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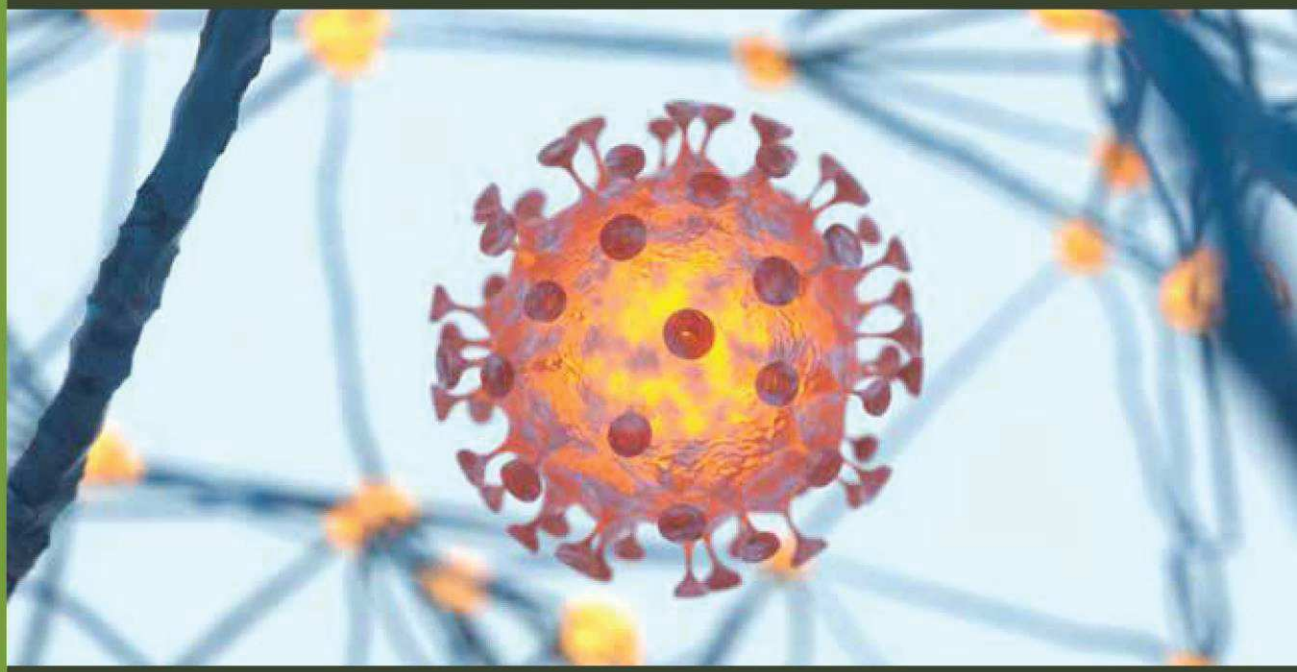

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Different courses of COVID-19

Iron-deficiency anaemia as the first sign of neoplastic disease

Lt. Col. Andrzej Żmudzki MD, PhD - the first military psychiatrist in post-war Warsaw

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Military Physician

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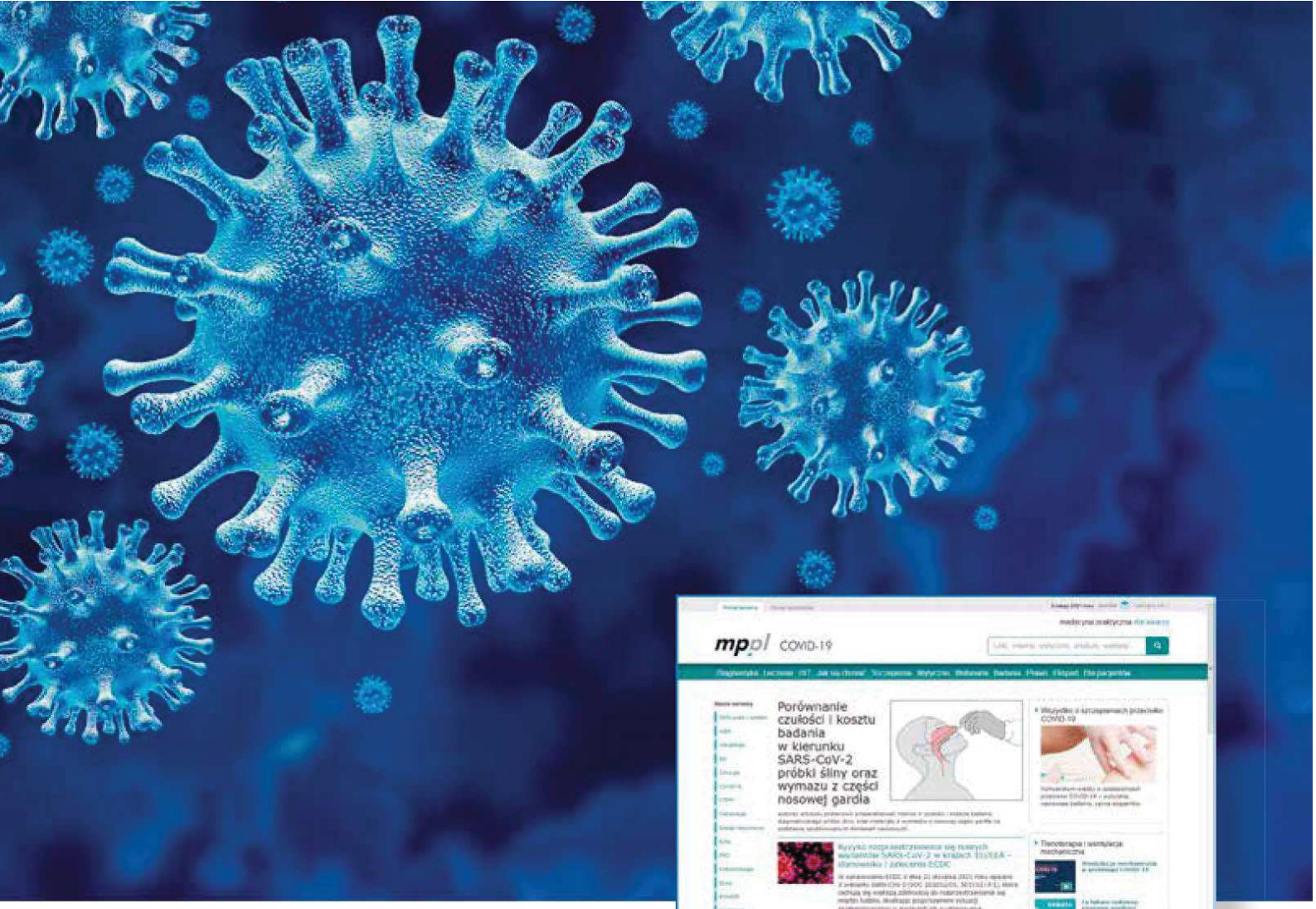

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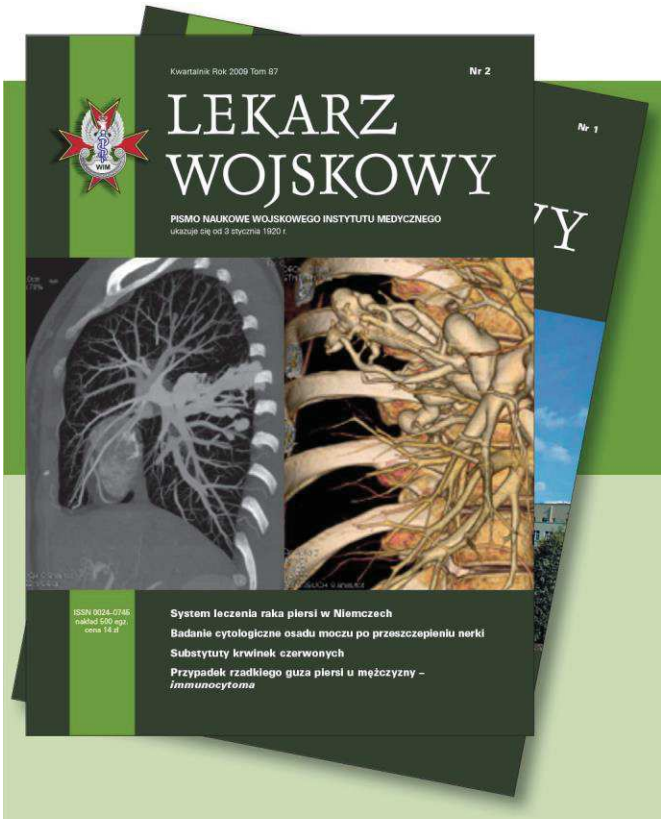

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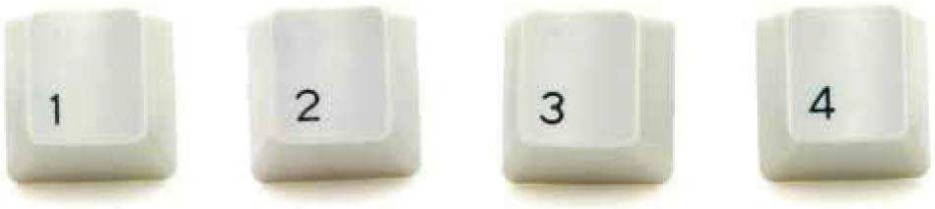

Inflammation of gastric mucosa in obese people

Zapalenie błony śluzowej żołądka u osób otyłych

Marta Wiśniewska, Janusz Rudziński, Paweł Gordon

Gastroenterology Unit, Department of Internal Diseases, 10th Military Clinical Hospital with Polyclinic at the Independent Public Healthcare Centre in Bydgoszcz; Unit Coordinator: Reserve Col. Janusz Rudziński MD, PhD

Abstract A questionnaire was completed by 144 people prior to elective bariatric surgery (laparoscopy sleeve gastrectomy - LSG) due to morbid obesity. The questionnaire related to dyspeptic symptoms and endoscopic examinations (panendoscopy) with mucosal specimens for histopathological evaluation. The clinical symptoms were then correlated with the histopathological picture and the incidence of *H. pylori* infection in the obese population assessed.
Keywords: gastritis, *Helicobacter pylori* infection, laparoscopy sleeve gastrectomy, obesity

Streszczenie U 144 osób przed planowanym zabiegiem bariatrycznym (LSG) z powodu otyłości olbrzymiej przeprowadzono ankietę dotyczącą dolegliwości dyspeptycznych oraz badanie endoskopowe (panendoskopia) z pobraniem wycinków błony śluzowej do oceny histopatologicznej. Skorelowano objawy kliniczne z obrazem histopatologicznym oraz oceniono częstość występowania infekcji *Helicobacter pylori* w populacji ludzi otyłych.
Słowa kluczowe: otyłość, rękawowa resekcja żołądka, zapalenie błony śluzowej żołądka, zakażenie *Helicobacter pylori*

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Corresponding author
Marta Wiśniewska
Gastroenterology Unit, Department of Internal Diseases, 10th Military Clinical Hospital with Polyclinic at the Independent Public Healthcare Centre in Bydgoszcz
5 Powstańców Warszawy St., 85-681 Bydgoszcz
e-mail: martawis83@wp.pl

Introduction

Obesity is considered one of the major diseases of civilisation in the modern world [1]. It affects the entire population, regardless of social status, age, sex, race or level of education. In 2002, World Health Organisation (WHO) included obesity on the list of the most serious threats to mankind [1]. According to NCD Risk Factor Collaboration (NCD-RisC), three out of five adult Poles are overweight, and one in four is obese [2]. The National Health Fund's 2019 report on the consequences of sugar consumption and the related development of obesity, prepared by the Department of Analysis and Strategy, estimates that by 2025 26% of adult women and 30% of adult men in Poland will be obese [3]. The analysis of the increasing rate of obesity indicates that in 2025 treatment of the conditions associated with the disease will cost 0.3 – 1.0 billion PLN more than in 2017. Obesity is a risk factor for cardiovascular diseases, diabetes and associated insulin resistance, sleep apnoea and osteoarticular disorders, including polyarticular pathologies [4].

There is an increasing belief in society that the fight against obesity involves not only various diets, but primarily regular physical exercise. A large group of obese patients decided to undergo radical, surgical treatment. For several years the available treatments for morbid obesity have included restrictive bariatric surgery, i.e. laparoscopic sleeve gastrectomy (LSG), which consists in reduction of the gastric volume and preservation of the normal intestinal passage [5]. Qualification of patients for this procedure involves panendoscopy and a urease test for *Helicobacter pylori.* If *H. pylori* infection is detected, an effective eradication treatment is necessary prior to the surgery. Histopathological assessment of the gastric mucosal membrane was previously performed using gastric specimens obtained during sleeve gastrectomy.

Aim of the study

The aim of the study was to assess the condition of the gastric mucosa in obese patients during the preparation for the LSG procedure, including the incidence of *Helicobacter pylori* infection and the correlation between the observed gastric mucosal lesions and dyspeptic symptoms.

Material and methods

The study was conducted between 2017 and December 2019. Following the guidelines of the Metabolic and Bariatric Surgery Chapter of the Association of Polish Surgeons, the principal indication for surgical treatment of obesity is the body mass criterion, based on the body mass index (BMI). For the patients to qualify for the procedure they must have BMI ≥40 kg/m^2 or ≥35 kg/m^2, and comorbidities associated with obesity, i.e. arterial hypertension, diabetes, lipid disorders, sleep apnoea etc. [6].

The study involved 144 patients aged 19-68 years old (mean: 42.6 years), with grade 1, 2 or 3 obesity, qualified for LSG procedure, including 111 females (77%) and 33 males (23%).

The subjects were divided into four age groups:

- group I - up to 30 years old (22 subjects - 15.3%),
- group II - 31-40 years old (41 subjects - 28.5%),
- group III - 41-50 years old (50 subjects - 34.7%),
- group IV - >50 years old (31 subjects - 21.5%).

All patients received a physical examination before the planned bariatric procedure. The patients qualified for the surgery completed a questionnaire regarding the most frequently occurring dyspeptic symptoms and gastro-oesophageal reflux, using the VAS scale, for example (Table 1).

Gastroscopy was performed using an Olympus gastro fiberscope (GIF-185), including an endoscopic assessment of the gastric mucosa, urease test and collection of specimens from the mucosal membrane in the body and prepyloric section of the stomach. The endoscopic assessment was based on the Sydney system, revised at the Houston Gastritis Workshop [7]. The histopathological examination of specimens was conducted at the Institute of Pathomorphology, 10th Military Clinical Hospital in Bydgoszcz, according to the Sydney scale [8].

The urease test for *Helicobacter pylori* and Giemsa stains of the direct preparations were assessed by the physician performing the endoscopy.

Results

In the study group 109 patients (76%) were diagnosed with morbid, grade III obesity (BMI ≥40), 35 patients (22.9%) with grade II obesity (BMI >35), and only 2 subjects (1.4%) with grade I obesity (BMI >30).

Tabela 1. Pytania użyte w ankiecie dotyczące wybranych dolegliwości ze strony przewodu pokarmowego
Table 1. Questions used in selected gastrointestinal complaint survey

№	Symptom	Characteristics
1.	Heartburn	Intensity, frequency
2.	Regurgitation	Intensity, frequency
3.	Eructation	Yes/No
4.	Abdominal pain	Intensity, frequency, location
5.	Borborygmus / abdominal gurgling	Yes/No
6.	Flatulence	Yes/No
7.	Stool frequency	Frequency
8.	Feeling of fullness in the upper abdomen after a meal	Yes/No
9.	Early satiety after a small meal	Yes/No

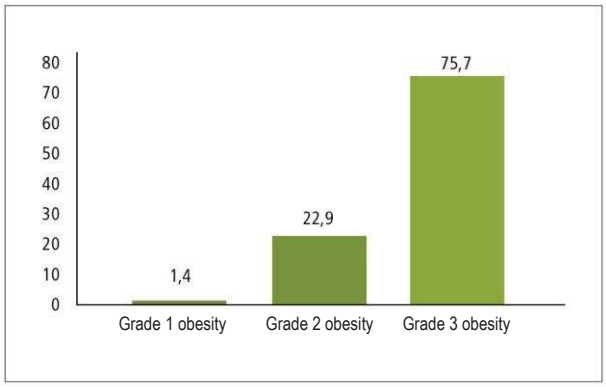
Intensity / presence of the symptom on a scale of 0 to 10 (0 - absence of symptom, 10 - maximum intensity)

The mean BMI of the study subjects was 44.57 kg/m^2. A statistically significant difference in mean BMI values ($p<0.05$) was found between females and males. Mean BMI values did not differ significantly in terms of age or comorbidities.

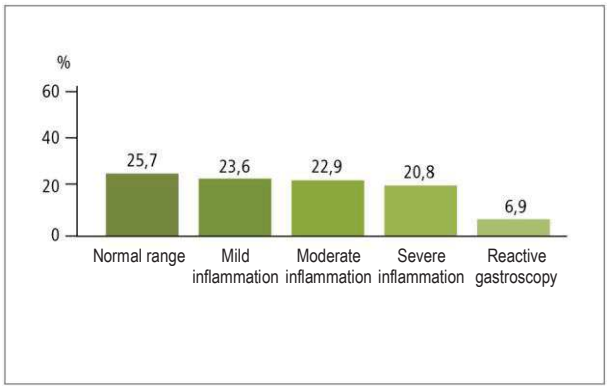
A total of 93 (86%) patients were diagnosed with the following comorbidities:

- arterial hypertension (51 patients - 29.5% of all the responses),
- type 2 diabetes (29 patients - 16.8% of all the responses),
- ischaemic heart disease (25 patients - 14.5% of all the responses),
- hypothyroidism (23 patients - 13.3% of all the responses).

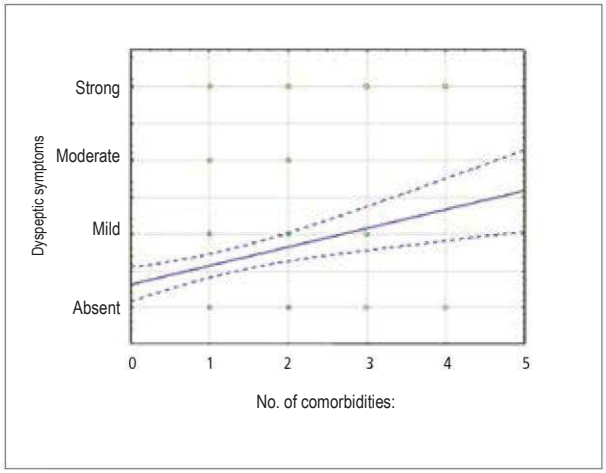
A total of 37 patients reported one or two comorbidities,15 reported three comorbidities, and 4 reported four comorbidities. The simultaneous occurrence of multiple diseases increased the symptoms of dyspepsia. In patients with several concurrent diseases the upper abdominal symptoms and signs of postprandial disorder syndrome (early satiety, postprandial feeling of fullness in the upper abdomen) were found more frequently. Such differences were not observed in the case of gastro-oesophageal reflux symptoms. A relationship was found between intensification of dyspeptic symptoms and intensification of gastro-oesophageal reflux disease (GERD) symptoms. (Fig. 2).



