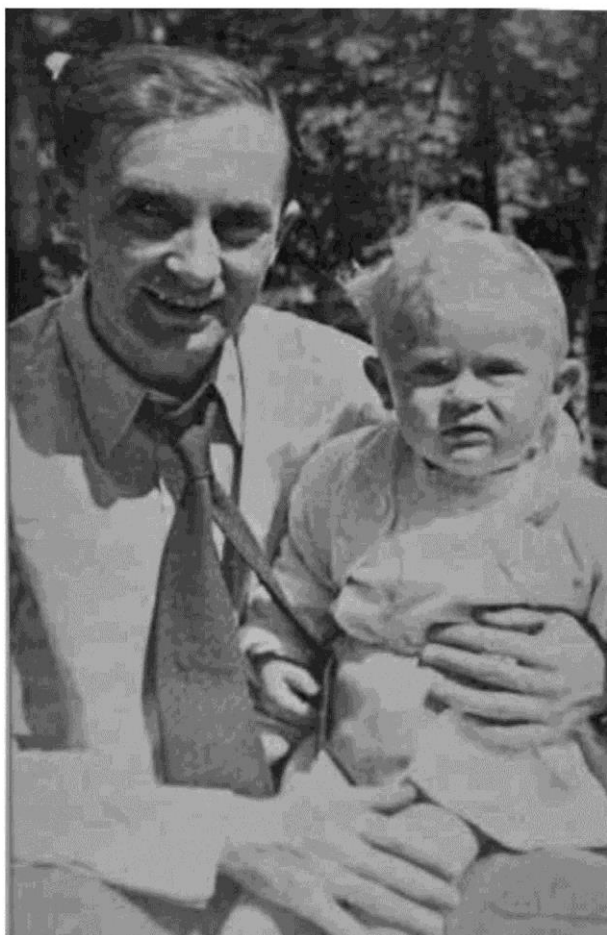
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**Figure 1.** Professor Bolesław Jałowy with his son Pawełek a few months before his death (source: Wojtkiewicz-Rok W. The years of glory and days of terror. Studies on history of Medical Faculty of the Jan Kazimierz University in Lviv. Adam Marszałek Publishing House, Toruń 2012: 81)

**Rycina 1.** Profesor Bolesław Jałowy z synem Pawełkiem na kilka miesięcy przed śmiercią (źródło: Wojtkiewicz-Rok W. Lata chwały i dni grozy. Studia nad dziejami Wydziału Lekarskiego Uniwersytetu Jana Kazimierza we Lwowie. Wyd. Adam Marszałek, Toruń 2012:81)

Ukrainian integral nationalism was an ideology that engendered a rich harvest of blood during the Second World War and had a significant influence on the tragic fates of Polish physicians and scientists from the Faculty of Medicine at the Jan Kazimierz University in Lviv. Lviv, which for hundreds of years had been a city of amicable co-existence between representatives of different nations living in the Republic of Poland (Poles, Jews, Russians, Ukrainians, Armenians, Germans, and Czechs), became a centre of activity for nationalist and terrorist organisations (Organization of Ukrainian Nationalists and the Ukrainian Military Organization). The height of their criminal activities took place after the city was taken by the Third Reich in June 1941. It is therefore no coincidence that a Ukrainian trail is also found in the notorious murder committed on Lviv's professors in the Wuleckie Hills during the night between 3 and 4 of July 1941 by Einsatzkommando under



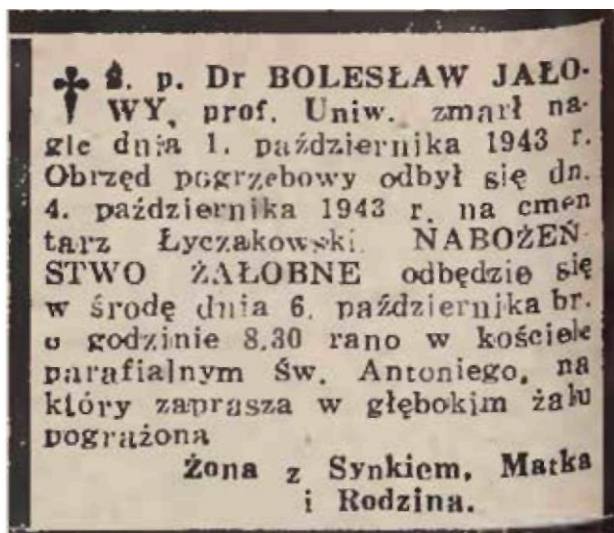
**Figure 2.** House where Professor Bolesław Jałowy and his family lived in 1930s, Lviv, 18 Wyspiański Street, October 20, 2017 (by Z. Kopociński)

**Rycina 2.** Dom, w którym w latach 30. mieszkał profesor Bolesław Jałowy z rodziną, Lwów, ul. Wyspiańskiego 18, 20 października 2017 (fot. Z. Kopociński)

the command of SS-Brigadeführer Eberharda Schongartha MD.

