DIAGNOSIS AND TREATMENT PATHWAY FOR COVID-19 PATIENT IN POLAND

Instytut Praw Pacjenta i Edukacji Zdrowotnej

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INDEX

Diagnosis and Treatment Pathway for COVID-19 Patient in Poland Report, *Institute for Patients' Rights & Health Education*, Warsaw, April 2022

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Authors in alphabetical order:

1. prof. dr hab. n. med. Leszek Czupryniak, specialist in internal diseases and diabetology, head of the Diabetology and Internal Diseases Clinic of the Medical University of Warsaw
2. dr n. med. Piotr Dąbrowiecki – allergist, internist, Military Institute of Medicine, chairman of the Polish Federation of Asthma, Allergy and COPD Patients
3. prof. dr hab. Marcin Drąg, biochemist, Wrocław University of Science and Technology, Faculty of Chemistry, Department of Infectious Diseases and Allergology, Department of Bioorganic Chemistry
4. prof. dr hab. med. Krzysztof J. Filipiak, rector of Medical University of Warsaw, specialist in cardiology, internist, specialist in hypertensiology, specialist in clinical pharmacology
5. dr n. med. Jakub Gierczyński, MBA, health care system expert, Institute of Healthcare Management, Lazarski University
6. Igor Grzesiak, vice president of the Institute of Patients' Rights and Health Education
7. dr hab. n. med. Jerzy Jaroszewicz, infectious diseases specialist, head of the Department and Clinical Department of Infectious Diseases and Hepatology of the Medical University of Silesia
8. prof. dr hab. n. med. Wiesław Jędrzejczak, internal medicine specialist, haematologist, oncologist, head of the Department and Clinic of Haematology, Oncology and Internal Diseases of the Medical University of Warsaw
9. prof. dr hab. n. med. Artur Mamcarz, internist and cardiologist, head of the 3rd Department of Internal Diseases and Cardiology at the Medical Faculty of the Medical University of Warsaw
10. father dr Arkadiusz Nowak, president of the Institute of Patients' Rights and Health Education, member of the Order of Fathers Serving the Sick, chairman of the Team for the development of a draft strategy for cooperation between the Ministry of Health and patient organizations
11. Patrycja Rzucidło-Zając, Institute of Patients' Rights and Health Education
12. dr Michał Sutkowski, specialist in internal medicine and family medicine, member of the National Development Council at the President of the Republic of Poland, president of Warsaw Family Practitioners in Poland
13. Anna Śliwińska, president of the Polish Diabetes Association
14. Krystyna Wechmann, president of the Federation of Breast Cancer Survivors Association "Amazonki"
15. Agnieszka Wołczenko, president of the EcoSerce Association

The report prepared on the basis of scientific workshops and sessions organized during the 16th Patient Organization Forum by the Institute of Patients' Rights and Health Education. It provides the state of the art as of April 2022.

Source: *Diagnosis and Treatment Pathway for COVID-19 Patient in Poland* Report, *Institute for Patients' Rights & Health Education*, Warsaw, April 2022

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INTRODUCTION TO THE REPORT

FATHER ARKADIUSZ NOWAK, PHD

We present to you the report entitled “Diagnosis and Treatment Pathway for COVID-19 Patient in Poland”. In order to prepare it, the Institute for Patients Rights and Health Education invited clinicians from various specializations, representatives of patients and health system experts. There was a substantive discussion on the current and optimal diagnostic and therapeutic pathway for a patient with COVID-19, with particular emphasis on chronically ill people, i.e. people at high risk of severe COVID-19 course.

As part of the project, during the 16th Patient Organization Forum, scientific workshops and the “Diagnosis and treatment pathway for COVID-19 patients in Poland” session took place. We are convinced that the discussion around COVID-19 will continue in the coming years - also in terms of access to new therapies. Developing optimal solutions for the diagnosis and treatment of COVID-19 patients is crucial from a social, systemic and ethical perspective.