Rycina 1. Rozkład BMI
Figure 1. BMI distribution



Rycina 3. Rozkład wyników histopatologicznych (wg klasyfikacji Sydney)
Figure 3. Distribution of histopathological results (acc. to Sydney classification)



Rycina 2. Wykres rozrzutu wyników objawów dyspepsji względem liczby chorób współistniejących
Figure 2. Scatter of results of dyspepsia symptoms *vs* number of comorbidities

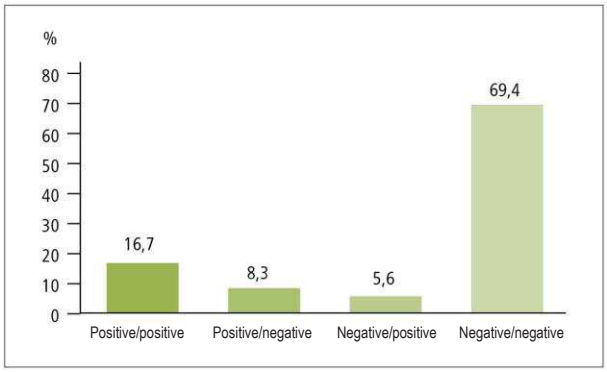
In the study group the histopathological examination of gastric specimens (non-selective specimens excised from the antrum and body of the stomach) revealed normal gastric mucosa in 37 patients (25.7%). Mucosal pathologies without inflammatory cells were found in less than 7% of patients. In the remaining 96 patients (67.3% of the study group) inflammatory invasion of the mucosal membrane was observed, severe in 22.9% of the subjects (Fig. 3).

The majority of patients, i.e. 92 (64%), did not report any dyspeptic symptoms, and gastritis in this group was clinically asymptomatic.

Helicobacter pylori infection was found in only 30% of the entire study group. In 25% of patients the infection was confirmed by a urease test, whereas in the remaining 5% it was diagnosed based on Giemsa stains of direct bioptate preparations. The tests were compliant in 16.7% (Tab. 2, Fig. 4).

Discussion

The available literature does not offer studies on assessments of mucosa in different groups of obese patients. The analysis of this problem raises the question whether obesity itself is a factor contributing to the destruction of gastrointestinal mucosa, or whether bad eating habits, including compulsive consumption of fast food, affect the condition of the mucosal membrane. In view of an increasing number of obese patients in the developed and developing countries, it should be the focus of further studies. Difficulties in maintaining proper body weight result primarily from bad eating habits. The various “miraculous diets” are mostly ineffective [9]. Great effort without effective and permanent weight loss, fast recovery of the baseline body mass or the yo-yo effect often prompt obese patients to undergo surgical treatment [10]. Bad eating habits and following weight-loss diets may result in more frequent gastric mucosal pathologies compared to the general population. This study demonstrated inflammatory lesions in the gastric mucosa in the majority of the patients (67.4%). These abnormalities did not correlate with the physical examination. Simultaneous occurrence of multiple diseases increased the symptoms of dyspepsia.



Rycina 4. Rozkład wyników testu ureazowego, infekcja *H. pylori* oraz zakażenia *H. pylori w* badaniach histopatologicznych
Figure 4. Distribution of urease test results, H. pylori infection and H. pylori infection in histopathology

Tabela 2. Wyniki testu ureazowego, infekcja *H. pylori* oraz zakażenia *H. pylori w* histopatologii
Table 2. Urease test results, *H. pylori* infection and *H. pylori* infection in histopathology

Urease test / histopathological examination	No.	%
Positive/positive	24.	16.7.
Positive/negative	12.	8.3.
Negative/positive	8.	5.6.
Negative/negative	100.	69.4.
total	144.	100.0.

Interestingly, in the study population of obese patients *Helicobacter pylori* infection was found in only approximately 30% of cases, whereas it is believed that approximately 80% of the adult population in Poland is infected with *Helicobacter pylori* [11]. As discrepancies were found in the results of tests for the oncogenic *Helicobacter pylori* bacteria, it indicates that the collection of bioptates of the gastric mucosa should become a standard procedure in qualification for bariatric surgery. The presented study demonstrates the presence of gastric inflammatory lesions, confirmed by a histopathological examination, in most obese patients, although they did not experience any upper gastrointestinal symptoms. Further research into this problem is required, as well as the development of principles for the qualification for gastric fibroscopy in patients with grade 2 and 3 obesity.

Conclusions

- Inflammatory lesions of gastric mucosa found in the majority of obese patients may be asymptomatic.
- *Helicobacter pylori* infection is less frequent in obese patients compared to the general population.
- It appears that introducing the histopathological examination with Giemsa staining of the bioptate from the gastric mucosa collected during a gastric fibroscopy should be considered in the qualification for bariatric surgery.

Literature

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Iron-deficiency anaemia as the first sign of neoplastic disease – case reports

Niedokrwistość z niedoboru żelaza jako pierwszy objaw choroby nowotworowej – opisy przypadków

Wiesław Wiktor Jędrzejczak, Jolanta Wieczorek, Leszek Kraj

Chair and Department of Haematology, Transplantology and Internal Diseases, Warsaw Medical University in Warsaw; Head: Prof. Grzegorz W. Basak MD, PhD

Abstract Two cases of women are described. One case involved a 25-year-old vegan with heavy menstruations, the main cause of iron deficiency anaemia was a stomach cancer, whose delayed diagnosis contributed to treatment failure and death. The other case involved a 60-year-old female, where the cause of iron deficiency anaemia was chronic bleeding from the gastrointestinal tract caused by a diffused large B cell lymphoma located in the small intestine, one difficult to access by standard gastro- and colonoscopy. The patient underwent standard immunochemotherapy and remains in complete remission. In conclusion, iron deficiency anaemia, particularly if it persists, should result in intensive diagnostic procedures aimed at exclusion/confirmation of neoplastic disease as the main cause.
Keywords: cancer diagnosis, gastrointestinal bleeding, gastroscopy

Streszczenie Opisano dwa przypadki kobiet. U jednej z nich, 25-letniej weganki z obfitymi miesiączkami, główną przyczyną niedokrwistości z niedoboru żelaza był rak żołądka, którego opóźnione rozpoznanie przyczyniło się do niepowodzenia leczniczego i zgonu. U drugiej - 60-letniej - kobiety przyczyną niedokrwistości z niedoboru żelaza było krwawienie z przewodu pokarmowego spowodowane przez rozlanego chłoniaka z dużych komórek B zlokalizowanego w jelicie cienkim, w okolicy trudno dostępnej badaniu gastro- i kolonoskopowym. Ta chora, poddana standardowej immunochemioterapii, pozostaje w remisji całkowitej. Podsumowując, niedokrwistość z niedoboru żelaza, zwłaszcza utrzymująca się dłużej, powinna być powodem do wszechstronnej diagnostyki zmierzającej do wykluczenia/potwierdzenia nowotworu jako jej przyczyny.
Słowa kluczowe: krwawienie z przewodu pokarmowego, gastroskopia, diagnostyka nowotworów

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Corresponding author
Prof. Wiesław W. Jędrzejczak MD, PhD
Chair and Department of Haematology, Transplantology and Internal Diseases, Warsaw Medical University
1a Banacha St., 02-097 Warsaw
telephone +48 22 599 28 18
e-mail: wieslaw.jedrzejczak@wum.edu.pl

Iron-deficiency anaemia, particularly in young women, is usually considered a mild condition resulting from heavy menstrual bleeding, poor nutritional decisions or habits, or - rarely - malabsorptive disorders. However, in males and post-menopausal females, i.e. individuals who do not experience regular physiological iron losses, anaemia due to iron insufficiency is typically caused by gastrointestinal or genital bleeding, which may be the first symptom of an oncological disease [1]. It is sometimes underrated, and treated symptomatically through administration of iron preparations or transfusion of red blood cell concentrate (RBC). However, underestimating this symptom may result in death or the need for a more aggressive, thus more toxic, treatment.

Presented below are two cases in which iron-deficiency anaemia was the first symptom of an oncological disease. In the first case the underestimating of this symptom led to death, while in the second it resulted in long-term anticancer therapy.

Case reports

Case 1

A 25-year-old female patient, with no history of pregnancy, with regular heavy menstruation, vegan for 6 years, visited a haematologist for a private consultation. She was very pale and complained of weakness, fatigue and the ineffectiveness of the iron and vitamin B_{12} supplementation prescribed by primary care physicians. A complete blood count revealed severe anaemia (Table 1), persisting despite the use of iron preparation and vitamin B_{12}. On admission the cardiac function was regular, 102/min, blood pressure 110/60, without any other significant abnormalities. The blood count demonstrated a very serious microcytic hypochromic anaemia (Hb 4.2 g/dL). It was associated with thrombocytosis and neutrophilia. Physical examination revealed only pain in the upper abdomen upon palpation. Other laboratory tests demonstrated: iron 11 µg/mL (normal range: 37-158), ferritin 8 ng/mL (normal range: 13-150), transferrin 232 mg/dL (normal range: 250-320), soluble transferrin receptor 21.03 mg/L (normal range: 1.79-4.63), vitamin B_{12} >2,000.0 pg/mL (normal range: 191-663), folic acid 11.21 ng/mL (normal range: 4.6-18.7). Moreover, hypoalbuminaemia (2.6 g/dL) and signs of inflammation (neu 12.83 10^3/µL, CRP 19.6 mg/L, fibrinogen 489 mg/dL, D-dimers 1748 ng/mL) were observed. The gastroscopy conducted the following day revealed an advanced gastric cancer. Despite three surgical procedures to manage the disease, the patient died.

Case 2

A 60-year-old female without any significant chronic conditions had a complete blood count performed after a sudden fainting episode. The test revealed a severe microcytic, hypochromic anaemia. Other laboratory tests demonstrated: iron 8 µg/mL (normal range: 37-158), ferritin 3 ng/mL (normal range: 13-150), transferrin 346 mg/dL (normal range: 250-320), soluble transferrin receptor 21.03 mg/L (normal range: 1.79-4.63), vitamin B_{12} 258.0 pg/mL (normal range: 191-663), folic acid 6.06 ng/mL (normal range: 4.6-18.7). Oncological markers: CEA, AFP, CA 19.9, CA 15.3, CA 125 were normal. The patient was not a vegan, but she avoided eating red meat. In her case the faecal occult blood test result was positive, but initial gastroscopy and colonoscopy did not identify the cause of the symptoms, which persisted despite correction of the deficit with the transfusion of red blood cell concentrate. The second gastroscopy revealed invasion of the duodenum and small intestine. The lesion was surgically removed. It was caused by a large B-cell lymphoma. The patient received immunochemotherapy for several months, and for the few years since she has been in complete remission.

Tabela 1. Parametry morfologii krwi, których wartości były podstawą do rozpoczęcia diagnostyki w kierunku choroby nowotworowej
Table 1. Complete blood count parameters serving as a basis to initiate diagnosis for neoplastic disease

Parameter	Case #1	Case #2
HGB (g/dL)	4.2	**5.3**
HCT (%)	14.7	18.2
RBC (10^6/µL)	2.33	2.68
MCV (fL)	63.0	67.9
MCH (pg)	18.1	19.8
MCHC (g/dL)	28.7	29.1
RDW (%)	20.4	16.7
PLT (10^3/µL)	628	454.
Neutrocytes (10^3/µL)	12.83	4.0
Lymphocytes (10^3/µL)	2.09	1.74
Monocytes% (10^3/µL)	0.83	0.77
Eosinophils (10^3/µL)	0.28	0.09
Basophils (10^3/µL)	0.06	0.05

Discussion

This differential blood count (microcytic hypochromic anaemia) is typical for iron-deficiency anaemia, in 1/3 of cases associated with secondary thrombocytopaenia, while neutrophilia may result from the inflammation. This has been confirmed by the outcomes of other studies on iron metabolism. Very rarely, severe anaemia may be also caused by a combination of factors such as heavy menstrual bleeding in young women, absence of meat, i.e. the main source of easily absorbable iron, in the diet and malabsorptive disorders. Few reports of similar cases can be found in the literature, and all of them have been cited.

It is difficult to determine whether the first patient could have been saved, if the diagnostics of anaemia had been started earlier (including gastroscopy). Regarding the presented case of lymphoma, whose first symptom was severe iron deficiency anaemia, the PubMed search of "iron deficiency anaemia as the first sign of lymphoma" did not reveal any such reports. The most frequent neoplastic cause of such a situation is colon cancer [2-4]. Other reported neoplasms include adenocarcinoma of the small intestine and sarcoma [5-7].

To sum up, detection of iron deficiency anaemia in post-menopausal women as well as in men should always be followed by active diagnostics to exclude/confirm a neoplastic origin; however, it should not be underestimated in young women who avoid eating meat, if the anaemia persists despite iron supplementation, or when it is severe.

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Different courses of COVID-19

COVID-19 o różnym przebiegu

Krzysztof Kłos,[1] Mirosław Dziekiewicz,[2] Agnieszka Jurek,[3] Andrzej Chciałowski,[1] Jerzy Kruszewski,[1] Krzysztof Piwowarek,[1] Artur Maliborski[4]

[1] Department of Infectious Diseases and Allergology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw; head: Assoc. Prof. Andrzej Chciałowski MD, PhD
[2] Department of Vascular and Endovascular Surgery, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw; head: Assoc. Prof. Mirosław Dziekiewicz MD, PhD
[3] Department of Cardiology and Internal Diseases, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine, Warsaw, Poland; head: Assoc. Prof. Paweł Krzesiński MD, PhD
[4] Department of Medical Radiology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw; head: Artur Maliborski MD, PhD

Abstract Despite many published studies and analyses, it is not known why the COVID-19 clinical picture may be so different. The paper presents two cases of COVID-19 patients, each with a different course despite the involvement of a similar area of the lungs.
Key words: COVID-19, SARS-CoV-2, pneumonia, venous thromboembolism

Streszczenie Mimo wielu publikowanych badań i analiz wciąż nie wiadomo, dlaczego obraz kliniczny COVID-19 może być tak zróżnicowany. W pracy przedstawiono dwa przypadki chorych na COVID-19 o różnym przebiegu, mimo zajęcia podobnego obszaru płuc.
Słowa kluczowe: COVID-19, SARS-CoV-2, zapalenie płuc, żylna choroba zakrzepowo-zatorowa

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Corresponding author
Krzysztof Kłos MD, PhD
Department of Infectious Diseases and Allergology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw
128 Szaserów St., 04-141 Warsaw
tel. +48 261817 519
e-mail: kklos@wim.mil.pl

Introduction

Based on the available observations, the consequences of SARS-CoV-2 infection in people can vary. The course of the disease is usually asymptomatic or oligosymptomatic, although we are only starting to learn about the long-term sequelae of such infections, especially in children [1, 2]. A mild course is also sometimes observed, involving classic COVID-19 symptoms, such as fever, dry cough, fatigue, rarely myalgia, sore throat, headache, diarrhoea, conjunctivitis, loss of taste or smell, skin eruptions and discolouration of fingers and toes. The occurrence of symptoms such as difficulty breathing, pain or pressure in the chest, or loss of speech or mobility, suggests a severe course of COVID-19, potentially associated with the involvement of various organ systems, primarily the respiratory system, with severe pneumonia as the dominant symptom [3-7].

Presented below are two cases of COVID-19 with pulmonary involvement, but following different courses: one typical, and one involving a relatively rare complication.

Case 1

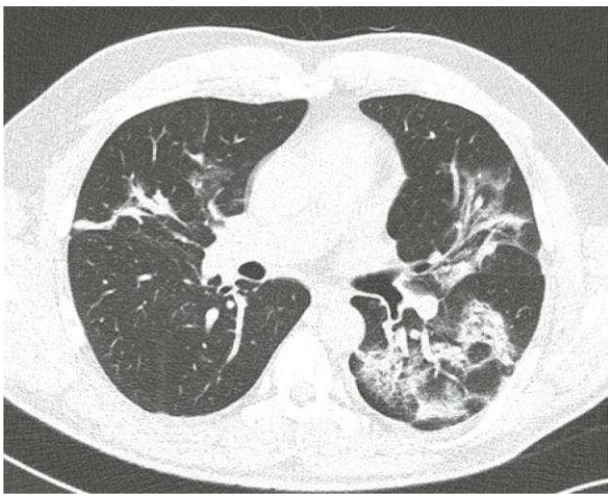
A 41-year-old male patient (a professional soldier, helicopter pilot), previously healthy and not receiving any chronic therapies, was urgently admitted to the Department of Infectious Diseases and Allergology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw, having been brought there by medical transport from an Independent Public Healthcare Centre in Krynica Zdrój, where he had been hospitalised on 12-13 October 2020 after a fainting episode and >39°C fever persisting for 8 days, unproductive, persistent cough, exercise dyspnoea, pressure in the thorax while inhaling deeply, a significant

general weakening and transient headaches. He received azithromycin and levofloxacin on an outpatient basis, without a result.

On 6/10/2020, the patient received a test for SARS-CoV-2, and the next day the results came back negative. However, the thoracic HRCT (high resolution computed tomography) performed the next day revealed massive infiltrating lesions in the right lung. The result of a test for SARS-CoV-2 conducted on 10 October 2020 was positive. A radiological thoracic test performed at that time revealed parenchymal opacities in almost the entire right lung and in the perihilar areas of the left lung. Ceftazidime, levofloxacin, dexamethasone and oseltamivir were prescribed. On 13 October 2020, the patient was referred to the Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw for further treatment.

On admission he was in good general condition, with a stable circulatory status, but with respiratory insufficiency, with saturation (SpO_2, measured with pulse oximetry) without oxygen therapy of 88%, whereas with passive oxygen therapy (a mask with a reservoir bag, flow rate of 6 L/min) it was 96%. The patient reported significant weakness, a dry, persistent cough, exercise dyspnoea that impaired basic hygiene activities, and loss of taste. Crackles up to the scapular angles, more pronounced on the right, were found on auscultation. Laboratory tests revealed slightly increased concentration of CRP (C-reactive protein) – 3.7 mg/dL (normal range: <0.8 mg/dL) and procalcitonin – 0.06 ng/mL (normal range: <0.046 ng/mL) and significantly increased ferritin concentration - 1115 ng/mL (normal range: 30-400 ng/mL). Antibiotic therapy was continued (ceftazidime and levofloxacin), and the following were introduced: steroid therapy (dexamethasone), anticoagulants (low molecular weight heparin), fluid therapy and Remdesivir (200 mg on the first day, then 100 mg q.d. for 4 days).

During the first days of hospitalisation a transient deterioration of the respiratory function was observed, with the patient requiring increased oxygen supply (flow rate up to 9 L/min through a mask with a reservoir bag). After 5 days, the patient's clinical status started improving gradually, the cough and dyspnoea subsided, and his well-being and physical capacity improved. The auscultatory abnormalities subsided gradually, and respiratory efficiency improved (after 7 days, the patient could breathe on his own, SpO_2 >95% while breathing atmospheric air). A follow-up thoracic HRCT without contrast enhancement revealed areas of ground-glass interstitial opacities, with thickening of the interlobular and intralobular septa (Fig. 1). The changes were more pronounced in segment 6 of the left lung, along the interlobar and interlobular sept, with band-like opacities and atelectatic lesions. Moreover, numerous small areas



Rycina 1. Obraz HRCT ewolucji zmian śródmiąższowych w COVID-19. Obszary zagęszczeń śródmiąższowych o typie matowej szyby z pogrubieniem przegród międzyzrazikowych i śródmiąższowych.