The firing squad that executed Polish academics consisted of 4-6 Ukrainians dressed in German uniforms, whereas the proscription lists with the names of the people to be liquidated were most probably prepared in Kraków by former Ukrainian students and graduates of universities in Lviv.

It should be emphasised that those selected to die included as many as 12 physicians, academics of the Faculty of Medicine at the Jan Kazimierz University in Lviv: Prof. Antoni Cieszyński (1882-1941), Prof. Władysław Dobrzaniecki (1897-1941), Prof. Jan Grek (1882-1941), Asst. Prof. Jerzy Michał Grzędzielski (1901-1941), Prof. Henryk Nusbaum-Hilarowicz (1890-1941), Asst. Prof. Stanisław Mączewski (1892-1941), Prof. Witold Walerian Nowicki (1878-1941), Prof. Tadeusz Ostrowski (1881-1941), Prof. Stanisław Progułski (1874-1941), Prof. Roman Rencki (1867-1941), Prof. Włodzimierz Sieradzki (1870-1941) and Prof. Adam Sołowij (1859-1941) [1-3].



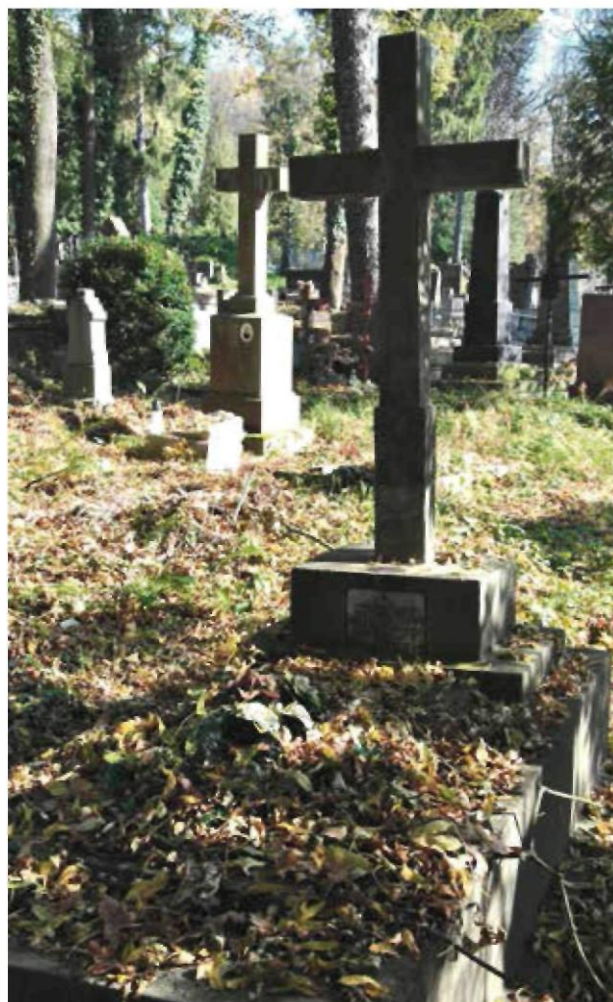
**Figure 3.** Obituary informing about death of Professor Bolesław Jałowy (source: Gazeta Lwowska. Galician district daily. October 5, 1943, year 132(3), no. 233)

**Rycina 3.** Nekrolog informujący o śmierci profesora Bolesława Jałowego (źródło: Gazeta Lwowska. Dziennik dla dystryktu galicyjskiego. 5 października 1943, rok 132 (3), nr 233)

The Germans liquidated the Lviv State Medical Institute (the former Faculty of Medicine at the Jan Kazimierz University) and transformed it into the State Medical Vocational Courses in Lviv (Staatliche Medizinische Fachkurse Lemberg), which significantly decreased the status of the university. The academic staff was mixed – Polish professors, assistant professors and physicians were still employed, but most of them were Ukrainian. The head of the courses was Prof. Karl Schulze from Berlin, and in 1944 this function was taken over by a Ukrainian – Jarosław Ginilewicz MD [2]. The head of the Department of Histology was Prof. Bolesław Roman Jałowy, a great physician and researcher, whose fate was determined by the nationalist ideology of the Organisation of Ukrainian Nationalists (OUN).

Bolesław Roman Jałowy was born on 11 September 1906 in Przemyśl, to Piotr and Franciszka née Wolik. He obtained a secondary school leaving certificate in 1925 at the Jan Kochanowski 9th State Gymnasium in Lviv. Then he moved on to study at the Faculty of Medicine at the Jan Kazimierz University. In the course of his studies he showed particular interest in histology and embryology, while he was still a student in 1928, and working in the Department of Histology and Embryology as a demonstrator. He was also active in student life.