KEY COVID-19 EPIDEMIOLOGICAL AND SYSTEMIC DATA IN POLAND

DR N. MED. JAKUB GIERCZYŃSKI, MBA

Coronavirus disease (COVID-19) is an infectious disease caused by SARS-CoV-2 virus. As a result of the infection, most people who develop COVID-19 will experience mild to moderate symptoms. These people will recover without special treatment. Other people, especially those with chronic comorbidities and those over 60 years of age, may become seriously ill and will need treatment[1]. According the Ministry of Health data from March 4, 2020 to April 26, 2022 there were 5 992 820 cases of COVID-19 reported in Poland, of which 115,977 people died and 5,334,451 people recovered[2].

Of the 206 deaths recorded on March 4, 2022, 153 (74%) reported comorbidities along with COVID-19, and 53 (26%) were COVID-19 deaths only. The report on deaths in Poland in 2020, published by the Ministry of Health in February 2021, showed that in 2020 (485,259 deaths) compared to 2019 (418,147 deaths) there were 67,112 more deaths. The number of deaths increased primarily among people over the age of 60, representing as much as 94% of the excess number of deaths compared to 2019.

Of the increase in the number of deaths in 2020 compared to the previous year, 43% (28,858)

1 https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-covid-19-how-is-it-transmitted.

2 Raport zakażeń koronawirusem (SARS-CoV-2), Ministerstwo Zdrowia 2022, https://www.gov.pl/web/koronawirus/ wykaz-zarazen-koronawirusem-sars-cov-2.

are deaths reported by sanitary and epidemiological stations with the SARS-CoV-2 cause of death.

Moreover, 27% of the surplus is the deaths of people who have been diagnosed with SARS-CoV-2 infection in the past. As much as 82% of the excess deaths were cases of people with comorbidities. The highest relative increase was recorded among people suffering from cardiovascular diseases – 16.69%, diabetes – 15.88%, neurological diseases – 14.63%, digestive system diseases –13.54%, psychiatric diseases – 12.69%, lungs diseases – 10.33% and oncological diseases – 4,7%[3].

TABLE: PERCENTAGE INCREASE IN THE MORTALITY AMONG PEOPLE SUFFERING FROM DIFFERENT DISEASES IN 2020 COMPARING TO THE YEAR 2019 (SOURCE: PESEL NUMBERS DATABASE, NFZ)

DISEASE	CHANGE IN RELATION TO 2019
Cardiovascular diseases	16.69%
Diabetes	15.88%
Neurological diseases	14.63%
Digestive system diseases	13.54%
Psychiatric diseases	12.69%
Lung diseases	10.33%
Oncological diseases	4.7%

SOURCE: Report on deaths in Poland in 2020, Ministry of Health 2021

According to the Ministry of Health, key activities in the field of COVID-19 prevention, diagnosis and treatment, and at the same time the pillars of the diagnosis and treatment pathway of a patient with COVID-19 are:

1. strengthening and promoting the importance of preventive vaccinations,
2. increasing the availability of COVID-19 tests,
3. implementing solutions that strengthen outpatient care, i.e. care for patients in the early stages of the disease or after disease, whose treatment does not require hospitalization,
4. increasing the number of inpatient treatment facilities,
5. the principles of social distancing, disinfection and wearing masks in closed spaces are still valid[4].

COVID-19 vaccines are one of the elements that can help to stop the COVID-19 outbreak[5]. The National COVID-19 Vaccination Programme is designed to plan activities that are to guarantee safe and effective vaccinations among Polish citizens. It includes not only the purchase of the appropriate number of vaccines and their distribution, but also monitoring of the course

3 Raport o zgonach w Polsce w 2020 r., Ministerstwo Zdrowia 2021, https://www.gov.pl/web/zdrowie/ raport-o-zgonach-w-polsce-w-2020-r.

4 Strategia walki z pandemią COVID-19. Zima/wiosna 2022, Ministerstwo Zdrowia 2021, https://www.gov.pl/web/zdrowie/ strategia-walki-z-pandemia-covid19.