Figure 1. HRCT image of the evolution of interstitial lesions in COVID-19. Areas of interstitial densities of the ground-glass opacities with thickening of interlobular and interstitial septa.

of ground-glass interstitial opacities were found in all the pulmonary lobes, less pronounced in the lower lobe of the right lung. The pleural cavities were free of fluid, and no other abnormalities were observed in the thoracic organs.

Following two RT-PCR (reverse transcription polymerase chain reaction) tests for the SARS-CoV-2 genetic material with negative results, the patient was discharged in a generally good condition, with recommendations to avoid effort for 4 weeks, remain under the care of the family doctor, take 40 mg/0.4 mL q.d. of subcutaneous enoxaparin for 2 weeks, and have follow-up laboratory tests in approximately 4 weeks: complete blood count with a smear, CRP, liver enzymes (AST, ALT), D-dimers and thoracic X-ray.

After 8 weeks of convalescence at home, the patient returned to active military service, following an authorisation of the Military Aviation Medical Commission to fly aircraft.

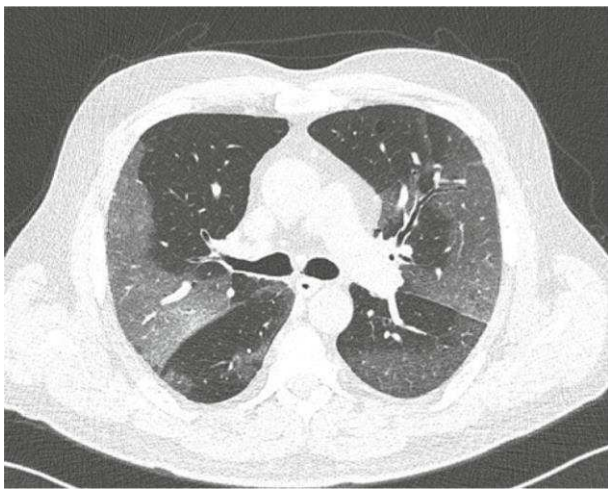
Case 2

A 66-year-old male patient with type 2 diabetes managed with oral medications, status post left-sided nephrectomy due to renal cancer in 2017 and cholecystectomy due to cholelithiasis in 2020, vaccinated against flu. For three consecutive days after the vaccination he experienced flu-like symptoms. On 22 October 2020, a nasopharyngeal swab was collected for an RT-PCR test to detect the presence of SARS-CoV-2 genetic material, with the result being positive. The patient then remained in household isolation; however, due to persisting significant

weakness, exhausting dry cough and transient fever of up to 39.5°C, on 30 October 2020, he visited the HED of the Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw, where thoracic HRCT revealed numerous, diffuse, peripheral interstitial ground-glass opacities in all the lobes of both lungs (Fig. 2). They were most pronounced in the lower lobe of the left lung an in the upper lobe of the right lung, significant thickening of the interlobular septa was also observed, which suggested typical radiological findings for COVID-19.

The patient was hospitalised at the Department of Infectious Diseases and Allergology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw, with a diagnosis of pneumonia due to SARS-CoV-2 infection. On admission, he reported significant weakness, dyspnoea during mild exercise and persistent dry cough. The patient denied chest pains, palpitations, fainting or syncope. Tachypnea of 30 breaths/min - SpO_2 without oxygen supply it was 88%, and with passive oxygen therapy (flow rate of 8 L/min) through a mask with a reservoir bag it was 96%. Laboratory tests revealed elevated concentrations of CRP – 14.5 mg/dL, D-dimers – 6.82 µg/mL (normal range: <0.05 µg/mL), LDH 521 U/L (normal range: 135-232 U/L). During the hospitalisation, only small molecular weight heparin was used, nadroparin, 0.3 mL = 2850 U/day). A gradual improvement of the clinical status, resolution of the auscultatory signs over the lung fields, and CRP reduction were observed. RT-PCR tests for SARS-CoV-2 infection, performed on the second and third day of hospitalisation, did not reveal any SARS-CoV-2 genetic material.

On the fifth day of hospitalisation, the patient reported a sudden pain in the right shin, associated with coldness, loss of sensation and muscular weakness. A physical examination did not reveal oedema of the limb, but pulse asymmetry on the popliteal artery and dorsalis pedis was found. An urgent computed tomography angiography (angio-CT) of the abdominal aorta and lower limb arteries was performed, which revealed minor paramural contrast deficits (probably small thrombi) in the distal section of the superior mesenteric artery, and paramural thrombi, with small restrictions of the lumen, were also found in the lower section of the abdominal aorta, over the bifurcation. Thrombi were also found in the right common iliac artery, at approximately 11 mm. Behind the bifurcation, no contrast was observed. The lumen was filled with soft lesions (thrombi) at approximately 35 mm; further, the iliac vessels were filled; paramural atherosclerotic plaques, small paramural thrombi, bilateral paramural thrombi with segmental significant stenoses in the internal iliac vessels were observed, at various levels; atherosclerotic plaques were found in the common femoral arteries, without



Rycina 2. Obwodowe zagęszczenia śródmiąższowe typu matowej szyby

Figure 2. Peripheral interstitial densities of ground-glass opacities

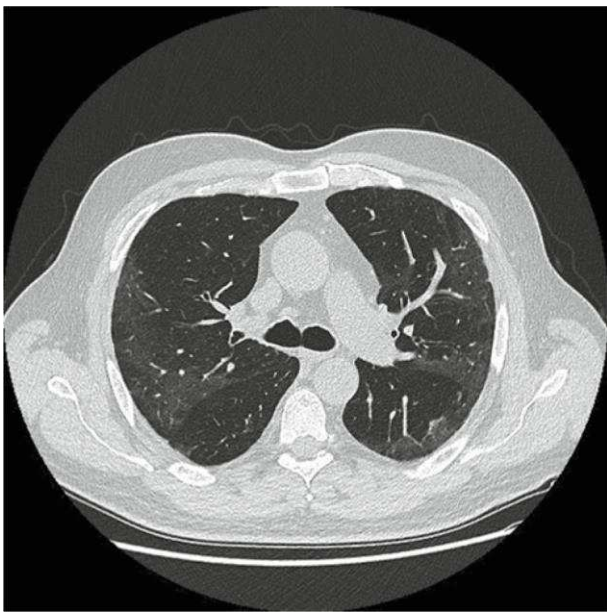
stenosis; the right superficial femoral artery was patent; the popliteal artery with tibiofibular trunk were obstructed at approximately 95 mm; the filling from the muscle pump in the right shin arteries was poor; slightly better filling of the posterior tibial artery, up to the distal aspect, was visible; the anterior tibial artery and the fibular artery were filiform up to 1/2 of the shin length, further – they were not filled distally; the arterial vessels of the right foot were not filled. No significant changes were found in the left lower limb.

A vascular surgeon was consulted, and the patient was qualified for surgical treatment on 5 November 2020. Continuous infusion of unfractionated heparin (Heparinum WZF) 25,000 U, diluted with 50 mL of 0.9% NaCl, was administered through an infusion pump.

On 5 November 2020, the patient was transferred to the Department of Vascular and Endovascular Surgery, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine, where an arteriography of the lower limb arteries was performed, and a coated stent was implanted in the right common iliac artery (Ventus 9x57), and a catheter was placed for targeted thrombolysis. A follow-up angiography on the next day revealed that a very good level of vessel patency had been achieved. The surgery and the post-operative period were uncomplicated. In a good general condition, with normal, palpable pulse on the right femoral artery, popliteal artery and posterior tibial artery, with a symmetrical temperature in the lower limbs, without any pain symptoms, without signs of haematoma at the vascular access site, after three days the patient was transferred to the Department of Cardiology for further treatment.

On admission to the department, the patient's status was moderately good, without pain symptoms in the chest, without dyspnoea at rest; however, he reported dyspnoea during mild physical exercise, after walking a few steps, and a persistent cough. The physical examination revealed regular cardiac function ~111/min, blood pressure of 92/60 mm Hg, no murmurs over the heart, discrete crackles over the lung fields, at the base of the right lung, oxygen saturation during oxygen therapy through a mask at approximately 96%, a soft and painless abdomen, without peritoneal symptoms, normal temperature in the lower limbs, and preserved pulse in the arteries. ECG demonstrated regular sinus rhythm, approximately 57/min, intermediate heart axis, without signs of recent ischaemia. Laboratory tests revealed CRP – 3.1 mg/dL, fibrinogen – 405 mg/dL (normal range: 200-400 mg/dL, D-dimers – 6.19 µg/mL, aminotransferases (ALT – 130 U/L, AST – 82 U/L), elevated concentration of high-sensitivity troponin T – 37 ng/L (normal range: <14.0 ng/L), and no other significant abnormalities. Echocardiography demonstrated heart chambers of normal size, normal thickness of the left ventricular muscle, no segmental contractility disorders. The left ventricular ejection fraction was approximately 65%, the ascending aorta was not dilated, without a haemodynamically significant valvular defect. The pulmonary trunk was not dilated, with normal acceleration rate. The inferior vena cava was not dilated, showing respiratory compliance. The pericardium was free of fluid, the interatrial septum showed no signs of leak in a colour Doppler examination. The applied therapy comprised passive oxygen therapy, nebulised bronchodilators, empirical antibiotic therapy (ceftriaxone, levofloxacin), intravenous steroid therapy, followed by oral steroid therapy, small molecular weight heparin at therapeutic doses, angiotensin convertase inhibitor, metformin, proton pump inhibitor, statin, and supplementation of water and electrolytes. The patient received general systemic rehabilitation and psychological care, following WHO (World Health Organization) recommendations.

The treatment led to a clinical improvement, confirmed by laboratory tests. Haematological diagnostics for coagulopathy were planned. On 16 November 2020, the patient was discharged from the hospital in a good general and local condition, with recommendations to continue the general systemic rehabilitation, exercise regularly, according to his physical capacity, drink up to 2L/day of liquids, restrict salt, animal fat and simple sugars in the diet, and to perform regular arterial pressure and pulse measurements (with a measurement diary), as well as to take the following medications: rivaroxaban 220 mg 1 tablet/day, prednisone 20 mg/day for a week, then gradually withdraw, perindopril 5 mg 1 tablet/day, atorvastatin 40 mg 1 tablet/day, metformin 500 mg 1 tablet/day, beclomethasone dipropionate with formoterol 1 dose b.i.d. Periodic follow-up tests on an outpatient basis at the primary care facility were also recommended, including complete blood count, ionograms, renal parameters, inflammatory markers and lipid panel.



Rycina 3. Częściowa regresja zagęszczeń typu matowej szyby z ich ewolucją w kierunku zmian włóknistych

Figure 3. Partial regression of the ground-glass opacities with evolution towards fibrotic changes

After six weeks, a follow-up thoracic CT presented a typical evolution of COVID-19 lesions, i.e. numerous, diffuse, peripheral ground-glass opacities in all the lobes of both lungs, particularly in the upper lobes. Compared to the previous test, a partial regression of the opacities was observed, with their evolution towards fibrous lesions (Fig. 3) – the lesions were less pronounced than before.

Discussion

The cases presented above illustrate various courses of COVID-19. In the first case, without any risk factors for a severe course, the disease was mild and limited to a pulmonary involvement. Some analyses suggest that in patients who do not experience severe respiratory insufficiency during COVID-19, the abnormalities in the pulmonary HRCT are maximally pronounced after approximately 10 days following the symptom onset [8]. In patients with severe respiratory distress the pulmonary lesions visible in HRCT show the greatest severity on days 6-11 of the disease [9]. The imaging tests performed at that period in our patient demonstrated inflammatory lesions in relatively large areas of the lungs, which resulted in respiratory insufficiency requiring oxygen

supplementation. Further on, there were no symptoms suggesting a significant vascular involvement or invasion of other vital organs to a degree that would result in a clinical manifestation. The respiratory insufficiency resolved quite quickly, the oxygen therapy could be discontinued, and the patient soon restored his physical capacity.

In the second case, the SARS-CoV-2 infection occurred immediately after a flu vaccination, and early symptoms of COVID-19 were interpreted as a reaction to the vaccination. When COVID-19 infection was confirmed, despite the risk factors for a severe course, nothing indicated a different course of the disease or that a serious complication would develop during the resolution of symptoms. In our opinion, the complication was not only due to the hospitalisation, but was also associated with the SARS-CoV-2 infection itself. It has been established that the expression of ACE 2 (angiotensin-converting enzyme 2), the principal receptor allowing virus penetration into cells, is particularly strong in the cellular membranes of vascular muscles and endothelium [10]. This results in endothelial dysfunction, activation of blood platelets, increased blood viscosity and disrupted blood flow, increased also due to hypoxia and immunological reactions, with leads to overcoagulation and thrombogenesis. Elevated concentrations of D-dimers, fibrin, fibrinogen and fibrinogen degradation products are observed, as well as reduced antithrombin values, prothrombin time activity and thrombin time [11]. Typically the consequences of these changes affect the venous system, and are clinically more pronounced in patients who previously suffered from venous thromboembolism [12]. However, in some cases, the consequences of vascular abnormalities due to COVID-19 manifest also in arterial vessels, especially the mesenteric and lower limb arteries. They can occur despite prophylactic anticoagulatory management [13]. Moreover, they develop suddenly, even in young, previously healthy individuals, and are associated with a serious risk [14]. In our patient the additional risk factor was atherosclerosis in the course of diabetes.

The risk of a severe course of COVID-19 differed in the presented patients. We know that the severity of COVID-19 is increased by various factors, such as age over 65 years, cardiovascular diseases, diabetes, pulmonary diseases (COPD, interstitial lung diseases and asthma), arterial hypertension, neoplasms, renal disorders, blood disorders (anticoagulatory therapy), hepatic, metabolic or neurological diseases, conditions such as obesity (BMI >30), smoking tobacco, pregnancy, immunodeficiency (e.g. therapy with certain biological drugs, anti-inflammatory medications, patients after transplantations, HIV infection) [10]. A severe, potentially fatal course of COVID-19 is particularly often observed in obese males, who smoke, aged 50-60 years old, with blood type A [14].

In the first patient, without any risk factors for a severe course, a relatively mild disease could be expected, but in the second case, a severe course was foreseen. However, initially, nothing indicated that such a serious complication could arise, although it is fortunate that its negative effects were prevented. A sudden deterioration in COVID-19 patients and development of certain complications appears to be typical for the disease.

Recently it has been suggested that the severity of COVID-19 may be genetically determined. Among the genes we inherited from the Neanderthals in the course of evolution, two groups can be distinguished: one determines a mild course of COVID-19, and the other is associated with a severe manifestation. It has been established that the baseline levels of 2′–5′ oligoadenylate synthetase 1, engaged in the innate immune reaction to viral infections and coded by OAS1 with the locus on chromosome 12, may play important role [16]. Elevated OAS1 levels were associated with protection against severe COVID-19 and hospitalisation [17]. It appeared that the Neanderthal isoform of OAS1 found in the modern population was of particular importance. Interestingly, some medicines, such as phosphodiesterase inhibitors, increased the OAS1 levels, so it seems reasonable to test their effect on the susceptibility to COVID-19 or the severity of the disease.

A gene cluster identified recently on chromosome 3 could be a risk locus for severe acute respiratory syndrome due to SARS-CoV-2 [18]. This risk could be conferred by a genomic segment of around 50 kilobases, also inherited from the Neanderthals and found in approximately 50% of people in south Asia and around 16% of people in Europe. Time will show if we can use these findings in practice.

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Cerebral small vessel disease – a great challenge for modern medicine

Choroba małych naczyń mózgowych – wielkie wyzwanie dla współczesnej medycyny

Jacek Staszewski
Department of Neurology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw; head: Prof. Adam Stępień MD, PhD
Article based on the Inauguration Lecture for Academic Year 2020/2021 at the Military Institute of Medicine

Abstract This article presents current achievements and challenges related to one of the most important neurological diseases of the 21st century, i.e. sporadic cerebral small vessel disease (sCSVD). The aim is to discuss the threats posed by the clinical consequences of the disease. Small cerebral vascular disease is an important clinical entity not only from the neurological but also from the general medical perspective. Epidemiological studies have shown that sCSVD is the most common vascular disease of the central nervous system and the main cause of cognitive deficits. It is also probably one of the most important pathological processes responsible for brain ageing. Despite the significant prevalence of cCSVD, especially in the elderly, and its significant clinical consequences, etiopathogenesis and optimal treatment of sCSVD have yet to be clearly defined.
Key words: etiopathogenesis, secondary prevention, sporadic cerebral small vessel disease, vascular dementia

Streszczenie W artykule przedstawiono dotychczasowe osiągnięcia i wyzwania, jakie stawia przed współczesną medycyną sporadyczna choroba małych naczyń mózgowych (sChMNM) - jedna z najważniejszych chorób neurologicznych XXI w. Praca ma na celu przybliżenie zagrożeń wynikających z następstw sChMNM. Choroba małych naczyń mózgowych to ważne zagadnienie nie tylko z perspektywy neurologicznej, ale także ogólnomedycznej. Badania epidemiologiczne wykazały, że jest ona najczęstszą chorobą naczyniową OUN oraz główną przyczyną deficytów poznawczych. Najprawdopodobniej należy także do najważniejszych procesów patologicznych odpowiedzialnych za proces starzenia mózgu. Mimo znacznego rozpowszechnienia sChMNM, zwłaszcza w populacji osób w wieku podeszłym, i istotnych konsekwencji klinicznych etiopatogeneza oraz optymalne leczenie sChMNM nie zostały dotychczas jednoznacznie określone.
Słowa kluczowe: sporadyczna choroba małych naczyń mózgowych, otępienie naczyniowe, etiopatogeneza, profilaktyka wtórna

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Corresponding author
Prof. Jacek Staszewski
Department of Neurology, Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine
128 Szaserów St., 04-141 Warsaw; e-mail: jstaszewski@wim.mil.pl

Cerebral small vessel disease

Cerebral small vessel disease (CSVD) is not a single disease affecting the cerebral arteries, but comprises various pathological processes observed in the small vessels of the brain, including the arteries, arterioles, capillaries and venules [1]. Their common feature is invasion of the vascular bed, whose diameter is <400 μm (less than the diameter of a human hair) [2]. At present there is no imaging technique that shows these vessels *in vivo*, which prevents the analysis of the associated pathological mechanisms. The anatomical basis for CSVD is the varied vasculature of the subcortical structures in the brain. Contrary to the cerebral cortex, characterised by a rich network of collateral circulation, the subcortical vasculature primarily comprises a system of poorly branched penetrating end vessels. They are the principal vessels engaged in circulatory autoregulation, and are highly susceptible to damage. The most common – sporadic – CSVD (sCSVD) results from a prolonged atherosclerotic process, arterial hypertension, lipohyalinosis and the processes associated with vessel

ageing. Less frequent causes of sCSVD include vasculitis and genetically determined microangiopathies [3].