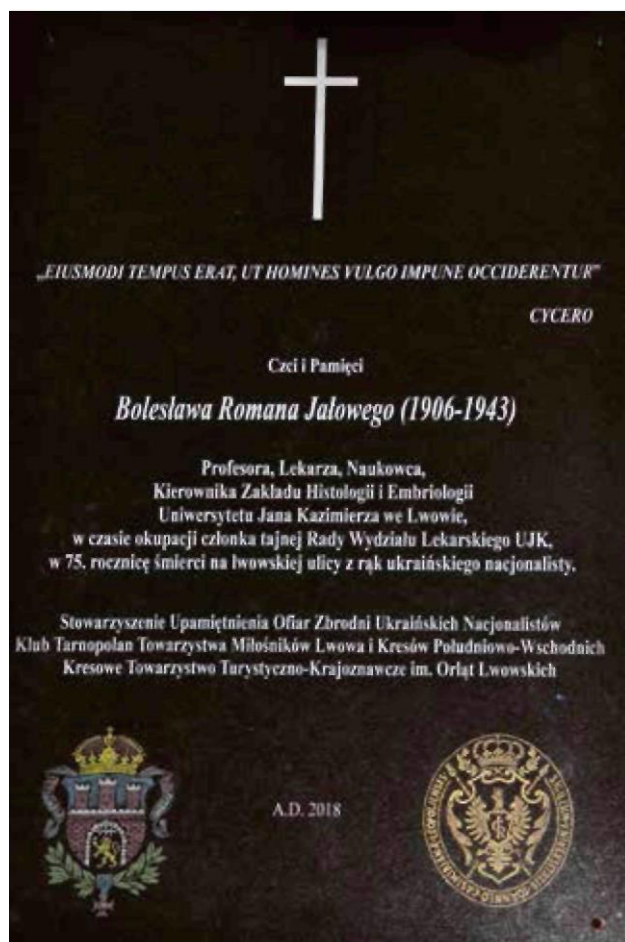
He was a member of the academic corporation *Aquitania*, and in the years 1929-1930 its president, the motto of which was "Per aspera ad astra". He received a PhD in all-medical sciences in 1931 and then became an assistant to Prof. Władysław Szymonowicz (1869-1939) in the Department of Histology and Embryology at the Jan Kazimierz University. In 1935, as a scholarship holder of the National Culture Foundation he studied in Utrecht and Amsterdam. After he returned, on 20 March 1936 he gave a lecture titled "O morfologicznej zmienności form zakończeń nerwowych" [On morphological variability of the forms of nerve endings], which simultaneously formed a basis for his postdoctoral examination in front of the Faculty Council. In January 1937 he was appointed a deputy examiner and assigned to conduct all the lectures on histology.



**Figure 4.** Untended grave of Professor Bolesław Jałowy at the Lychakiv Cemetery in Lviv, October 19, 2017 (by Z. Kopociński)

**Rycina 4.** Zaniedbany grób profesora Bolesława Jałowego na Cmentarzu Łyczakowskim we Lwowie, 19 października 2017 (fot. Z. Kopociński)

In 1938, when Prof. W. Szymonowicz retired, he became the head of the Department of Histology and Embryology and then he was appointed an Associate Professor of the Jan Kazimierz University [2, 4-6]. Regardless of his relatively young age he had a serious track record in academic achievements and published the results of his works in Polish and foreign journals. The subject matter of his academic pursuits focused not only on the issues related to histology and embryology, but also on dermatology and venereology, a field of medicine in which he was a specialist and for which he had a private practice. One of his co-workers in the 1930s was Wiesław Hołobut (1907-1988), at the time of the Second World War an officer physician of the Polish Second Army, one of the founders of the 8th Field Mobile Surgical Hospital (currently the 105th Kresy Military Hospital with Outpatient Clinic in Żary), and after the end of the war activities a Professor and Rector of the Academy of Medicine in Lublin, together with whom they conducted original experiments on the regenerative capabilities of the nervous system [7-16].



**Figure 5.** The commemoration plaque with inscription in honour of Professor Bolesław Roman Jałowcy (1906-1943), Żary, May 17, 2018 (by Z. Kopociński)

**Rycina 5.** Tablica z inskrypcją ku czci profesora Bolesława Romana Jałowcy (1906-1943), Żary, 17 Maj 2018 (fot. Z. Kopociński)

The outbreak of the Second World War interrupted the brilliant academic career of B. Jałowcy. During the Soviet occupation he continued to act as a head of the Department of Histology and Embryology at the Lviv State Medical Institute, and once Lviv was taken over by the Germans at the State Medical Vocational Courses in Lviv. In 1941 was lucky to avoid death during the execution of a part of the academic staff in the Wuleckie Hills. Starting from that year he became a member of the secret Council of the Faculty of Medicine at the Jan Kazimierz University. At the same time he worked as a lice feeder at the Institute of Prof. Rudolf Weigl (1883-1957), where vaccines were made against typhus [2, 4, 5].