5 https://www.gov.pl/web/szczepimysie/informacje.

and effectiveness of vaccination and the safety of Poles[6]. As of April 26, 2022, the total number of vaccinations against COVID-19 was 54,188,360, and the number of fully vaccinated people - 22,420,907[7]. According to the National Institute of Public Health NIH "Analysis of the risk of death due to all causes and due to COVID-19 of vaccinated and unvaccinated against COVID-19" report, there was a much higher risk of death due to all causes of unvaccinated people compared to those vaccinated against COVID-19 in all age groups[8]. This is confirmed by the data of the Ministry of Health from February 2022 stating that among all deaths of people infected with the SARS-CoV-2 coronavirus, only 5.69% were cases of death of vaccinated people. These deaths were not related to vaccination[9].

Diagnostic and therapeutic pathway is a complex intervention aimed at comprehensive decision-making and organization of care processes for a well-defined group of patients at a strictly defined time[10]. Model diagnostic and therapeutic pathways should be based on clinical guidelines / standards / recommendations of scientific societies, which are developed on evidence-based medicine (EBM). Clinical guidelines should be followed by interdisciplinary care teams to ensure effective and safe patient care — usually in the formula of procedures developed by individual clinical centres. In this respect, clinical protocols should be tools for evidence-based health care. Their aim should be to translate the recommendations of clinical practice guidelines into the clinical processes of care in the environment of a given health care institution in order to standardize care in the case of a specific clinical problem, procedure or health care episode in a specific population.[11].

An exemplary diagnosis and treatment pathway for a COVID-19 patient was developed by the World Health Organization (WHO) and is regularly updated on the WHO website[12]. It is designed to be a living tool to support health care workers visualize the current clinical and therapeutic recommendations to be considered in the care plan for patients with COVID-19. COVID-19 pathway CARE is aligned with the ninth version of the guidelines "WHO

6 https://www.gov.pl/web/szczepimysie/narodowy-program-szczepien-przeciw-covid-19.

7 https://www.gov.pl/web/szczepimysie/raport-szczepien-przeciwko-covid-19.

8 Analiza ryzyka zgonu z powodu ogółu przyczyn oraz z powodu COVID-19 osób zaszczepionych i niezaszczepionych przeciw COVID-19, NIZP-PZH 2021, https://www.pzh.gov.pl/raport-analiza-ryzyka-zgonu-z-powodu-ogolu-przyczyn-oraz-z-powodu-covid-19-osob-zaszczepionych-i-niezaszczepionych/.

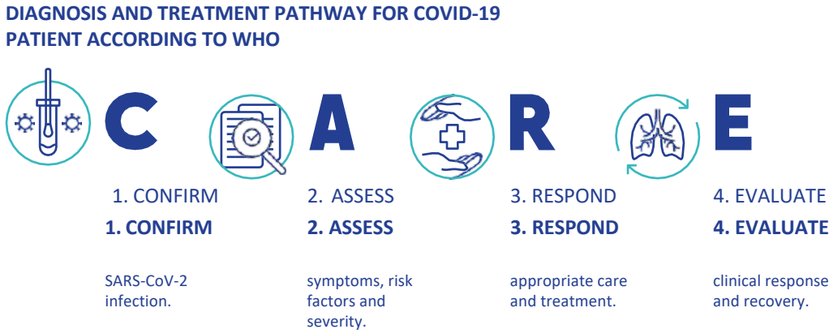
9 https://twitter.com/mz_gov_pl/status/1464257638326226945.

10 European Pathway Association, źródło: http://e-p-a.org/care-pathways/.

11 Rotter T., de Jong R.B., Lacko S.E. et al., Clinical pathways as a quality strategy, [In:] Busse R., Klazinga N., Panteli D. et al., editors, Improving healthcare quality in Europe: Characteristics, effectiveness and implementation of different strategies [Internet], Copenhagen (Denmark): European Observatory on Health Systems and Policies 2019, (Health Policy Series, No. 53.) 12, https://www.ncbi.nlm.nih.gov/books/NBK549262/.

12 The COVID-19 Clinical Care Pathway, WHO Updated on 3 March 2022, https://www.who.int/tools/covid-19-clinical-care-pathway.