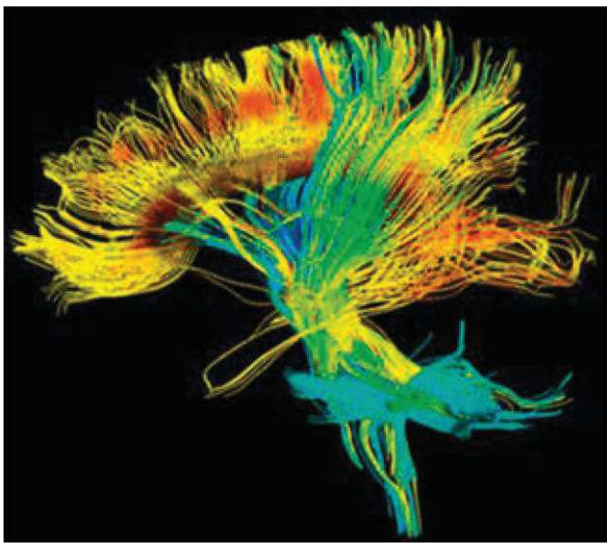
The course of sCSVD vessel obstruction or critical stenosis, followed by hypoperfusion and impaired flow autoregulation, is caused by atherosclerotic plaque and segmental disorganisation of the vascular wall. Isolated fibrinoid necrosis and atherosclerotic processes may result in progressive ischaemic focal lesions in the brain, as well as damage to and local weakening of the vascular wall, resulting in microaneurysms, microhaemorrhaging or acute blood extravasation (intracerebral haemorrhage).

Small vessels supply mainly the white matter, basal ganglia, and brainstem. These structures are responsible for interlobar integration, inter-hemispheric integration, planning of the movement pattern, control of body posture, emotions, movement automation and executive memory. Figure 1 presents neuroimaging of the white matter tracts using diffusion tensor imaging. White matter is a highly complicated and extensive structure, which forms various tracts connecting the individual regions of the cortex and extracortical areas [4]. A minor injury of such a vast area can be asymptomatic, but it may also lead to a number of different clinical symptoms. A typical symptom of lacunar stroke, an acute manifestation of sCSVD, is dysarthria and clumsy hand syndrome, involving dysarthria, facial paresis and ataxia of the ipsilateral upper limb.

Sporadic cerebral small vessel disease

Sporadic cerebral small vessel disease is responsible for over 25% of ischaemic strokes (lacunar strokes) and 30% of intracerebral haemorrhages (located primarily in the subcortical structures). It is also among the main causes (50%) of cognitive function impairment and dementia, often concurrent with Alzheimer's disease. It contributes significantly to balance disorders in elderly patients, as well as to vascular Parkinson's disease [5].

Short-term prognosis in lacunar stroke is usually favourable, but the mean survival is approximately 4 years. Even in the case of a single focus, lacunar stroke is associated with a risk of vascular dementia, if it is strategically located (e.g. in the thalamus or basal ganglia). With multiple foci, significantly more often than in strokes due to large vessel atherosclerosis, the cognitive functions are impaired (50% within the first year following the stroke) and depression develops (25% within the first year). The risk of recurrent lacunar stroke is estimated at 20% per 4 years. Our understanding of the risk factors of lacunar stroke is incomplete. Based on population studies, it has been established that the vascular profile of the risk factors for a lacunar stroke differs from a non-lacunar one (e.g. lack of strong correlation with atrial fibrillation and hypercholesterolaemia or ischaemic heart disease).



Rycina 1. Obrazowanie szlaków istoty białej tensorem dyfuzji (zmodyfikowano na podstawie ryciny T. Schultz, www.sci.utah.edu/~gk/DTI-data/)

Figure 1. Diffusion tensor imaging tractography of white matter tracts (modified basing on T. Schultz work, www.sci.utah.edu/~gk/DTI-data/)

Intracerebral haemorrhage in the course of sCSVD is typically located in the deep brain structures. It is usually found in patients with poor control of arterial pressure. The prognosis depends on the extent of the haemorrhage, but it is rarely favourable. Short-term and long-term mortality rates (40% after a month, 54% after a year) are similar to those in intracerebral haemorrhages in the course of amyloid angiopathy or anticoagulation complications. The annual risk of recurrence is estimated at 2%; it is higher in elderly patients, and can be reduced with proper blood pressure control. Intracerebral haemorrhage involving the deep structures is also a risk factor for ischaemic vascular incidents, including lacunar strokes (annual risk of 6%), and cardiovascular mortality (annual risk of 3%).

Vascular dementia (VD) due to focal subcortical lesions is one of the most common types of dementia. Focal lesions in the white matter are also an important risk factor for dementia of various aetiologies, including Alzheimer's dementia (AD) and Lewy body dementia. The clinical presentation of vascular dementia changes depending on the extent of the lesions in the white matter or location of injuries. Many patients are aware of their "problems with memory", suggestive of AD; however, the clinical profile of cognitive disorders in VD patients differs considerably. Difficulties in solving even simple problems, delayed information processing and apathy are the dominant symptoms. Operational and functional memory disorders, with a significant adverse impact on the daily

life of patients, are much more frequently observed in VD than in AD. The annual incidence of VD among individuals aged 60-69 years old is up to 20-40/100 thousand people, and it increases to 700/100 thousand people aged over 80 years! The life-long risk of developing the disease is estimated at 34.5% in males and 19.4% in females, which is higher than in AD. Five-year mortality is up to 63% and over 30% of patients require care in nursing homes (32% and 20% in AD, respectively). Optimal causal treatment has not been determined. At present, the only known strategy for AD prevention is to reduce the vascular risk. Prophylactic use of acetylsalicylic acid in elderly patients with limited vascular risk is not recommended.

Apart from cognitive functional disorders, chronic sCSVD may be manifested by Parkinson's-like symptoms (dominating postural and gait impairments, early and symmetrical involvement of the lower limbs, slight limb tremor) with focal symptoms constituting axial symptoms of vascular parkinsonism. Vascular parkinsonism is currently underdiagnosed. It is estimated that it accounts for approximately 10-20% of parkinsonism cases, and is the second most common cause of parkinsonism. It differs significantly from idiopathic Parkinson's disease (iPD), for instance by a limited reaction to dopaminergic therapy. In vascular parkinsonism atrophy of substantia nigra or presence of Lewy bodies are not observed, although they are the basis of a histopathological diagnosis of iPD. At least one symptom of Parkinson's syndrome is found in approximately 30% of patients following a lacunar stroke, and symptom severity correlates with the burden of subcortical focal lesions, especially in the frontal and parietal areas, as well as in the basal ganglia.

Secondary prevention (optimisation of the treatment of arterial hypertension, diabetes, hyperlipidemia or obesity) and rehabilitation are of great importance in the therapy of patients. Despite a weak response to L-dopa preparations, they result in certain improvement in 15-30% of patients.

Cerebral small vessel disease may also present as a syndrome of various clinical symptoms of minor intensity and chronic nature., and include primarily: memory and concentration impairment that does not meet the criteria of dementia, uncharacteristic balance, posture and gait disorders, mood disorders and depression, tinnitus, impaired sphincter function and pseudobulbar palsy. The symptoms increase gradually, resulting in progressive physical incapacity, cognitive disorders and loss of independence. Balance disorders are caused by the damage to the white matter in the periventricular area, and the rupture of the cortico-thalamic and cortico-cerebellar connections. The main symptoms in the physical examination include postural reflex disorders, impaired movement pattern and concurrent presence of Parkinsonian gait and posture. Patients may fall suddenly. The presented syndromes are mainly treated with symptomatic therapy, movement rehabilitation and psychotherapy.

Radiological phenotypes of sCSVD

Considering the availability of magnetic resonance imaging (MRI), the radiological phenotypes of the disease have been carefully studied. Apart from lacunar or haemorrhagic stroke, they include: presence of microhaemorrhages in the deep structures, hyperintense focal lesions in the white matter (most common) and lacunae. The latter are radiological traces of a stroke, typically a symptomatic one, but often presenting with few or no symptoms. Recent population studies with the use of MR imaging demonstrated that the radiological course of sCSVD is often unfavourable [6, 7]. Initially asymptomatic, the lacunar lesions or periventricular lesions in the white matter progress in up to 30-40% of patients, or transform into other types of changes. The mathematical models based on the mean results of diffusion tensor imaging demonstrated that, compared to healthy individuals, patients with even minor white matter deficits reveal a significant reduction of white matter tracts, already at the initial stages of a clinically manifesting disease. It may indicate that the small focal lesions found in neuroimaging tests constitute merely the tip of the iceberg of the disease process that has been developing for some years [8, 9]. It also explains a significant limitation of the cognitive reserve and reduced effectiveness of rehabilitation, e.g. compared to the patients who experienced strokes of a different aetiology.

Latent strokes and focal lesions in the white matter

Little is known about the causes and course of sCSVD, especially in the preclinical phase. The disease may remain asymptomatic for a number of years, manifesting only with neuroimaging changes, such as clinically silent focal lesions in the white matter or lacunae. Lacunae, previously referred to as "silent strokes", are currently known as "latent strokes", as they have been demonstrated to cause subtle neurological deficits, e.g. regarding the cognitive functions. These radiological changes are found in the general population in up to 40% of individuals aged over 65 years old, and diffused periventricular lesions are observed in as many as 90% of people over 80 years of age [10]. Interestingly, most of them result from sCSVD, not from thromboembolism or cardioembolism. Detection of these focal lesions is associated with adverse prognosis. Research conducted at the Department of Neurology, Military Institute of Medicine, revealed that their presence, independently of

other vascular risk factors, is a predictor of ischaemic strokes, haemorrhagic strokes, dementia, balance disorders, falls and disability [11]. Depending on the advancement of the radiological signs of sCSVD, the risk of cardiovascular death or disability increases significantly; it is 25% to 60% at 6 years [12]. The principal risk factors for lacunae include advanced age, nicotinism and arterial hypertension. Recently, it has been found that the risk factors for lacunae vary according to the size of the lacuna, with a stronger correlation between diabetes, systolic blood pressure and lacunae of <7 mm in diameter, as opposed to larger lacunae, which correlate more strongly with LDL hypercholesterolaemia and nicotinism. Lacunae and periventricular lesions are predictors of microangiopathies in locations other than the brain, e.g. retinopathy, nephropathy or small coronary vessel disease [13]. Therefore, focal lesions of vascular origin in the white matter, detected accidentally in a clinically asymptomatic patient, should not be considered a normal variant, or a sign of physiological ageing processes [14].

The management after detection of asymptomatic radiological signs in the course of sCSVD has not been determined, due to lack of randomised studies in this population of patients. Collecting a detailed history is recommended to verify if the patient experienced a symptomatic episode, and conducting a neurological examination is advisable. In the case of asymptomatic changes in neuroimaging, the general management principles following the AHA/ASA guidelines apply, based on the vascular risk factors, and the treatment following the rules of primary prevention of vascular diseases and stroke should be introduced [15]. Diagnostics for atrial fibrillation, patent foramen ovale with right-to-left shunt, and stenosis of the cephalad arteries should be considered. The effectiveness of the treatment with acetylsalicylic acid in patients with latent stroke/lacunae in the course of sCSVD has not been established. A recently completed study did not demonstrate any effect of restrictive control of the vascular risk factors on the development of focal lesions in the white matter. Only delayed progression of the lesions was observed with very intensive hypotensive therapy, reducing blood pressure to <120/80 mm Hg, but exclusively in patients with the most advanced focal lesions [16]. Therefore, despite well-established and precise guidelines for the therapeutic and diagnostic management of patients with symptomatic stroke, strong recommendations have not been developed for those with latent stroke and analogous cerebral damage. This is *terra incognita* in the guidelines for the management of vascular diseases, and should be urgently addressed. Due to the gap in our understanding of this medical problem, the current recommendations do not include diagnostic testing when silent focal lesions are found, although most experts indicate that the presence of these radiological markers of the disease should be considered when establishing therapeutic goals in the treatment of arterial hypertension, hyperlipidaemia, or in the assessment of the risk of embolism and haemorrhaging during anticoagulation therapy [17].

Pathophysiology and risk factors for sCSVD

There are a few theories explaining the development of focal lesions and leukoaraiosis in the course on sCSVD. One of them attributes lacunae formation to obstruction of the blood flow through a vessel due to an embolus from a ruptured atherosclerotic plaque, closure of the lumen due to lipohyalinosis or chronic hypoperfusion. According to another hypothesis, acute or subacute cerebral injury results from impaired permeability of the walls of the perforating vessels due to a damaged vascular endothelium, mostly because of arterial hypertension or diabetes. As a result, the blood-brain barrier is damaged, blood elements are extravasated, oedema of the extravascular space occurs, and the cells in this area are damaged. There is no consensus regarding the mechanism in which chronic “leak” of various blood elements outside the vessels could contribute to “acute” symptoms of lacunar stroke, for example. Previous observations demonstrated that the atherosclerotic process (primarily in the parent artery or in the proximal section of the perforating artery) accounts for only approximately 30% of lacunar strokes, and for 10% of focal lesions in white matter [18]. Studies indicate that following distal vascular involvement, the significance of the atherosclerotic process in the pathogenesis of CSVD decreases, while the impact of impaired autoregulation and chronic hypoperfusion increases [19].

Chronic impairment of the blood-brain barrier is confirmed by advanced MRI tests which demonstrate extravasation of the contrast medium in the area of lacunar focus and in the regions of apparently unchanged white matter [20]. Due to the damage to the blood-brain barrier, proteins and cellular blood component are extravasated, resulting in perivascular oedema and distally expanding hypoperfusion. The impairment of the blood-brain barrier is only one of the elements contributing to a functional impairment of a greater unit, i.e. a neurovascular unit. It comprises both the vascular structure and the perivascular space, including microglia, astrocytes and neurons. This structure is responsible for proper functioning of the vascular bed in reaction to changes in the systemic arterial pressure, for proper cerebral perfusion and for immunological homeostasis [21]. The causes of progressing damage of the blood-

brain barrier and neurovascular unit are probably multifactorial, and have yet to be fully determined. It is assumed that classic vascular risk factors, especially long-term hypertension, probably contribute to the progressive destruction of these structures. An animal model of refractory arterial hypertension demonstrated that focal lesions in the CNS develop many years prior to the hypertension, which also indicates the multidimensional role of genetic factors [22]. Recently, the adverse effect of sodium chloride on the vascular endothelium has been emphasised, as well as the resulting damage to the blood-brain barrier, particularly in individuals with gut-brain axis dysfunction and microbiomic abnormalities [23]. The risk of sCSVD is high also in patients with chronic inflammation, e.g. chronic kidney disease (kidney-brain axis) and persistent infections (e.g. of the respiratory system) due to chlamydia, or chronic periodontium diseases [24]. Small vessel disease may be the first stage and the fundamental element in the development of neurodegenerative processes, as impairment of the blood-brain barrier facilitates accumulation of β-amyloid and Tau protein in the brain due to reduced clearance of these substances and reduced neuronal plasticity and cognitive reserve.

New clinical studies on sCSVD

A number of studies have been published recently demonstrating that abnormal daily arterial pressure variations may be an important risk factor for the development of focal lesions in the CNS, due to the adverse effect of excessive pulsation of blood flow (blood-hammer effect) through microcirculation [25]. It has also been observed that both systolic and diastolic arterial hypertension demonstrate the most harmful effects on the development of focal lesions not in elderly patients, but in middle-aged individuals, for many years, even decades, before the clinical diagnosis is established. Later, the effect of arterial hypertension control on the course of sCSVD decreases [26]. Newly proposed risk factors for sCSVD include depression (doubles the risk of lacunar stroke and lacunae), obstructive sleep apnoea syndrome (doubles the volume of focal lesions in white matter), insomnia or sleep deprivation (four times higher risk of cerebral atrophy and/or focal lesions in the CNS – probably due to reduced clearance of brain metabolites during the shortened REM phase) and air pollution (especially with $PM_{2.5}$ – the risk of focal lesions in white matter is increased by 46%).

Conclusions

The introduction of new therapies for sCSVD and modification of the vascular risk factors are important, as despite the currently applied prevention methods, the risk of ischaemic stroke has increased in the past 25 years in Poland by 6%. This effect is associated with longer life expectancy, but also with other modifiable risk factors. In the recent years, a constant reduction in the incidence of atherosclerotic strokes has been observed in Western Europe; however, the rates of strokes due to sCSVD has been increasing continuously. In Poland, approximately 30 thousand patients with strokes due to small vascular disease are hospitalised, while the number of patients with latent strokes is at least twice as high, and also require preventive treatment. The last three decades are referred to as “decades of the brain” – a range of new diagnostic and therapeutic methods has been introduced, and mortality rates due to vascular diseases of the CNS have decreased significantly. This decade will certainly witness further scientific research and implementation of effective therapies for CSVD. In this context, it is important to introduce interdisciplinary vascular clinics and provide a wide access to rehabilitation and neuropsychological therapy. I would like to close with a quote from Thomas Sydenham, known as the English Hippocrates: “a man is as old as his arteries.” It aptly describes the clinical presentation of cerebral small vessel disease.

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Asthma and allergic diseases in terms of COVID-19

Astma i choroby alergiczne a COVID-19

Jerzy Kruszewski

Department of Infectious Diseases and Allergology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw; head: Assoc. Prof. Andrzej Chciałowski MD, PhD

Abstract The study presents a current state of knowledge following a year of experience with a COVID-19 pandemic, especially regarding the issues that arose while caring for asthma and allergy patients. It generally shows the cellular mechanism of SARS-CoV-2 infection, its clinical presentation and consequences. The risk and course of infection in patients with asthma or allergies, as well as the COVID-19 potential impact on asthma flare-ups were discussed. The paper describes how to treat asthma flare-ups during the COVID-19 pandemic, how to proceed with asthma flare-up patients infected with COVID-19, how to treat chronic asthma during the COVID-19 pandemic and which medical and diagnostic procedures should be limited. It presents guidelines for allergists during the pandemic and for individual protection of health professionals delivering asthma and allergy care in the era of the pandemic.
Key words: Keywords: asthma, COVID-19, SARS-CoV-2

Streszczenie W pracy przedstawiono stan wiedzy po upływie roku doświadczeń z pandemią COVID-19, ze szczególnym uwzględnieniem problemów, jakie pojawiły się w opiece nad chorymi na astmę i choroby alergiczne. Ogólnie przedstawiono mechanizm zarażania komórek przez SARS-CoV-2 oraz obraz kliniczny i następstwa COVID-19. Omówiono takie problemy, jak ryzyko zakażenia SARS-CoV-2 chorych na astmę i choroby alergiczne, przebieg COVID-19 u takich chorych oraz czy zakażenie SARS-CoV-2 może wywołać zaostrzenie astmy. Wyjaśniono, jak należy leczyć zaostrzenia astmy w czasie pandemii COVID-19 i zaostrzenie astmy u chorego na COVID-19, a także jak leczyć przewlekle astmę w czasie pandemii COVID-19 oraz jakie procedury diagnostyczno-lecznicze trzeba ograniczyć. Przedstawiono zasady pracy alergologa w czasie pandemii COVID-19 oraz wytyczne odnośnie do indywidualnego zabezpieczenia personelu medycznego wykonującego procedury u chorych na astmę oraz choroby alergiczne w dobie pandemii.
Słowa kluczowe: SARS-CoV-2, COVID-19, astma

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Corresponding author
Prof. Jerzy Kruszewski
Department of Infectious Diseases and Allergology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw
128 Szaserów St., 04-141 Warsaw
e-mail: jkruszewski@wim.mil.pl

Introduction

The COVID-19 (coronavirus disease 2019) pandemic due to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infections has been ongoing for over a year [1].

According to official statistics, approximately 70 million people across the world have been infected, and nearly two million died. In Poland, almost 1.5 million people have been infected, and 30 thousand died.