The overtaking of the south-eastern borderlands of the Republic of Poland by the Third Reich caused an unprecedented intensification of the criminal activities of the Ukrainian Insurgent Army and the Organisation of Ukrainian Nationalists. In large cities, such as Lviv, where

Poles were the majority, the situation was more advantageous, as the Banderites were not able to commit mass murders, but terror and single murders were commonplace.

One of the most far-famed murders that was widely noticed in the entire Polish medical community, and which had long-term results, was the shooting of Prof. Jałowcy on 1 October 1943. On that tragic Friday he finished work at the medical practice of Asst. Prof. Stefan Łukasz Kwiatkowski (1898-1944). While he was returning home along Teatyńska Street, a Ukrainian nationalist, probably a nephew of Prof. Marian Panczyszyn (1882-1943), shot him in the back of his head [2, 17, 18].

The funeral of Prof. Bolesław Jałowcy on 4 October 1943 in an intimidated Lviv was a great manifestation of Polish patriotism. The funeral procession was led by medicine students carrying bouquets of white and red flowers and the casket from the chapel of the Department of Anatomy, whereas the funeral ceremony was led by Archbishop Rev. Bolesław Twardowski, PhD. The body of the murdered physician found its resting place at the Lychakiv Cemetery, in section 13.

Bolesław Jałowcy widowed his wife Stanisława (1907-1969) and one year-old son Pawełek (1942-1989), while his sudden death caused depression and almost panic among the Polish intelligentsia of Lviv. The result of this dramatic situation was the first major emigration of academic staff from the Jan Kazimierz University. The people who left the city included Prof. Bolesław Popielski, Prof. Adam Gruca and Prof. Wiktor Bross. The murderer has never been punished for his act [4, 19-21].

The young killer of this 37-year-old Polish physician, brought up in the spirit of a criminal nationalist ideology and convinced about its righteousness, carried out the heinous order without any hesitation, probably convinced of his heroism. The death of Professor Jałowcy should be a source of reflection for every decent person, regarding the continuously valid need to bring up the young generation in a spirit of mutual respect and not hatred, which is becoming particularly significant in this age of reviving nationalism, relativisation and tampering with history. Let us hope that an ideology allowing the commitment of the worst crimes in the name of its own interests will never triumph again.

The co-authors of this publication were the originators, designers and founders of the memorial intended to honour Professor Bolesław Roman Jałowcy, which was revealed and consecrated on 17 May 2018 at the Church of the Exaltation of the Holy Cross in Żary, during a ceremony under the honorary patronage of the President of the Medical Council of the Military Medical Chamber.

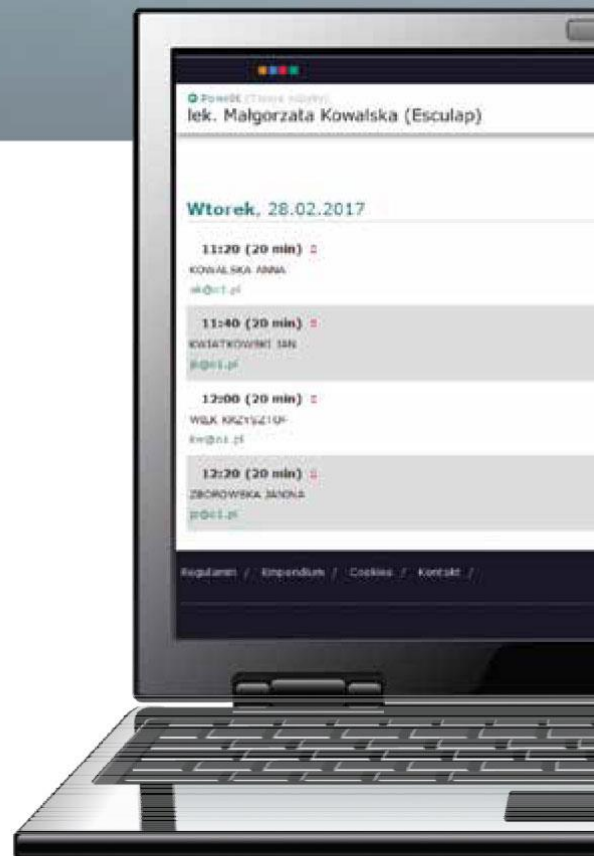
We should certainly appeal to all Poles, especially those in medical circles, and who visit the Lychakiv Cemetery in Lviv, to always light a candle on the rather neglected and unjustly omitted grave of Prof. Bolesław Jałowcy, to at least to pay him respects in this way and to muse upon his tragic fate.

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