Therapeutics and COVID-19: living guideline", published on March 3, 2022[13], and the third edition of the "WHO COVID-19 Clinical management: living guidance", published on November 23, 2021[14]. The diagnostic and therapeutic pathway of a patient with COVID-19 according to WHO is based on the activities within the CARE acronym:

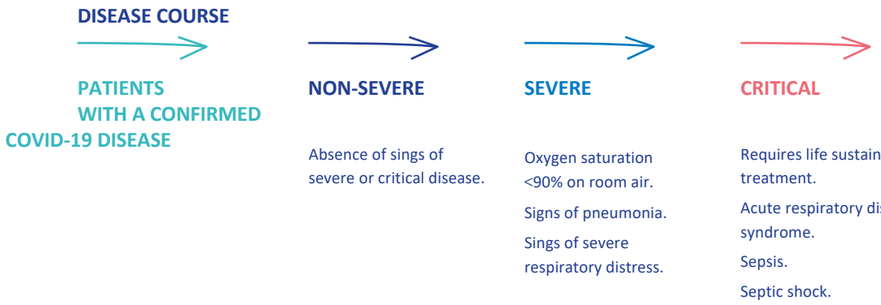


Ad. 1. Confirm SARS-CoV-2 infection

Ensure prompt diagnosis using a molecular (NAAT/PCR) or antigen-detection test (i.e. Ag-RDT).

Ad. 2. Assess symptoms, risk factors and severity

Provide early clinical assessment and evaluation to determine if the patient has emergency signs, symptoms or risk factors that may warrant treatment, clinical referral or admission to hospital care. Disease severity staging is: non-severe, severe and critical.



Risk factors: >60 years, hypertension, diabetes, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression (including HIV), obesity, cancer and unvaccinated against COVID-19. Risk factors in pregnant or recently

13 WHO Therapeutics and COVID-19: living guideline, WHO, 3.03.2022, https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.2.

14 WHO COVID-19 Clinical management: living guidance, WHO 23.11.2021, https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2.

pregnant: advanced maternal age (≥ 35 years), obesity, chronic diseases and pregnancy-specific disorders (e.g. gestational diabetes and pre-eclampsia / eclampsia). Emergency signs are: obstructed or absent breathing, severe respiratory failure, cyanosis, shock, coma and / or convulsions.

Ad. 3. Appropriate care and treatment

Treatment selection is determined by severity of disease and risk factors. For patients with COVID-19 presenting with early onset of mild or moderate COVID-19 (non-severe symptoms) without risk factors for severe disease the treatment care plan includes:

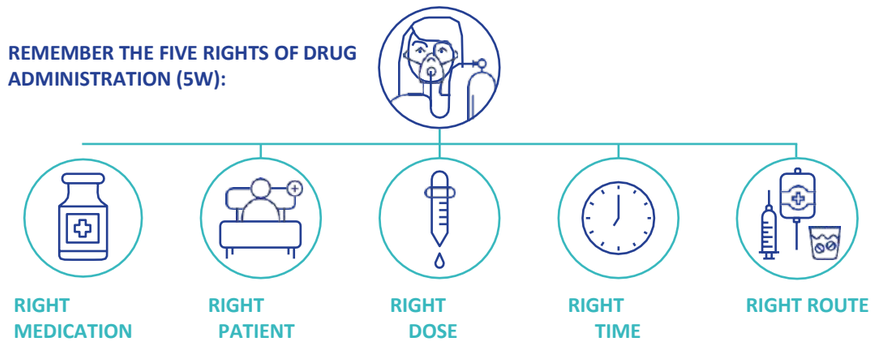
- symptom management and supportive care,
- Monitoring (at home, or in the community).

For patients with COVID-19 presenting with early onset of mild or moderate COVID-19 (non-severe symptoms) and with risk factors, for severe disease consider including treatment with one of the following options:

- molnupiravir OR
- nimatrelvir (PF-07321332)/ritonavir, OR
- sotrovimab, or casirivimab and imdevimab (neutralizing monoclonal antibodies).

For patients presenting with severe or critical COVID-19 immediately assess for emergency signs. For patients with severe or critical COVID-19, the treatment care plan includes:

- oxygen therapy and corticosteroids, and venous thromboembolism Prophylaxis, AND
- interleukin-6 receptor blocker (tocilizumab or sarilumab) or baricitinib. For seronegative patients, consider including casirivimab and imdevimab[15] (neutralizing monoclonal antibodies).