Compared to other known SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) viruses, SARS-CoV-2 appeared more infectious, but much less deadly.

This study summarises the present state of knowledge (end of 2020) regarding the effects of the COVID-19 pandemic on the management of patients with asthma or allergic diseases.

Mechanism of cellular infection with SARS-CoV-2

SARS-CoV-2 penetrates into the human body through the nose, the throat, and then continues to the lower respiratory system.

Although not all the mechanisms of the fusion of the SARS-CoV-2 virus with cells have been explained, we know that the key protein necessary for infection is the S (spike) protein, comprising three subunits: S1, S2 and S2' (a total of 1272 amino acids). The S1 subunit combines with ACE2 (angiotensin-converting enzyme 2), found in many human cells (lungs, arteries, heart, kidneys and intestines), especially in the pulmonary alveoli [3]. The affinity of SARS-CoV-2 to ACE2 is exceptional, as it is 10 times stronger than in the case of SARS-CoV-1, responsible for the 2002 pandemic. Also, the virus variants, characterised by differences in protein S, demonstrate different abilities to infect human cells. The VUI-202012/01 variant with V501Y mutation, found in Europe since September 2020, presents an even higher infectious potential, and replaces the older variant, e.g. with the VD614G mutation - European variant from February 2020, and A222V - the Spanish variant from the summer of 2020. While the older variants differed by 1-2 mutations, the VUI-202012/01 variant varies by at least 22 loci of mutation in its genome. However, at present it is considered to be of no practical consequences in the diagnostic process, although it may limit the effectiveness of the available RNA vaccines against SARS-CoV-2 (Fig. 1).

Probably the already known genetic polymorphisms for ACE2 may also be of importance for the effectiveness of binding between the virus and human cells, i.e. the risk of infection for some people. Among several studied alleles of ACE2, two interacted with protein S of SARS-CoV-2 in a different way than others [4]. Interestingly, there is no data presently to confirm that the commonly used ACE2 inhibitors or sartans modify the expression of ACE2 in humans in a way that could contribute to infections with SARS-CoV-2. Dutch researchers are conducting studies on monoclonal antibodies against SARS-CoV-2 protein S, and Canadian scientists are working on the development of antibodies binding human ACE2 receptors to prevent the fusion between the virus and cells [5].

It has been established that co-receptors play an important role in cell infection by coronaviruses, including SARS-CoV-2. These co-receptors include serine protease 2 (TMPRSS2), activating the process of cellular fusion with protein S of the virus, and lymphocyte antigen 6E complex (LY6E), strongly reducing infections with numerous viruses, including SARS-CoV, SARS-CoV-2 and MERS-CoV [6,7]. Other proteins are also being studied as potential co-receptors for coronaviruses, e.g. furin enzyme, CD147 molecule, or proteins GRP78 and ADAM17 [1].

Consequences of SARS-CoV-2 infection

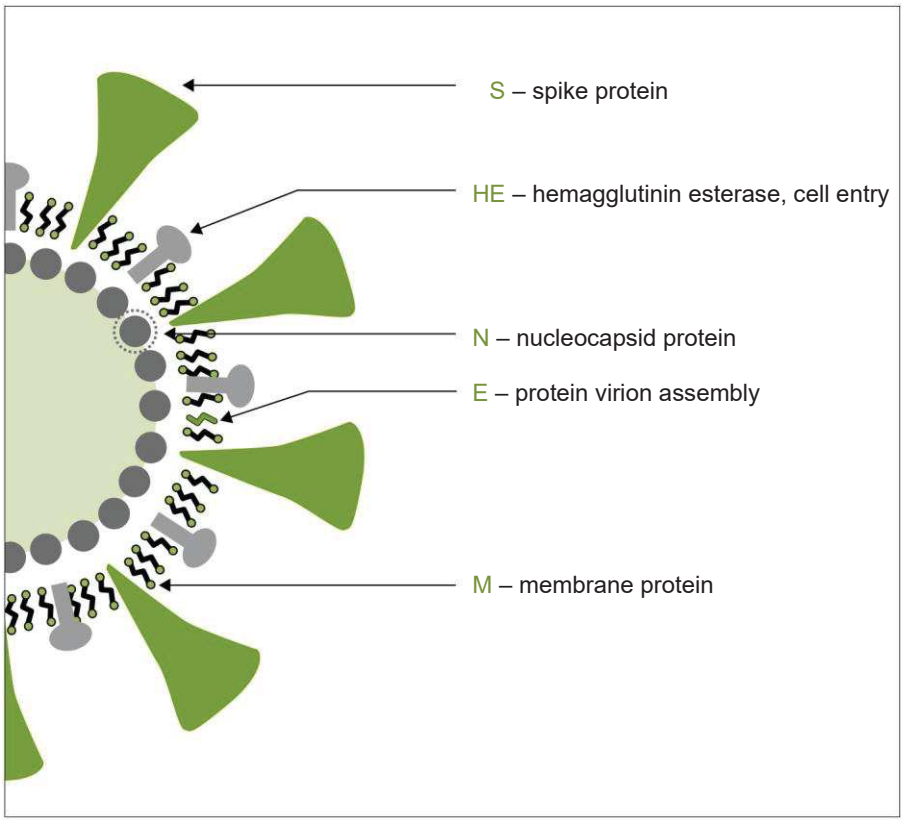
The known consequences of SARS-CoV-2 infection in humans may vary: from asymptomatic disease (we are only beginning to learn about the sequelae of such presentation, especially in children) to classic symptoms, including fever, dry cough, fatigue, rarely muscle pain, sore throat, headache, diarrhoea, conjunctivitis, loss of taste or smell, skin rash and discolouration of fingers and toes.

The occurrence of symptoms such as difficulty breathing, pain or pressure in the chest, or loss of speech or mobility, suggests a severe course of COVID-19, potentially associated with the involvement of various organ systems, primarily

- respiratory – acute atypical pneumonia, in severe cases associated with acute respiratory distress syndrome, but also:
- nervous – neurological symptoms (loss of smell and taste, headache, nausea, confusion, consciousness disorders), in severe cases development of cerebrovascular disease with brainstem involvement;
- gastrointestinal – diarrhoea and vomiting,
- urinary – acute renal damage,
- circulatory – embolism, acute heart failure.

SARS-CoV-2 infection may also, especially in elderly patients, induce excessive immune response, expressed by elevated cytokine levels (cytokine storm). This is manifested by high fever, extreme fatigue and nausea, and results in multi-organ damage and a severe, life-threatening course of COVID-19, often fatal.

Susceptibility to SARS-CoV-2 is common and high, although it appears that some individuals may be considerably less susceptible. The causes of lower susceptibility are being sought, for example, in the differences in ACE2 expression (lower in children and elderly individuals; in this case a severe disease manifestation is determined by ageing of the immune system, chronic inflammation of minimal intensity, and comorbidities), and in various genetic polymorphisms for ACE2 in individual people. Hussain et al. found that among 17 different ACE2 alleles, two of them: rs73635825 (S19P) and rs143936283 (E329G), demonstrated different intermolecular reactions with protein S of SARS-CoV-2 than other analysed alleles [4].



Rycina 1. Ważniejsze białka w strukturze SARS-CoV-2
Figure 1. More important proteins in SARS-CoV-2 structure

Total mortality due to COVID-19 is still difficult to establish, due to a lack of reliable data regarding the actual infection rates. It is estimated to be relatively low (<2-3%), but analysis of various groups of patients demonstrates that, for example, among hospitalised patients in Poland it exceeds 6%. In patients admitted to hospital with partial pressure of O_2 >95% the mortality rate is 12.3%, in those who require supplementary oxygen it increases to 17.3%, in the patients admitted at the age of >80 with partial pressure of O_2 <90% it is 29.8%, and in those requiring mechanical ventilation it is 67% [8].

The risk of death due to COVID-19 increases with age and presence of comorbidities. Severe, life-threatening COVID-19 is observed in obese smoking males aged 50-60 years old, with blood type A. In patients who meet these criteria and those at high risk of severe disease course the recommended preventive measures (isolation, social distancing, personal protection equipment) are particularly important.

We know that various factors worsen the manifestation of COVID-19:

- age over 65 years old (fatalities in patients >70 years old – approximately 8%, in those >80 years old – 14.8%),
- cardiovascular diseases,
- diabetes,
- lung diseases: COPD, interstitial lung diseases and asthma (fatalities in this group – approximately 6.3%),
- arterial hypertension,
- neoplasms,
- obesity (BMI >30),
- smoking tobacco,
- pregnancy,
- renal diseases, blood disorders (anticoagulatory therapy), liver diseases, metabolic disorders, neurological diseases,
- immunodeficiency (e.g. use of biological medications, anti-inflammatory drugs, patients following transplantations, HIV infection).

It is expected that COVID-19 caused by new, more infectious virus variants (British, South-African and Brazilian) will be also associated with higher mortality rates.

Does asthma increase the risk of SARS-CoV-2 infection?

The clinical presentation of COVID-19 acute phase and its course are mainly determined by the interaction between SARS-CoV-2 and the cells at various levels of the respiratory system. Therefore, at the beginning of the pandemic there were concerns that allergic diseases, asthma and COPD would be risk factors for infection with

the virus and the development of COVID-19. In addition, the fact that these diseases tend to exacerbate during viral respiratory infections, including those caused by various coronaviruses, was taken into consideration.

The first reports from China, where the pandemic started, indicated that asthma and allergic diseases did not increase the risk of infection with SARS-CoV-2 [9, 10]. In a cohort of 140 COVID patients admitted to a hospital in Wuhan between 16 January and 3 February 2020 there were no patients with asthma, and only 1 patient with COPD. A total of 11.4% of the patients in this group were hypersensitive to drugs, with different manifestations. Due to absence of patients with asthma, also in other Asiatic cohorts of approximately 100 individuals infected with SARS-CoV-2, scientists considered whether an increased Th2 immune response in asthma could protect against the infection with this virus.

Further analyses from the USA, based on data from cities on the East Coast revealed, however, that the rate of people with asthma among the patients hospitalised due to COVID-19 was up to 14-17% [11, 12]. Similar estimates were presented in Great Britain, where researchers demonstrated that asthma was found much more frequently in children and adults with mild to severe COVID-19 than previously reported in Asia and Europe [13]. In other European and non-European countries asthma was observed in 4-5% of patients, i.e. at a level comparable to the general population [14, 15]. A detailed assessment of history of allergic diseases and asthma performed in a group of 113 patients admitted to a regional hospital in Spain due to COVID-19 revealed that 22% of patients suffered from these conditions, which was similar to the prevalence of allergic diseases and asthma in Spain, estimated at 21.6% [16]. Nearly half of the patients were allergic to drugs (4 patients were allergic to beta-lactams, 2 demonstrated intolerance to NSAIDs, and 5 to other drugs and contrast media). Five patients had allergic rhinitis and asthma, 3 patients had rhinitis, 2 had asthma, 2 had seasonal allergy and 2 had urticaria. One of the patients had asthma, rhinitis and urticaria. In the data from the Department of Infectious Diseases and Allergology, Military Institute of Medicine, covering almost 400 COVID-19 patients requiring hospitalisation (with confirmed SARS-CoV-2 infection) only 4% suffered from chronic asthma. Study design may partially account for the American and British results, diverging from the general trend, but the comments to these reports highlight the problems with asthma management in countries where healthcare is mostly commercialised, and many patients cannot afford it. Due to the difficult access to drugs, patients do not receive treatment at all, or are treated on an emergency basis, and their asthma is poorly controlled.

It seems that the problem of asthma as a risk factor for SARS-CoV-2 infection is summed up well in the first part of the analysis conducted by the South Korean researchers, involving 7340 patients with positive test results for SARS-CoV-2 (out of 291,959 patients tested) [17]. The general odds ratio for SARS-CoV-2 infection in patients with asthma was deemed low – 1.10, with 1.06 for allergic asthma and 1.34 for non-allergic asthma (to compare: the odds ratio for SARS-CoV-2 infection in patients with allergic rhinitis was 1.2, and in those with atopic dermatitis was 0.93).

Despite such divergent outcomes, we can now declare that initial concerns that asthma and allergic respiratory diseases may be associated with increased risk of infection with SARS-CoV-2 have not been confirmed, especially when these conditions are well treated and managed.

Is COVID-19 more severe in patients with asthma?

Different measures are used in the assessment of COVID-19 severity, from indications for hospitalisation, necessity to prolong hospitalisation, necessity to treat the patient at ICU, to death. The mentioned analysis by Spanish researchers regarding hospitalised COVID-19 patients suggests that the following were associated with an increased risk of prolonged hospitalisation: advanced age and reduced O_2 saturation and bilateral pneumonia at admission [16]. Previous use of calcium channel blockers and proton pump inhibitors, as well as low oxygen saturation, high leukocytosis and high D-dimer levels at the time of hospital admission indicated a risk of transfer to ICU. The risk of death was increased in elderly patients, with a history of cerebrovascular disorders, using oral anticoagulants and selective serotonin re-uptake inhibitors, and demonstrating elevated IL-6 concentration. Asthma and allergic diseases were not mentioned as risk factors for severe COVID-19 in adults, and only in relatively young patients were allergic diseases slightly increased the risk of hospitalisation.

Similarly, French researchers demonstrated that arterial hypertension, diabetes and hypothyroidism significantly increase the risk of severe COVID-19, whereas asthma does not [18].

However, the mentioned analysis by the Korean researchers revealed that concurrence of asthma and allergic diseases may increase the risk of severe COVID-19, associated with hospitalisation at ICU, invasive ventilation or death [7]. Generally, the odds ratio for asthma was 1.67, for allergic asthma – 1.40, for non-allergic asthma – 4.09 (for comparison: for allergic rhinitis the value was 1.40, and for atopic dermatitis – 0.72).

However, even if we assume that asthma is associated with a risk of severe COVID-19 outcomes, it must be emphasised that such risk is minimal, much lower than in the case of other diseases, such as cardiovascular diseases, neurological disorders, diabetes, obesity, neoplasms etc.

Can SARS-CoV-2 infection exacerbate asthma?

At present, little is known about it. However, it has been established that coronaviruses can cause seasonal upper and lower respiratory inflammation, and they are found in nearly 10% of patients with asthma exacerbation [19].

There are no data currently illustrating the course of asthma in patients with SARS-CoV-2 infection who are not hospitalised due to COVID-19. According to some authors the information in the current guidelines of the American Centres for Disease control and Prevention that SARS-CoV-2 infection in patients with moderate to severe asthma may exacerbate the underlying disease is not sufficiently substantiated [20]. In patients hospitalised due to severe COVID-19, asthma exacerbations may result from the recommended use of dexamethasone.

How can asthma exacerbations be treated during the COVID-19 pandemic?

Epidemiological data demonstrate that good control of asthma may reduce the risk of SARS-CoV-2 infection. If a patient with well-controlled asthma is infected, COVID-19 may take a milder course.

According to many authors maintaining or restoring good asthma control during the pandemic is the most important recommendation for asthma patients, and a goal for their doctors [14, 21]. In periods of asthma exacerbation, systemic glucocorticosteroids (GCsys) are acceptable, if SARS-CoV-2 infection is not confirmed, and no symptoms are observed [22].

How can asthma exacerbations be treated in patients with COVID-19?

An analysis by Schulze et al., covering over 800 thousand asthma patients from British registers, demonstrated that therapy with inhaled glucocorticoids (IGC), especially in high doses, may increase the risk of death in patients with asthma (or COPD) and COVID-19 [23]. In patients using high doses of IGC the odds ratio is 1.55 compared to 1.14 in the patients using moderate or low IGC doses. It is often postulated, however, that IGC should be the basic therapy in asthma, also in the time of a pandemic [21, 24, 29]. Studies on the use of IGC in COVID-19 patients without asthma are being conducted to determine whether such treatment could reduce the severity of the disease [25].

At present, there is no consensus regarding GCsys therapy during asthma exacerbations in COVID-19 patients. GINA, WHO and CDC statements recommend avoiding GCsys in these patients, as they may extend the length of COVID-19 [21, 24, 26]. On the other hand, some studies indicate that GCsys (dexamethasone) may have beneficial effects on COVID-19 outcomes in hospitalised patients in severe condition [27-29], which is reflected in the guidelines. According to Polish guidelines, in asthma patients with SARS-CoV-2 infection the decision regarding the use of GC p.o. should be taken by the physician providing treatment [30].

There is no data indicating that other medications for asthma (SABA and LABA or antileukotrienes) can affect the course of COVID-19 [23, 30].

Long-term therapy of asthma during the pandemic

During the COVID-19 pandemic, if asthma is well-controlled, no treatment plan modifications are necessary [21, 30]. Continuation of previous inhalation treatment, based on anti-inflammatory IGC, is recommended. All inhaled medications should be administered using MDI or DPI inhalers. It is worth noting that studies are being conducted (to be completed in 2022) to determine a potential effect of IGC therapy on reducing the risk of COVID-19 in people without asthma [31].

During the pandemic the use of nebulised medications should be discouraged, as the aerosol may contribute to increased spreading of the virus. Continuation of previous long-term GCsys therapy is also justified.

If the asthma is not properly managed, the treatment plan should be modified, and the previously used drug doses should be increased, or new medications should be introduced, following the GINA recommendations [21].

Patients with severe asthma qualified for biological therapy programmes should not discontinue or modify their treatment. Pre-registration clinical trials of biologic drugs for the treatment of severe asthma and allergic diseases, such as omalizumab, mepolizumab, reslizumab, benralizumab and dupilumab demonstrated that they do not increase significantly the risk of viral infections. Therefore, continuation of the previous biologic treatment with anti-IgE (omalizumab) or anti-IL-5 (mepolizumab, benralizumab) in patients with severe asthma is recommended during the COVID-19 pandemic. It is also acceptable to initiate and continue biologic therapies with anti-IgE or anti-IL-5 in patients with severe asthma or chronic spontaneous urticaria, following the National Health Fund drug programmes.

Biologic drugs should not be administered to patients with acute symptoms of SARS-CoV-2 infection. In a reported case of a patient with mild COVID-19,

omalizumab administration soon after the resolution of clinical symptoms was not associated with any adverse effects [32]. The practitioner supervising the biologic treatment should decide whether and how to continue the therapy after the resolution of acute symptoms of COVID-19, following the principles presented in the drug programmes. There are no studies on the effect of biologic therapy on the course of COVID-19 in this group of patients, but it has been suggested that in patients treated with omalizumab, according to theoretical premises, the disease can be milder [33, 34]. It is not clear yet if adverse interactions can occur between biologic drugs and medications recommended in the treatment of COVID-19 (azithromycin, antiviral medications, immune plasma).

In patients with asthma due to inhalation allergy who receive subcutaneous allergen-specific immunotherapy (AIT), the treatment should be continued for at least three years [30, 35]. This requires visits to a clinic. In such situations, the doctor – in consultation with the patient – should consider various epidemiological and organisational aspects, including the patient's concerns, that could result in temporary suspension of the AIT, and its continuation in safer circumstances. The patient should be informed in detail about the potential risks/benefits of such decision, and about the plan for therapy continuation after the epidemiological situation improves. The necessity to limit social contacts during the pandemic justifies extension of the intervals between injections to a maximum specific for each vaccination: up to 4-6 weeks in the first year, and up to 8 weeks in the following years of therapy [30].

In the case of inhalation allergies, sublingual AIT may be an alternative for subcutaneous desensitisation as it requires fewer contacts with a physician and visits to the clinic, as it is administered by the patient. The final decision regarding a switch from the subcutaneous to sublingual therapy in individual cases, after consultation with the patient, lies with the physician.

During the pandemic, the decision to start AIT with inhalation allergens should be taken considering the current epidemiological situation, and the possibility to meet the patient safety requirements. The therapy could be delayed until the circumstances improve.

AIT using insect venom is recommended to be continued following the current principles for 3 years or longer. During the pandemic, it is possible to start AIT using insect venom using fast protocols, especially in patients with absolute indications for such treatment.

Experts from the European Academy of Allergy and Clinical Immunology do not recommend administration of vaccines used in AIT to patients with SARS-CoV-2 infection (confirmed by PCR-RT), or people who have had contact with infected individuals [35]. It appears that AIT may be continued after virus eradication or resolution of the symptoms of COVID-19, following the principles applicable to other viral infections.

Patients with asthma are bound by the same obligation to wear face masks as healthy individuals.

At present, it is believed that asthma therapy with the use of IGC, AIT and biologic drugs should be continued, as improved control of asthma can reduce the risk of infection with SARS-CoV-2 in asthma patients, and alleviate the symptoms of COVID-19 by improving the antiviral defence and suppressing inflammation [34]. Such treatment can possibly also reduce the *ACE2* gene expression in the nasal and bronchial cells [36].

Which procedures should be limited?

It is recommended to limit various *in vivo* procedures, as well as those associated with generation of small molecule aerosols which can increase dissemination of the SARS-CoV-2 virus [30]. The procedures include:

- skin prick tests (SPT), to be replaced by blood tests – determination of allergen-specific IgE;
- intradermal tests,
- patch tests with hapten contact (PT),
- spirometry,
- peak exploratory flow (PEF) tests in the office,
- induced sputum tests,
- measurement of fractional nitric oxide (FeNO) concentration in exhaled breath,
- non-specific bronchial hyperresponsiveness tests,
- inhaled allergen bronchoprovocation or nasal provocation tests,
- food allergen oral provocation tests,
- oral drug provocation tests,
- drug nebulisation.

The principles for allergologists during the pandemic

Asthma is a chronic disease and, following the guidelines, patients (at least majority of them) should have individual treatment plans. This allows to limit patient visits to a minimum [21, 30]. Patients who do not have treatment plans, especially in the case of disease exacerbation, should be provided with them as soon as possible, via the Internet or phone.

At the time of the pandemic, e-visits and televisits/teleconsultations became popular forms of contact between patients and doctors, allowing to receive medical advice without leaving the house.

They offer a way to avoid high risk of infection associated with the close contact between a patient and healthcare professional. Televisit/teleconsultation for a patient with asthma can be a good solution in the following cases [37]:

- to verify whether a visit in person is necessary (e.g. in the case of first visit),
- to repeat a prescription, especially on patient's request,
- for a general follow-up of properly managed and recently stable asthma (well-controlled symptoms in ACT), when treatment modification is not required, but only minor corrections could be introduced,
- to interpret and assess the results of additional studies, when patient's status is good/stable,
- to discuss with the patient any doubts regarding the individual plan of prophylactic and therapeutic management, e.g., oral AIT, especially when dosing modification may be required,
- before the pollen season, when treatment initiation should be recommended to patients with seasonal asthma, before the local pollen season starts.

Televisit/teleconsultation should not be used [37]:

- whenever physical examination is required (unstable disease, exacerbation, necessity to conduct additional *in vivo* studies, administration of a vaccine or biologic drug, episodes of severe anaphylaxis),
- when education on medication dosing / control of medication use is required,
- in other situations when the physician decides that contact in person is necessary.

If a visit in person is required, patients should use personal protection equipment (mask, hand disinfection), their route to the place of the visit should be possibly short, and proper distance between the patients in the waiting room should be ensured. During visits to a clinic, safe practices should be used not only for the patients, but also for their representatives and the medical personnel.

Personal protection equipment for the personnel performing procedures on patients with asthma during the pandemic

The general principles of protection for the medical personnel treating patients with COVID-19 were quickly developed in China [38]. At present, we know that the risk of SARS-CoV-2 infection is equally high for the entire medical staff, regardless of the services they provide. Many patients visiting a clinic may be asymptomatic, but still carry and spread the SARS-CoV-2 virus.

Knowing that coughing and sneezing are typical symptoms of asthma and allergic diseases, as well as factors contributing to SARS-CoV-2 dissemination, allergologist and the medical personnel in a clinic should take special precautions regarding the space where patients are admitted, and should include distancing (plastic barriers, spacial distance), regular airing and disinfection of rooms, equipment and furniture. Equally important is the use of personal protection equipment (proper face masks, e.g. N95, non-woven barrier gowns, disposable gloves, disinfectants with 60% alcohol content), following the general recommendations and current guidelines of the Ministry of Health, which can be found on the Internet [39, 40]. It is also important to limit the procedures mentioned above, and to avoid using nebulisation, as well as to use and utilise personal protection equipment properly.

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Distant memories*

Odległe wspomnienia

Andrzej Żmudzki

MD, PhD, Specialist in Psychiatry and Neurology, Retired Lt. Col. of the Polish Army, Falls Church, Virginia, USA

Abstract Participant observation of the military social environment in Poland after WWII by a military psychiatrist. Images of incongruent behaviours and attitudes generated by antagonism between ingrained Christian cultures and new norms, values and patterns imposed by the communist political system.
Keywords: Polish military psychiatry after WWII, Polish military case law of forensic psychiatry after WWII

Streszczenie Obserwacja uczestnicząca środowiska społecznego zawodowego oficera, psychiatry wojskowego w powojennej Polsce. Obrazy niezgodnych ze sobą postaw i zachowań wynikających z antagonizmu między zakorzenioną kulturą chrześcijańską a nowymi normami, wartościami i wzorami narzucanymi przez komunistyczny system polityczny.
Słowa kluczowe: psychiatria wojskowa w Polsce po II wojnie światowej, orzecznictwo sądowo-psychiatryczne w Wojsku Polskim po II wojnie światowej

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Corresponding author
Dr. Andrzej Żmudzki
318 Pennsylvania Avenue, Falls Church VA 22046, USA
e-mail: azmudzki@gmail.com

Someone once said that luck is what we sometimes experience when good preparation meets favourable circumstances. My parents prepared me well for the vicissitudes of life, and I have had a fair share of favourable circumstances. Unfortunately, I grew up and lived for many years in a country where some were introducing "social justice" using lies, deceit and force, whereas others collected the fruit of this justice: constant intimidation, limited ability to decide about one's own life or place of residence, inability to speak the truth or have honest conversations with neighbours, especially those with different views. Many paid for this historical catastrophe with broken – or taken – lives. My situation was easier, as I functioned in a "protective environment": I was a doctor, working for the army, and living in the capital city.

My father was an atheist, but he had me christened and made sure I attended religion classes. He taught me that everything is "relative": "In Christianity, God is the most important thing, but God is little more than Santa Claus for adults. Do not waste your time pondering the relativity of god's existence or non-existence, it is better to remember that you happen to live in a country with a Christian culture, so you must learn all about this culture".** He also used to say that "life is hard, you always need to make choices and take decisions". My mother would say: "Daddy likes to philosophise. Taking decisions is not really such a big deal, as you always try to choose the things that are good, useful and feasible, and to pick those you care about. Our lives consist of the constant performance of tasks, and it is important to perform them well: at once, thoroughly, and from beginning to end. And always clean up afterwards. Life is not difficult, it is tiring". She also told me never to lie to defend myself, and to always be good and helpful to others, never to harm them, tease them or act out of spite. For my parents, social inequality, poverty and ignorance were part of reality, constant and unchangeable, overlooked or ignored.

* As it turned out, I am a kind of an exhibit. When Professor Ilnicki, physician and medicine historian, a friend of mine, was dusting me off, he noticed that I was still breathing, and asked me to write down a few memories about my military medical services in communist Poland, and how the army and communism affected me.

** The words I "quote" often are not exactly what someone said; I was only trying not to change the meaning and tone of what I actually heard.

Since childhood I have been an avid reader, I went to a humanities secondary school where the books we read (back then, there were no lists of obligatory or forbidden authors) made me somehow more sensitive to progress and justice than to patriotism. At the same time, I easily absorbed the teachings of our new bards, as it appeared they were addressed to me specifically. I became an activist in a political organisation at our school. After a few years, while I was still a university student, I wrote: "I don't believe in God, but I respect him as a person. When I think about him, I see my secondary school religion teacher, wearing a frayed cassock, and explaining his simple and noble religion. When I took the cross off the wall behind the teacher's desk, and stuck it in a hole behind the tile stove, the whole school was outraged. He only said: 'Jędruś, Jędruś. You are so stupid, so utterly stupid. What will become of you'".

A few years later, when I was already working as a physician, one day I submitted to the secretary of the local "party unit" an application to become a party member. He put the document in a briefcase and left. Right afterwards, he broke his arm or leg, and lost the briefcase. My application was never mentioned again. Maybe it was a result of father Kałuszko's prayers to his God.

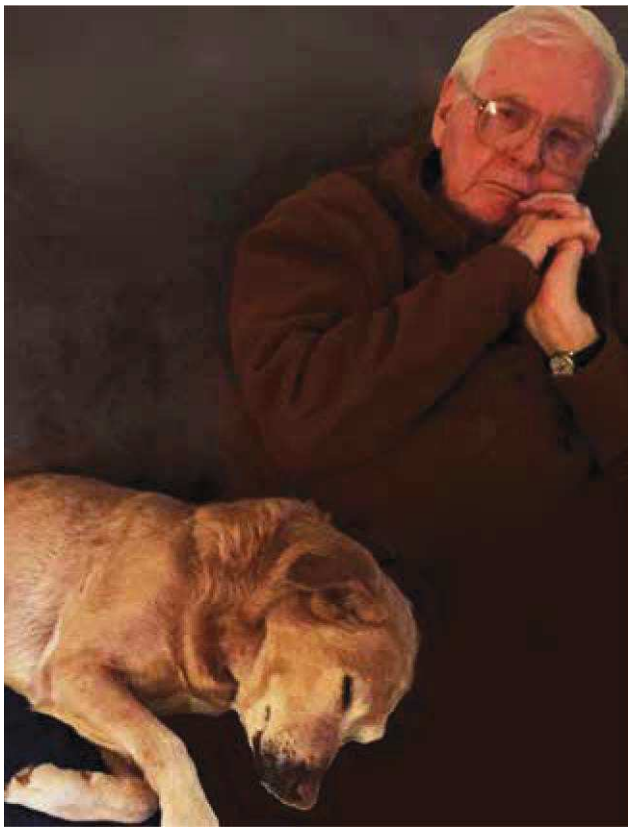
During my first two years of work, I was a doctor at a psychiatric department in Kraków. From the start, recognising symptoms of mental disorders fascinated me. After an hour of the first interview with my first patient about her two failed marriages, I went to the assistant professor and said that in my opinion she had a bad husband, but was mentally stable. He only said: "Interesting, I think you should spend another hour with this patient". I came back and started by reminding her that we were talking about her second husband. She said that maybe she had been unclear before, but she had only one husband. The other man was not her real husband, but was one set up by the security police.

One of my tasks in the hospital was to go to the court with Antoni Kępiński or Wanda Półtawska; I was also Władysław Stryjeński's apprentice in adjudication. One of them warned me that I should watch my steps when adjudicating, as psychiatric adjudication is sticking one's nose into other people's lives. After my internship at the hospital, I passed the specialisation exam in psychiatry.

Then I was conscripted into the army, following the act on mandatory two-year military service for medical university graduates (In my case the service was postponed, as I had received the specialisation internship at the Psychiatry Department: my work there was considered "socially indispensable", based on a completely arbitrary opinion, which allowed me to delay the duty). Initially, I was assigned to the Ministry of Internal Affairs Hospital in Wrocław, where I worked in the neurological clinic, and provided opinions regarding the "suitability" of candidates for security police officers. A few months later, I was transferred to the Department of Neurology at the central Military Hospital in Warsaw, where soon I went back to writing forensic psychiatric adjudication reports, under the supervision of the head of the department, Stefan Bogusławski, whom I considered a saint in a uniform. Together we went to the court or the prison where intellectually handicapped soldiers or those with personality disorders, symptoms of mental disorders or suspected of simulating such conditions were sent. They were accused or convicted of "desertion", or "absence without leave" from the army – an environment where they had been placed under compulsion, without a chance to adapt. The fate of these poor people, sentenced to many years of prison, was the subject of my doctoral thesis, which I wrote while working at the Military Institute of Postgraduate Education, at the psychiatric clinic at the Department of Neurology run by Dr. Teofan Domżał. Medical adjudication reports for the army and forensic psychiatric adjudication reports were usually given in the clinic, but I still sometimes went to court with one of two dear friends of mine: Stanisław Ilnicki, a psychiatrist, and Agnieszka Foss, a psychologist.

One day, at the beginning of my medical career, while I was searching for a solution to practical life problems of a patient, an idea firmed in my mind, not entirely in compliance with "doctor's principles" or legally binding regulations, that the *primum non nocere* rule applies not only to the patient, but also to his or her family. That in certain situations I should take decisions, instead of leaving them to the family, thus placing the weight of responsibility for the consequences, or the physical and material burden associated with such decisions on the family members. That, for instance, instead of pressuring the family to take their relative home, it is better to keep the dying patient in the hospital, or to arrange the admission of a mentally handicapped child with a severe physical disability to a care facility.

My ethically unclear activity was gradually expanding. It allowed me to arrange a free of charge abortion in an illegal private medical office for a patient who was helpless and broke; to offer advice on how to end their own life to a person completely exhausted by a chronic, progressive, incurable disease; to issue a false medical certificate to save someone from further political persecution, or to protect another person against nonsensical, severe damages due to bureaucratic omnipotence and impunity. I came to terms with the personal responsibility for my actions much later: at some point in my forties, I finally acknowledged that if I had been involved in anything, even when my conscious contribution had been no more than 5%, I was fully responsible for the results. To simplify the maths, my responsibility should be **equal** to that of people who



participated in 95% of the endeavour. Also, I bear the responsibility for the situations when I did not know what I was doing, or what was happening, but I could have and should have known. This helped me in times of doubt, but with the passing years I collected significant baggage of complete responsibility for the consequences of my decisions that in hindsight I consider wrong. Along the way, I was slapped on the face by an outraged general, and once I was stabbed with a knife. The wound was not serious.

Contacts with my superiors were sometimes enlightening. One day, the commandant in my hospital, a physician, called a staff meeting. He announced that the next day was to be work-free. In the morning we were to put on civilian clothes, and to ride the trams. In pairs, we were to "mould public opinion" – have loud conversations supporting the current controversial decisions of the party and the government. We were paired by the hospital administration; my partner was a man slightly older than me, whom I did not know. The next day, at an arranged time we got on the tram, rode a few stops in silence, then my partner pointed to the door, and we got off. We got on the tram going in the opposite direction, we talked a little about subjects unrelated to the current affairs, only to ease the tension, and we said goodbye at the place of our original appointment. It was one of these days when one suddenly matures. Thinking about the commandant, I realised that the meaning of the biblical "forgive them, for they know not what they do" (Luke 23:34) is not as easy and simple as I had believed. Thinking about myself, I experienced that confusing feeling I had known since childhood, when I was lost on a trip.

Another time, I asked my superior for a personal favour. When he heard my request, he called the head of human resources and said: "Krysia, Dr Żmudzki's sister, a paediatrician, moved to Warsaw, and she would like to work in our clinic". Ms Krysia responded: "But Colonel, there is no way it can be done". To which he replied: "I know that, but it is not your job to make comments like this. I called you, not someone else, because the reason we keep you here is sometimes to get impossible things done. Here are Dr Żmudzka's documents. That would be all, thank you. Please keep me informed about the outcome". My sister was employed on the first day of the following month, and she worked diligently at the clinic for many years.

One day, an older colleague, a neurologist, came to my office and informed me that he had been ordered to supervise my work. He sat in the corner and did not say a word. I did not object, or ask any questions. Someone needed him to keep an eye on me for a few hours, and I knew why: it was the second day of testing of candidates suddenly drafted into the army based on the new regulations we did not know. The patients were students exempt from military duty until they graduated. They were selected according to some pattern: many of them appeared to be "of Jewish origin". I learned about it from them; one by one, they protested. The situation took place in the short period of preparation for entering "rebellious" Czechoslovakia. The next day my colleague did not come. Nobody ever said a word about it to me.

The reverse also happened: a member of a military medical board, whom I knew a little, invited me for a talk, and gave me a long lecture. He said: "I want you to know that we are aware that sometimes your adjudication reports are stretched, so that their results are in line with the personal needs of patients, not with the requirements of the military service. We have nothing to pick on, as the reports are well prepared and documented, but remember that we bear the responsibility for your adjudication, not you". He did not stop there, but added something that astounded me: "We also sometimes, very rarely, stretch our reports if we believe that it is our absolute duty. We are bound to make these exceptions by the unwritten rules: the sense of human decency, only when we have no doubts; the sense of absolute need to prevent a clear, unnecessary and irreversible harm to our patient caused by the adjudication (we chose the lesser evil), and higher power – once we modified a report at the demand of a person who could decide about the fate of our hospital.

And that is it. Importantly, **we never do anything out of kindness**. Beware of charity: everything you do here you only do because it is your duty. Working in this way will allow you to be at peace with yourself, and you will be able to sleep at night. You have a good and quiet job, providing bread, butter and ham with horseradish. Many could envy you. Of course it is a private conversation. I hope you do not get in trouble." I did not get in trouble, I did not sleep well.

My professional performance, as well as my personal life, was deeply affected by the fact that I had to learn, and did learn, to talk with my patients about politics, just as I learned to talk to them about sex. Neglecting one of these areas would be a "medical malpractice", but honest conversations about political views, the political situation in the country, its effect on patients' lives and families were sometimes surprising for them, and caused anxiety or suspicion. In the long run, however, these conversations formed foundations for openness, trust, bonds, or even a sense of responsibility for mutual safety.

At times my patients heard something else than what I thought I was saying. I learned the hard way that what is important is not what you say, but what people hear. However, speaking face to face is the most comprehensible way of communicating crucial information. One day a patient (ironically, it was a political officer, mentally broken by the incompatibility between his conscience and his duties) corrected me while we were talking about politics: "Collaboration? Independence? Why are you using these words in a conversation that is not taped? There are no such things. It is simply a modern version of another Russian occupation".

Once I brought to my office, and put on the window sill, a figurine of Marshall Piłsudski. My father wanted to get rid of it, as a useless trinket, but he "could not force himself to throw it away". One of the doctors from the institute came to the office and, after a few casual remarks, he said: "I'm here, because someone told me that you have a statuette of 'Grandpa'. What do you see when you are looking at him? Poland? Or a dictator? If a dictator, you should better take 'Grandpa' out of here, for your own good. If it is Poland you see, feel invited to my office for a shot of vodka after work".

I was on the phone with a journalist I knew, who must have felt safe, as he liked to start provocative discussions on controversial political topics. When we finished, suddenly a voice in the receiver said: "For God's sake, doctor, what are you doing! Such a conversation on the phone! Forgive my boldness, but I suggest you have your head checked". I responded immediately: "And what about your head, you think you are safe?", but there was no one on the other end.