15 Kasirivimab and imdevimab are active against the alarming alpha, beta, gamma and delta variants. Local epidemiological data should be taken into account as preclinical in vitro and in vivo evaluations show no efficacy against the omicron BA1 variant. The use of kasirivimab and imdevimab should be limited to cases where rapid viral genotyping is available and confirms infection with the SARS-CoV2 variant that is sensitive to the neutralizing effect of this combination of monoclonal antibodies.

Ad. 4. Evaluate clinical response and recovery

All patients receiving COVID-19 treatment require clinical monitoring and follow up by a health care professional throughout their illness and recovery, including those who develop post COVID-19 condition. If patients have emergency signs OR SpO2 <90%, seek urgent medical assistance. If patients have SpO2 between 90-94%, worsening symptoms, side-effects or concerns, patient or caregiver should immediately seek advice from a health care professional. It is important that all COVID-19 treatments are prescribed, completed or stopped under guidance of a health care professional. Ensure reporting of any adverse events (AE) through local or national reporting systems. Advise patient or caregivers to monitor for change or worsening of symptoms, such as chest pain, fast or difficulty in breathing (at rest or while speaking), fast heart rate, palpitations, confusion, altered mental status, or any other emergency signs. If present, instruct patient or caregivers to call for emergency help according to national protocols[16].

“Model diagnostic and therapeutic pathways should be based on clinical guidelines of scientific societies, which are developed on evidence-based medicine (EBM). Clinical guidelines should be followed by interdisciplinary care teams to ensure effective and safe patient care.”

DR N. MED. JAKUB GIERCZYŃSKI

16 https://www.who.int/tools/covid-19-clinical-care-pathway.

DIAGNOSIS AND TREATMENT PATHWAY FOR COVID-19 PATIENT*

1. **INFECTION CONFIRMATION SARS-COV-2** – positive result of PCR test or Ag-RDT (prescribed by a doctor or performed by the patient)
2. **URGENT CONTACT WITH A CLINIC**
3. **CONTACT WITH A DOCTOR** – preferred personal visit on the day of notification
4. **CAUSAL ORAL TREATMENT** (assessment of symptoms, risk factors and disease severity)
5. **INITIATING THERAPY** (a doctor will prescribe an oral drug for COVID-19 after determining that at this clinical stage the course of the disease is mild or moderate and the patient does not require oxygen therapy)
6. **PATIENT CONDITION MONITORING** – evaluation of clinical response and recovery

TIME MATTERS - WE HAVE ONLY 5 DAYS TO START THERAPY

ORAL COVID-19 TREATMENT SHOULD BE GIVEN ASAP AFTER DIAGNOSING INFECTION WITH SARS-COV-2 CORONAVIRUS.

You have 5 days to start treatment after the symptoms of the disease appear.

CRITERIA FOR INTRODUCING ORAL TREATMENT

The decision to initiate oral treatment is taken by the physician based on the implementation criteria in line with the Summary of Product Characteristics and the guidelines. These are:

Confirmed COVID-19 (antigen or PCR test). Clinical

Symptoms last no more than 5 days.

Patients over 18 years of age from the high-risk group of severe course of COVID-19.

At this clinical stage, the course of the disease is mild or moderate, and the patient does not require oxygen therapy.

HIGH-RISK GROUPS FOR SEVERE COVID-19

> 60 years
hypertension
diabetes cardiac
disease
chronic lung disease
cerebrovascular disease dementia mental disorders chronic
kidney disease
immunosuppression (including HIV)
cancer
obesity (BMI ≥ 35)
unvaccinated against COVID-19

* management of mild / moderate disease with the presence of risk factors (high-risk groups for severe COVID-19)