After I graduated from secondary school, my father said: "Do what you want, but you may not sign up for anything that requires carrying a gun, you must go to university immediately. You have no talents, you are lazy, so you should become a doctor". I did not listen to the first recommendation. In the dark times I spent a lot of time in the Armed Section of the Party, awkwardly trying to choose between good and evil. Not only did I have a service gun, but I also got a small revolver "for personal use", engraved with the words "For loyal service".

My parents tried to prepare me for the life they had, and wanted to bring up a "good man". Like many others, I do not know if I became one. Progress, science and history helped us learn new things about who we are, but the worst was known for ages. Two thousand years ago we formulated the "Lord's Prayer", realising that **we have never been able to take responsibility for ourselves**: "give us this day our daily bread; forgive us our trespasses; lead us not into temptation; deliver us from evil". We constantly counted on God, who never intended to deal with our affairs, although priests insist otherwise. Unfortunately, we have to do everything ourselves (at once, thoroughly, from beginning to end), and clean up afterwards. However, we are very bad at it.

Lt. Col. Andrzej Żmudzki MD, PhD, the first military psychiatrist in post-war Warsaw

Ppłk dr med. Andrzej Żmudzki, pierwszy psychiatra wojskowy w powojennej Warszawie, 1957–1973

Stanisław Ilnicki MD, PhD
Department of Psychiatry, Combat Stress and Psychotraumatology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine in Warsaw;
head: Col. Radosław Tworus MD, PhD.

Abstract The subject of this publication involves a large part of the professional life of Andrzej Żmudzki, a psychiatrist: the years of his military service in post-war Poland and his endeavours to reveal the need to introduce amendments to the terms and methods of psychiatric and psychological treatment, referral and certification in the army. The paper provides a description of Żmudzki's cultural and professional environment in Kraków during the 1950s, a place and time where his humanistic approach to individuals with intellectual disabilities and psychiatric disorders began to crystalise. The circumstances of his conscription and a course of his service in central military hospitals in Warsaw in 1957-1973 are described. The paper discusses his activity related to establishing the first mental health outpatient clinic in the Polish Army, his involvement in the field of policies and procedures of psychiatric certification (both forensic and medical) for conscripts, and his views on the psychosocial determinants of maladaptation to military service among officers. Also presented are a few of his fine art prints.
Keywords: history of the Polish military psychiatry, military forensic psychiatry, military psycholegal opinion, Polish psychiatrists

Streszczenie Przedmiotem publikacji jest znaczna część życia zawodowego psychiatry Andrzeja Żmudzkiego: lata jego służby wojskowej w powojennej Polsce oraz podejmowane przez z niego wysiłki zmierzające do ujawnienia potrzeby wprowadzenia zmian w zasadach i metodach postępowania psychiatrycznego i psychologicznego w leczeniu, poradnictwie i orzecznictwie w wojsku. Przedstawiono opis środowiska kulturalnego i zawodowego, w którym Andrzej Żmudzki żył w Krakowie w latach 50. ubiegłego wieku; to właśnie tam i wtedy kształtować się zaczęło jego humanistyczne podejście do osób z niepełnosprawnością intelektualną lub objawami zaburzeń psychicznych. Opisano okoliczności wcielenia go do służby wojskowej i przebieg tej służby w centralnych szpitalach wojskowych w Warszawie w okresie od 1957 do 1973 r. Omówiono jego działalność związaną z utworzeniem pierwszej poradni zdrowia psychicznego w Wojsku Polskim, działalność w zakresie zasad i procedur psychiatrycznego orzecznictwa wojskowo-lekarskiego i sądowego odnoszących się do żołnierzy z poboru oraz jego poglądy na psychospołeczne determinanty nieprzystosowania do służby wojskowej u oficerów. Przedstawiono też kilka jego druków artystycznych.
Słowa kluczowe: polscy psychiatrzy, historia polskiej psychiatrii wojskowej, ekspertyza wojskowo-psychiatryczna, wojskowa psychiatria sądowa

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Corresponding author
Prof. Stanisław Ilnicki MD, PhD
Department of Psychiatry, Combat Stress and Psychotraumatology, Central Clinical Hospital of the Ministry of National Defence, Military Institute of Medicine
128 Szaserów St., 04-141 Warsaw
e-mail: silnicki@wim.mil.pl

The ninetieth birthday of Andrzej Żmudzki, a medical doctor and military psychiatrist of great merit, living in the United States since 1983, provides an opportunity to remind Polish readers of his achievements and his role in the organisation of psychiatric care and forensic psychiatric adjudication in the Polish Army. It also allows us to demonstrate in Poland his original art.

Andrzej Żmudzki was born in Kraków on 25 June 1931. His father, a licensed dental technician who studied dental medicine after the war and became a dentist (he

began and graduated from the university in his 50s), was a social campaigner, a non-partisan activist at a trade union, and a member of the Kur's Fraternity Shooting Society in Kraków, where at some point he was appointed a marshal. Żmudzki's mother, a graduate of a Teachers' University, eventually became a housewife and a devoted mother to her son and daughter, Izabella, two years' younger (a future medical director of the Children's Hospital in Warsaw). Apart from the period of displacement during the war, the family lived in a tenement house at 43 Main Market Square in Kraków.

Andrzej Żmudzki started his primary education in 1938, and he completed it by taking secret courses during World War II. After the war, he attended the Jan Kochanowski No. 3 Secondary School, where he passed the final exams in 1949. In the same year, he started studies at the Medical Faculty of the Jagiellonian University, later transformed into the Medical Academy in Kraków. At the secondary school and the university, in the period preceding "the October thaw" of 1956, he was actively engaged in youth organisations (Youth Organisation of the Workers' University Society, OMTUR, and Association of the Polish Youth, ZMP). As a university student, he published his poetry in the *Medyk Krakowski* magazine. When asked about the quality of these poems, Bolesław Gołubiew [1] said that their author might be equally good as a poet as he is a doctor. According to Dr. Żmudzki, it reduced his interest in the arts.

During the final exam in psychiatry, Prof. Eugeniusz Brzezicki [2] encouraged Żmudzki to specialise in this field. Having received his medical diploma on 30 December 1954, and a specialisation grant on 1 April 1955, Dr. Żmudzki began work at the Psychiatric Department of the Medical Academy in Kraków (Fig. 1). After one year, he became a lecturer's assistant, whose tasks included the selection of patients and summarising their medical histories for the lectures given by a professor. His masters: classic of Polish psychiatry, Antoni Kępiński [3], Wanda Półtawska [4] and Władysław Stryjeński [5], were exemplary doctors and humanists.

He reminisced: "I'll repeat what has been said about Kępiński many times, in different words: he was a great doctor, and an outstanding person. Kępiński decided that I should learn how to prepare forensic psychiatric adjudication reports. He and other experienced colleagues often took them with them to courts as the second expert. With this goal in mind, Kępiński also sent me to Stryjeński, who was a great teacher. He demanded that the adjudication report be always an independent document, that it contain no references but only quotations from the sources of information used, and clearly explained premises for the conclusions, so that the reader did not have to search the literature".

Rycina 1. Lekarz A. Żmudzki, Klinika Psychiatryczna AM w Krakowie, 1955

Figure 1. A. Żmudzki, MD, Department of Psychiatry, Kraków Medical Academy, 1955

During the two years Dr Żmudzki spent as a resident, he met all the requirements necessary for the first degree of specialisation in psychiatry. On 9 May 1957, he was called for the mandatory two-year military service for the graduates of medical schools, which had been delayed for two years, due to the specialisation grant he had received [6]. He took the specialisation exam as a military physician. He had to give up the familial atmosphere of the Psychiatry Department, and the artistic life of Kraków, in which he socialised with interesting artists related to Tadeusz Kantor's Cricot 2 Theatre (once he even performed in a Grand Guignol show) [7].

After a short period of awaiting for the Polish Army Chief Quartermaster's decision, Lt. Andrzej Żmudzki, MD (Fig. 2), was assigned as an assistant at the Department of Neurotic Diseases at the 2nd Central Hospital of the Ministry of National Defence in Warsaw, in 1958 renamed the 2nd Central Clinical Hospital of the Military Medical Academy (2 CSK WAM) [6]. The head of this department was Col. Stefan Bogusławski MD, PhD, a military neurologist of great merit, a participant in both world wars, a humanist with a medical-artistic background [8, 9].

Rycina 2. Por. lek. A. Żmudzki, Oddział Neurologiczny CSK MON w Warszawie, 1957

Figure 2. Lt A. Żmudzki, MD, Department of Neurology, Central Military Hospital in Warsaw, 1957

Doctor Żmudzki found in him a friendly superior and mentor, which probably influenced his decision to continue professional military service.

After five months of work at the12th Transport Battalion in Warsaw as a physician, Dr Żmudzki was promoted to captain. On 15 June 1962, he passed the specialisation exam in neurology, with very good results. He saw patients in outpatient clinics at Nowowiejska Street and Koszykowa Street, and he continued preparation for the 2nd degree specialisation in psychiatry [6].

On 1 January 1963, Żmudzki was delegated to the School of Professional Training and Specialisation at the Military Medical academy in Łódź. There he had a specialisation internship at the Psychiatry Department of the Medical Academy in Gdańsk, run by Prof. Tadeusz Bilikiewicz [10], a year-long internship at the Psychiatry Department of the Psychoneurological Institute in Pruszków, run by Dr Jan Jaroszyński [11], and an internship at the Forensic Psychiatry Department run by Dr Lidia Uszkiewiczowa [12], at the same institution. He published a scientific article about the molecular memory mechanism [13], he was delegated by the Healthcare Department of the Polish Army to the Psychiatry congress in Moscow, and participated actively at the 6th Polish Mental Hygiene Conference. He gave a few lectures in psychopathology at the Military Political Academy, and in sexology at the Military Medical Academy in Łódź. Moreover, he translated Robert Frost's poems for Polish Radio [6].

On 11 December 1964, Capt. Żmudzki passed the exam and became a 2nd degree specialist in psychiatry. On 17 May 1965, the Chief Quartermaster of the Polish Army assigned him as Senior Assistant at the Department of Neurology with Mental Health Clinic, EEG laboratory, and four doctors' offices at the 2nd Central Clinical Hospital of the Military Medical Academy with Polyclinic and Offices in Warsaw (this was the full name of the Department of Neurology in the hospital at Szaserów St.). The department was created on 22 February 1964, as a result of a merger between the Department of Neurology at the 2nd Central Clinical Hospital of the Military Medical Academy at Koszykowa St., and the Department of Neurology at the Military District Hospital at Nowowiejska St. [6].

He took this position with the following opinion from Col Stefan Bogusławski: "Capt. Andrzej Żmudzki MD is a conscientious and dutiful officer and physician, who dedicates a lot of time and effort to his work. (...) He demonstrates a great sense of honour and dignity, as well as ambition to extend his medical knowledge. He is righteous, honest and direct. He shows great manners and social skills. (...) He forms independent opinions (at times with a hint of youthful contradiction), has a great memory, learns fast, can easily express his thoughts in speech and writing, thinks logically, can present theoretical problems in a synthetic framework, and demonstrates a sense of humour. He easily adapts to new conditions, thanks to his ability to form close and friendly relationships with people. His honesty, moral attitude, behaviour during his service and in his personal life, as well as his approach to the environment are impeccable. Mistakes made by Dr. Żmudzki (...) were never results of ethically questionable motivation. (...) The project of open consultations for patients regarding neurosis, mental disorders, sexology and psychiatric prophylaxis in the hospital's polyclinic presented by Dr. Żmudzki was approved by his superiors. (...) Due to his manners, helpfulness and friendliness, he is universally liked. Loyal to his superiors, he respects their authority and opinions. (...) In his work and medical practice Dr Żmudzki gained the trust of his patients, as he pays a lot of attention to their symptoms, devoting his time outside the consultation hours, and offers skilful psychotherapy. Dr Żmudzki is a physician of great promise in the chosen area of specialisation" [6].

At that time, in the hospital at Szaserów St. Dr Żmudzki (Fig. 3) was the only specialist in psychiatry, but the head of the Mental Health Clinic was a neurologist, head of the Department of Neurology, Lt. Col. Dr Teofan

Domżał [14,15]. This was due to the fact that in the 1960s, there was no specialisation in psychiatry for healthcare officers, and neurologists were considered specialists in this field. Both groups of physicians, independently, diagnosed the following conditions for the Military Medical Commission: "§65 Chronic neuroses, §71 Psychopathic degeneration and chronic, refractory substance dependence, §72 Minor mental handicap, mental retardation, psychoses, mental disorders" [16]. There were frequent diagnostic controversies between psychiatrists and neurologists [17].

Two years later, in 1967, the Mental Health Clinic had one office at the Polyclinic of the 2nd Central Clinical Hospital of the Military Medical Academy at Szaserów St. Doctor Żmudzki saw patients there, alternately with a civilian psychiatrist, Maria Pietrzyk. Most patients were compulsory military service soldiers (approx. 65%), professional soldiers (approx. 20%), retired soldiers and pensioners (approx. 10%), and family members of military personnel (approx. 5%). Soldiers were referred to the clinic by their unit's physicians, and by the Military Medical Commission. On average, approximately 20-30 patients were seen daily - outpatients, those referred by the commission, and individuals from other departments of the hospital.

Due to the difficulties associated with the implementing the tasks of the Mental Health Clinic, Dr Żmudzki, promoted to major in 1966, developed and presented to the commandant of the 2nd Central Clinical Hospital of the Military Medical Academy a proposal for an instruction defining the tasks, organisation, required staff and premises, as well as the functioning of the Mental Health Clinic. This document from 3 February 1967 can be considered a model design of the first Mental Health Clinic in the Polish Army [18]. Although the proposal was in the form of a manuscript, the principles it outlined were implemented in daily operations of the clinic. They included referral of soldiers to the clinic under a supervision, with professional and medical opinions, procedures to follow in frequent cases of self-harm or swallowing objects (so-called fakirs), and the documentation principles.

On 16 November 1967, Maj. Andrzej Żmudzki MD became an Assistant Professor at the Department of Neurology - the head of the Mental Health Clinic (Fig. 4) [6]. Some of his wishes were granted: five offices were opened in the Polyclinic – one for the head of the clinic, two for psychiatrists, one for the psychologist, and one for the nurse - receptionist, as well as a waiting room. Agnieszka Foss, a psychologist, was hired, and when Maria Pietrzyk left, two specialists in psychiatry were hired: Maria Gedych and Alina Ferszt. On 5 September 1968, a graduate of the Military Medical Academy, Lt. Stanisław Ilnicki, MD was hired as "assistant psychologist", to specialise further in psychiatry. The first nurse-receptionist at the clinic was Maria Rudalska.

Rycina 3. Mjr dr med. Andrzej Żmudzki, Klinika Neurologiczna IKP WAM w Warszawie, 1970

Figure 3. Maj A. Żmudzki, MD., PhD., Neurology Department, Postgraduate Institute of the Military Medical Academy, Warsaw, 1970

Dr Żmudzki's request to open a psychiatric subunit for patients with acute psychotic disorders and for adjudication observations was not approved by his superiors. He asked for "a 3-bed room, a 2-bed room, and a doctor's office, as well as assigning a nurse to the department where such subunit would be formed". He tried in vain to explain that "sending away patients with acute psychosis for a few days to a psychiatric hospital, (...) is an outdated solution, and appears to be an organisational error in a hospital hiring psychiatrists" [18]. Until 2005, when the Department of Psychiatry and Combat Stress was created, compulsory military service soldiers were referred to psychiatric hospitals in Tworki and Drewnica. In the years 1967-1970, approximately 200 soldiers were treated there annually [19]. The professional military personnel were referred to the 5th Military Garrison Hospital in Kraków, and to the Department of Psychiatry at the Military Medical Academy in Łódź.

The rejected requests of Dr Żmudzki included the following: establishment of a long-term scientific

Rycina 4. Psychiatrzy mjr dr med. A. Żmudzki i por. lek. S. Ilnicki (ostatni rząd u góry) wśród lekarzy Kliniki Neurologicznej IKP WAM w Warszawie, 1970

Figure 4. Psychiatrists Maj A. Żmudzki MD, PhD and Lt. S. Ilnicki MD (the top row) among physicians of Department of Neurology, Postgraduate Institute of the Military Medical Academy, Warsaw, 1970

consultant position, establishment by the Healthcare Department of procedures for neurosis requiring hospitalisation in professional soldiers, organisation of patient flow to eliminate collisions in the order of admissions of first-time patients, professional soldiers and compulsory service soldiers, commission examinations, patients with chronic conditions and individuals consulted in all the hospital departments [18].

In 1968, the provisions regulating adjudication process were amended. Now they included Chapter 16 - Mental condition, with the following diagnoses: “§67 Neuroses, organ neuroses, nocturnal enuresis; §69 Character abnormalities and reactive situational, transient character disorders (psychopathic conditions); §70 Infantilism; §71 Exogenous, alcohol-induced and endogenous psychoses; §72 Low intellectual capacity and intellectual impairment; §73 Substance dependence without defects (alcoholism)" [20]. These conditions were to be assessed for the Military Medical Commission by psychiatrists.

The above provisions, following the defence policy at that time, accepted calling for the compulsory military service and in self-defence formations candidates with intellectual impairment and with personality disorders (character abnormalities), classified as military capacity categories C and D. These soldiers were sent to Territory Defence Units, railway and road military units, and building units. They formed the majority of patients of the Mental Health Clinic, as well as perpetrators of typically military offences, referred to the MHC for forensic psychiatric tests. In the years 1968-1970, 219 opinions were issued in such cases [21].

Dr Żmudzki was particularly interested in the functioning of individuals with intellectual impairment and with psychopathic personality (character abnormalities) in the military environment. In 1968, together with Agnieszka Foss, a psychologist, they conducted a study on the usefulness of soldiers with intellectual impairment in the military service. Based on the analysis of records from the Mental Health Clinic and the Military Medical Commission, they established that “lack of usefulness of

individuals with retardation, with borderline mental handicap and with low intellectual capacity is due to not only the reduced intellectual potential and the corresponding decreased maladaptation, but (...) to the tendency such individuals demonstrate during the military service to develop maladaptation syndromes and reactions of particular burden for the army (...)" [22].

These authors also analysed 130 forensic psychiatric adjudication reports issued at the Mental Health Clinic in 1969, of which 110 (84.7%) were for compulsory military service soldiers, the remaining 20 (15.3%) for the professional soldiers, candidates, reserve soldiers called for training and civilians. The analysis demonstrated that approximately 2/3 of the examined compulsory service soldiers should have been considered, following the applicable military-medical adjudication standards, unfit for military service. Approximately 1/3 of the examined individuals were found to demonstrate reduced sanity. A few typically military offences, mainly desertion and absence without leave, were the cause for 90% of opinions. In 99% of perpetrators non-psychotic disorders were found: personality disorders, "mental immaturity", and intellectual impairment [23].

In 1969, Dr Żmudzki and Lt. Stanisław Ilnicki MD conducted a field study in a Territory Defence Unit, at the Petrochemia Płock building site. It revealed that of 119 randomly selected soldiers, 55% had mental abnormalities qualifying them for discharge from the army. However, catamnestic analysis demonstrated that nearly half of them adjusted to the service, and only one in ten were discharged due to psychiatric indications. The authors concluded that soldiers with low intellectual capacity and character abnormalities that only slightly impair social functioning can adapt to the conditions of military service in a Territory Defence Unit equally well as soldiers without such impediments [24].

In 1969, Maj. Żmudzki defended a doctoral thesis "Studies on the percentage of psychopaths in the group of perpetrators of the most common military offences: desertion and absence without leave" at the Medical Faculty of the Military Medical Academy in Łódź [25]. The thesis was supervised by the head of the Department of Psychiatry at the Military Medical Academy, Lt. Col. Zdzisław Rydzyński MD, PhD. The study comprised 1700 rulings of the Warsaw Military District Court in cases closed within the previous 2 years: 1962 and 1963. Among them 330 concerned soldiers convicted of desertion or absence without leave, including 64 individuals convicted for these offences two or more times. Statistical analysis of the data regarding these perpetrators demonstrated that in the group of psychopaths the tendency to break the law was twice as high as in the entire population of soldiers committing military offences, and in the group of recidivists ("special recidivism"), it was four times higher. Referring to the statement of Col. Jan Nelken MD, PhD, a psychiatrist [26], who said that military regulations serve as a fishing rod for psychopaths, Dr Żmudzki added that articles 108 (desertion) and 109 (absence without leave) in the military criminal code from 1957 are the hook for this rod. He found that the recidivism of these offences can be treated almost as a symptom of abnormal personality, and he distinguished the factors whose presence in a perpetrator of such crime should signal the need for a forensic psychiatric opinion. Apart from the assessment of sanity, these opinions indirectly contribute to the evaluation of soldiers' fitness for service and, further, determine whether their actions will be considered punishable or not.

Apart from a deep analysis of the literature on psychopathy, Dr Żmudzki presented in his work his original theoretical reflections on the differences between military forensic psychiatric adjudication and the analogous adjudication outside the military context, and he described in details, step by step, a model decision process of an expert psychiatrist adjudication in typically military offences.

Prof. Stanisław Cwynar [27], head of the Department and Chair of Psychiatry at the Medical Academy in Łódź, wrote in his review of Andrzej Żmudzki's doctoral thesis: "This work is an important contribution to the Polish literature on the usefulness of psychopaths and the purpose of their conscription for compulsory military service. (...) The author demonstrated a deep understanding of the problems related to military psychiatric adjudication. (...) His observations comprise valuable material for readers seeking the right approach to psychopathy. (...) The reflections on certain difficulties regarding psychopaths' functioning in the military environment are doubtlessly original, and are based on the author's own findings. (...) Some of the conclusions on the response of psychopaths to educational influence appear to be too pessimistic, and the methods to correct abnormal personality should be explored, at least for some of the patients diagnosed as psychopaths, also at the time of their military service" [25].

Despite a high grade, and suggestion from the reviewer to publish the thesis, its manuscript was classified until 1999. Also four articles written by Maj. Żmudzki, based on his doctoral thesis, and sent on 7 January 1971 to the editorial board of *Military Physician* to be published in the classified issues of the journal were rejected [28, 29].

In the professional evaluation report for the years 1966-1969, the head of the Department of Neurology of the 2nd Central Clinical Hospital of the Military Medical Academy, Lt. Col. Dr Teofan Domżał, presented the following description of Maj. Dr Andrzej Żmudzki: "Very intelligent, ambitious. (...) He is disciplined, although

military discipline does not correspond to his nature. (...) He is open and honest when presenting his views, sometimes maybe showing too much self-criticism. He participates actively in the scientific work of the department (...) He runs the Mental Health Clinic well. He ensures continuous education of his employees, but sometimes shows a too liberal approach towards them. (...) He actively participates in the organisation of military psychiatry, and in the conferences of military psychiatrists. He continuously improves his professional knowledge. (...) Sometimes he forgets about the uniform regulations. (...) If he changes his attitude to military service, I see no obstacles to his remaining at the currently held position" [6].

On 5 February 1970, Maj. Dr Żmudzki sent the Minister of National Defence a report which stated: "I request permission to be released from professional military service. (...) My request is motivated by a growing sense of unsuitability to the requirements of military service, following the increase in the number of professional tasks and the associated responsibility, which results in a constant nervous strain. I find it difficult to follow the decisions and orders of my superiors, which has become a cause of conflicts on several occasions, and disturbed the harmony of the relationships between us. (...) As a psychiatrist, I realise that this situation, if prolonged, may adversely affect my health. I would like to avoid it, as well as to prevent my discharge from the army as an unworthy officer, due to my increasing inability to perform professional duties" [6].

Referring to the above report, Maj. Żmudzki's direct superior, Lt. Col. T. Domżał wrote: "From the beginning of his work at the Department [Maj. Dr Andrzej Żmudzki] demonstrated an unwillingness to perform military service, and cannot follow proper regulations. This results in frequent conflicts. I support Maj. Żmudzki's request, as I can see the increasing emotional tension, leading to conflicts, and I believe that his further employment will not demonstrate beneficial effects of the efficiency of work, but the contrary may be the case" [6].

Higher-level superiors confirmed that "in the past few years, Maj. A. Żmudzki MD, PhD, has requested several times permission to be released from the military service. (...) He was encouraged to adapt to the military service (...). However, in the long-time perspective, these attempts were in vain". They concluded that "release of the applicant is possible if another psychiatrist is assigned for his position as the head of the Mental Health clinic – an officer, or a civilian physician with a potential to begin professional military service" [6].

Expecting a negative response to his report, on 1st March 1970, Maj. Żmudzki talked to the deputy Chief of the Polish Army Healthcare, Gen. Dr Jerzy Ejmont [30], whom he had met personally at a university course, when Ejmont was a lecturer at the Military Study of the Medical Academy in Kraków. He reminisced: "The second time I talked to him I was a commandant of a field surgical hospital during some military exercises. We went to the German Democratic Republic. The General came to visit my hospital (he was surprised that there was still some spirit left in the hospital pharmacy). For the third time, he met me, at my request, in Warsaw, Mokotów, when I wanted to leave the army. He said: 'We need you at the moment, but we'll try to find you a new workplace. Maybe that will calm you down. Then we'll see'".

Following this conversation, on 3 March 1970, the Chief of the Polish Army Healthcare, Gen. Prof. Władysław Barcikowski [31] wrote: "I do not support Maj. Żmudzki's report, as there is a significant shortage of specialists in psychiatry in military healthcare. As a change in the work environment is needed, I suggest moving him to the Military Institute of Aviation Medicine, after a suitable replacement has been found, to which Maj. Żmudzki agreed" [6].

After providing a written consent to the "proposed transfer to a lower position of (lieutenant colonel) assistant professor - psychiatrist at the Military Institute of Aviation Medicine", by the Ministry of National Defence order from 11 July 1970, Maj. Andrzej Żmudzki MD, PhD, was transferred to the Military Institute of Aviation Medicine (Fig. 5) [6]. However, it appeared that there was no such position at the institute, so he became "assistant professor at the Laboratory of Neurophysiology at the Experimental Centre". In fact, he worked from the beginning as a psychiatrist at the Psychoneurological Department at the Military Institute of Aviation Medicine, run by Col. Dr Eugeniusz Marks [32].

He reminisced: "I could divide my experience at the Military Institute of Aviation Medicine into two periods: the first, shorter one, at the beginning of which Marks informed me that I was employed against his will. My desk was placed in a storage room for cleaning materials. It coincided with the time when Radio Free Europe aired material about a group of people in the Ministry of Justice, who extracted information from political prisoners using pharmacological substances. A black list with their names was published. My name was on that list, but it was not me! At that time, a psychologist with the same first name and surname was employed at the Ministry of Justice. It was a catastrophe for me, many people turned away from me. They believed it was me, not someone else. I told Marks about it during a conversation, and I asked him to check for himself, using his influence, that I was not the man from the list. Sometime later, his approach towards me changed significantly. One of the patient rooms was turned into my office. Later, on his own initiative, Marks said: 'We'll give you an outside consultant, so that you can discuss clinical matters." The consultant was Prof. Halina

Wardaszko-Łyskowska, head of the Department of Psychiatry at the Medical Academy in Warsaw [33]".

At the Military Institute of Aviation Medicine, apart from diagnosing and treating patients and preparing opinions for the Military Aviation Medicine Commission regarding adjudication in cases regarding flight personnel and ground security, Dr Żmudzki conducted scientific research, whose outcomes were published after he left the army. The studies focused on the examination of personnel working within the range of microwaves (MW). In one of the studies, Żmudzki and neurologist Col. Jan Chrzanowski MD, PhD, established that symptoms and disorders affecting adjudication opinions were found in one in ten professional soldiers working within the range of MW. Neurological abnormalities accounted for 2/3 of all anomalies found during medical examination. Over half of the neurological abnormalities were neuroses; one in two people demonstrating neurological anomalies was deemed permanently unfit for work within the range of MW radiation. It meant that every year 3% of professional soldiers working in close proximity of MW radiation was considered permanently unfit for this type of work, due to neurological contraindications [34].

Another publication on the same subject, prepared together with Col. Prof. Eugeniusz Marks, revealed that: "Using the term 'microwave neurosis' with reference to the neurotic symptoms, symptoms of disturbed autonomic nervous system function, and other symptoms of central nervous system dysfunction (sometimes in the form of psycho-organic, or even focal symptoms) found in soldiers serving within the range of microwave radiation raises fundamental doubts. (...) The hypothesis that MW emitted by the devices used in the army have a permanent traumatic effect on the central nervous system of healthy individuals working in their proximity even in the conditions of military service, at present considered safe, has not been proven sufficiently. (...) It is a fact that military service in many workplaces equipped with MW generators is associated with difficult conditions. It can be an extreme example of the limitations and sacrifices required by the military service during a time of peace. The work shifts are exhausting, and the service itself, regardless of the effect of MW, is associated with a strong neurosis-inducing effect, which should be considered in differential diagnosis. (...) Qualification of individuals with discrete symptoms of central nervous system defect for work within the range of MW may be one of the basic sources of diagnostic and adjudication errors, next to neurotic reactions due to environmental factors" [35].

On 5 October 1971, Dr Żmudzki was promoted to lieutenant colonel. He was still employed as assistant professor at the Laboratory of Neurophysiology at the Experimental Centre, which was not the work he actually performed. Therefore, he did not receive the bonus for

Rycina 5. Lt. Col. A. Żmudzki, Klinika Psychoneurologiczna WIML w Warszawie, 1973

Figure 5. Lt Col A. Żmudzki, MD, PhD, Psychoneurological Department of the Military Institute of Aviation Medicine, Warsaw, 1973

psychiatrists, although due to his work at the department, all other employees did. This absurd situation was remedied only after 7 April 1972 [6].

Two months earlier, on 12 February 1972, at a scientific conference of the Military Institute of Aviation Medicine, Żmudzki read the paper "Unwillingness to perform professional military service as a military adjudication problem" [36]. It was the first attempt in the Polish Army to explore the problem of burnout syndrome, currently included in the International Statistical Classifications of Diseases and Health Problems ICD-10 and ICD-11.

Doctor Żmudzki proposed: "The need for a clear approach to the diagnosed or treated professional soldiers, who are unwilling to continue service, occurs frequently in the daily work of a military physician. Identification of such an attitude in a professional soldier, and the need to address it, are sources of complicated psychotherapeutic and adjudication problems for the physician, and commanders must face equally difficult administrative problems. (...)

From a medical point of view, the unwillingness to continue military service typically results from the difficulties in adapting to the highly specific conditions and requirements of military service, or it may be caused by modification of personal plans, and the associated personal perspectives. However, both in the professional environment, and in the medical adjudication, the approach to individuals who demonstrate or declare reluctance to continue service reveals insufficient consideration and objectivity. At times such reluctance can even be considered as indicative of adverse character traits, or negative political views".

Following a detailed discussion of the phenomenon, and presentation of numerical data illustrating the theses of the paper, Dr Żmudzki formulated the following conclusions, prophetic for that regime:

1. In military medical adjudication, the unwillingness to perform service should be treated without adversity or emotions, as an important factor that negatively affects the prognosis of long-term adaptation to the conditions and requirements of professional military service.
2. The factors justifying the refusal to release a soldier from the service need to be specified and listed.
3. The rights of professional soldiers as employees should be precisely defined, so that the decisions convenient for low-rank commanders are not considered necessary for the defence of the country.
4. Military medical adjudication is not a machine to eliminate problems with personnel, as it delays the development of proper solutions, and pushes the military service down from its rightful position, making it subordinate to administration.

Doctor Żmudzki reminisced: "Despite the friendly gestures of my boss, I was tired of working in the army, and I dreamt of being released. At the Military Institute of Aviation Medicine they wanted to help me, but at that time being released on one's own request was unimaginable".

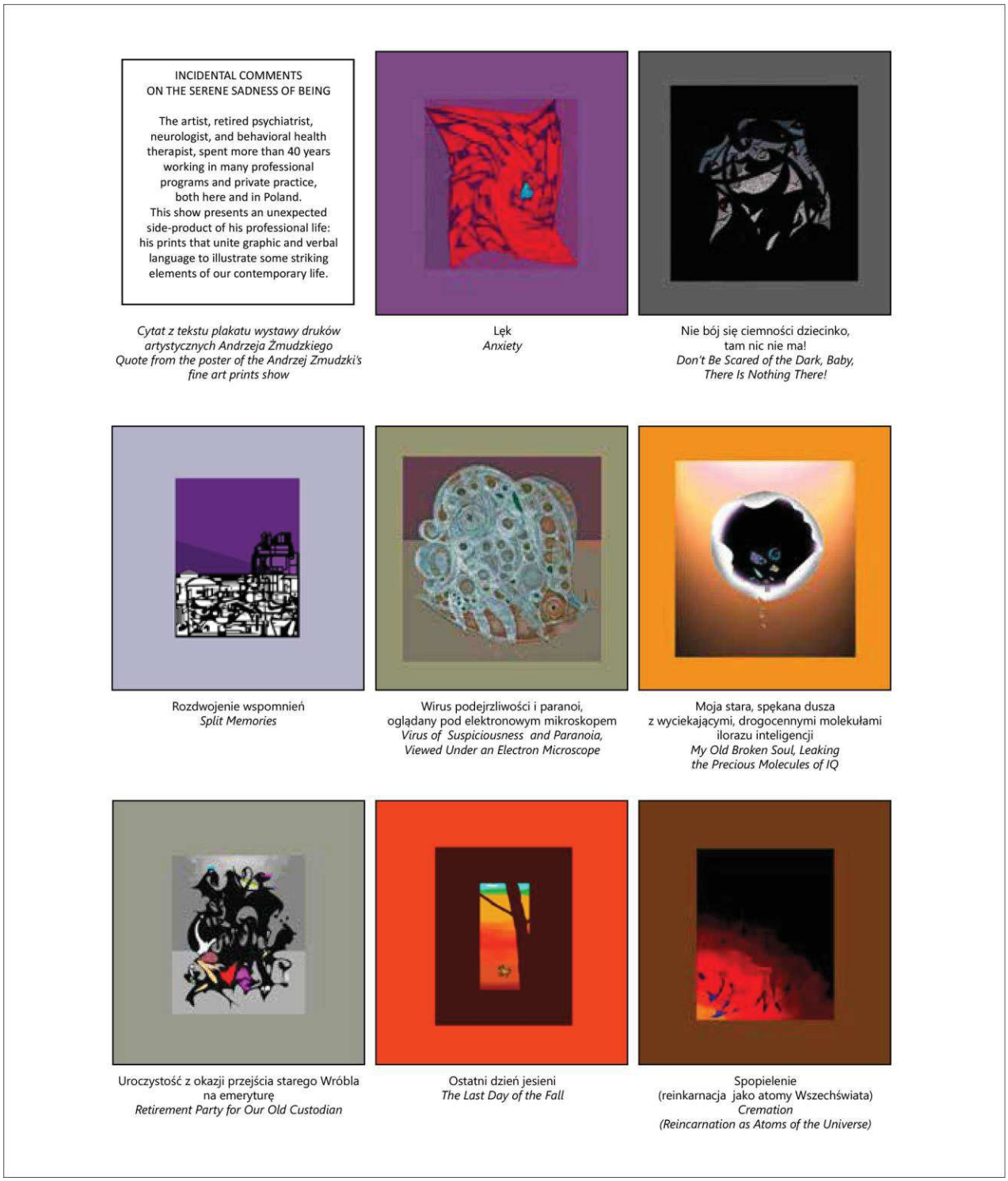
Following tests and observation at the Department of Internal Diseases of the Military Medical Academy, Dr Żmudzki was referred to the Military Medical Commission, which diagnosed him with six diseases, including two associated with military service; however, it adjudicated that he could still be a professional soldier "with limitations" [6]. In this situation, like several years before, he wrote a report to the Minister of National Defence with a request to be released from the army. He mentioned the same arguments. This time, due to lack of objections from superiors, by the decision of the Commander of Air Forces of 6 June 1973, Lt. Col. Andrzej Żmudzki MD, PhD, Assistant Professor at the Psychoneurology department of the Clinical Units of the Military Institute of Aviation Medicine, after 16 years of service, "at the request of the officer", was released from professional military service and moved to the military reserve [6].

Regardless of the difficulties that Dr Andrzej Żmudzki experienced during his military service: his ironic, jocular and dismissive approach to psychiatry, and despite the general lack of understanding for individuals incapable of adapting to the conditions of military, the absence of basic conditions for in-patient psychiatric treatment of ill soldiers, the attempts to use psychiatry for non-medical purposes, and the wasting of his research efforts, thanks to his humanistic approach to patients he passed on to his younger colleagues - including the author of this article - a model of decent behaviour in a situation of trial; the same model he had been taught to believe in at the beginning of his medical career from his teachers of humanistic psychiatry.

The fate of Lt. Col. Andrzej Żmudzki MD, PhD, after his release from the army is quite another story, and will not be explored in this article. The titles of works published before he left Poland reflect his scientific interests at that time [37-42]. Although he left the country, he never abandoned it mentally. He also preserved the bonds with the "psychiatry department from Szaserów Street", which he had started half a century ago. While visiting Poland in 2016, Żmudzki participated in the 1st Polish Conference of Military Psychiatrists and Psychologists in Rynia, and in 2019 he took part in the "100th Anniversary of Military Psychiatric Therapy" Conference in Warsaw. He assisted in forming scientific cooperation between the Military Institute of Medicine and a leading American military psychiatrist, Retired Col. Elspeth Cameron Ritchie MD, PhD [43], who agreed to be a member of the *Military Physician's* Programme Council The fine art prints offered by Dr Żmudzki, inspired by his work as a psychiatrist, the "illustrations and metaphors of daily life and ageing" now decorate the department (Fig. 6) [44].

On his 90th birthday, we wish our dear doctor the best of health, and we hope he will remain actively present in Polish military psychiatry, which he co-created.

Finally, following his request, we enclose his "poem", once dedicated to us (in the original form):



Rycina 6. Druki artystyczne Andrzeja Żmudzkiego w Wojskowym Instytucie Medycznym w Warszawie, 2020
Figure 6. Andrzej Żmudzki's fine art prints at the Military Institute of Medicine, Warsaw, 2020

serene old age

65
when you finally stop rushing
when your hopes come true
and the equation is solved
your plans will go awry
what was to last, will perish
the unwanted will stay
85
when future becomes blurred
when past moves to
the pages in the album
you will learn to cherish the unwanted
and start the final wait
alone in the crowd

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