CLINICAL GUIDELINES FOR DIAGNOSTICS AND TREATMENT OF COVID-19 PATIENTS IN POLAND

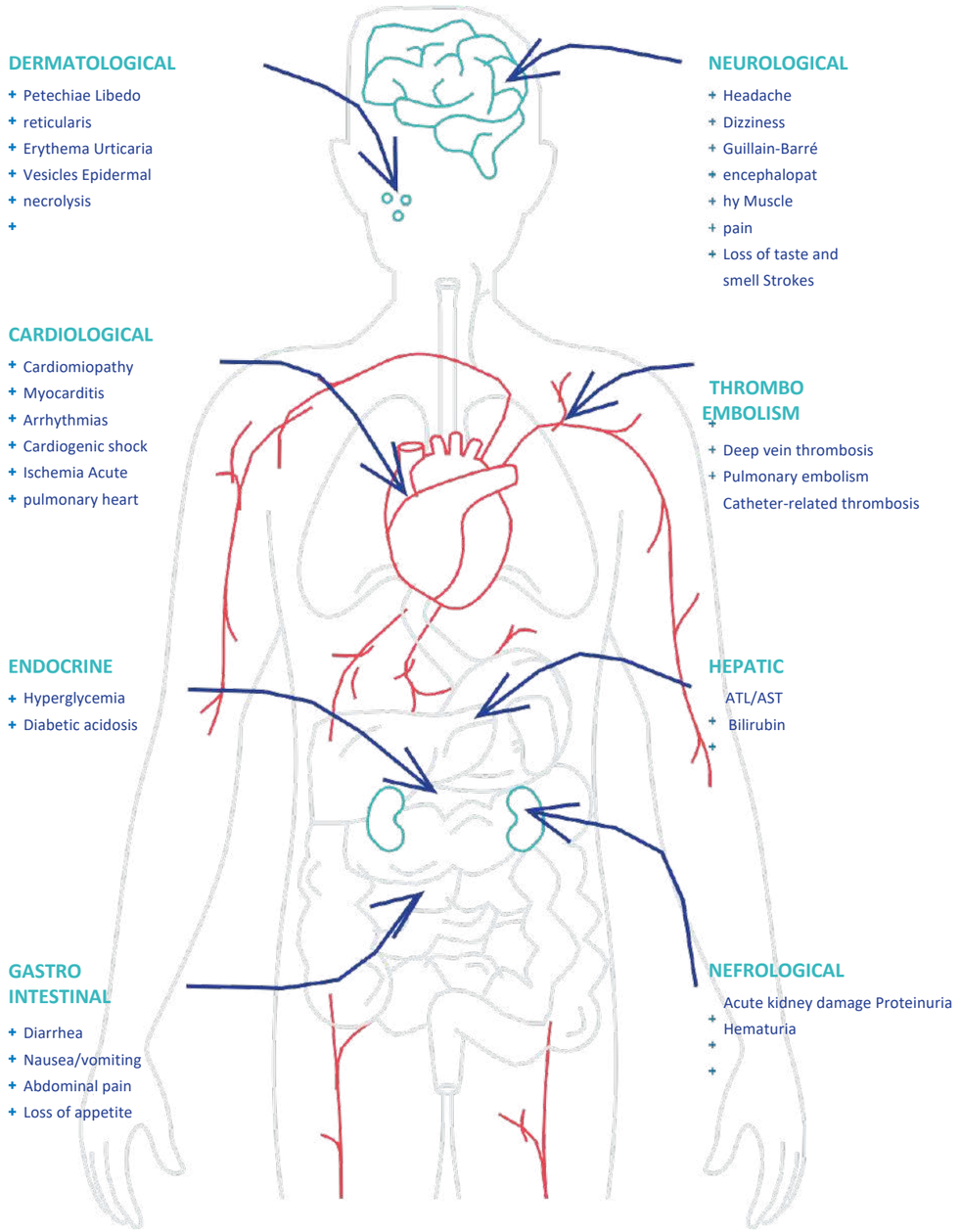
DR HAB. N. MED. JERZY JAROSZEWICZ

COVID-19 is an interdisciplinary disease, therefore its diagnostics and treatment are performed by physicians of various specializations. COVID-19 is not only a lung disease, but it also affects heart, blood vessels, skin, kidneys, nervous system, liver and endocrine organs.

"Remember that antiviral drugs only work when the SARS-CoV-2 coronavirus is multiplying.
So at a very early stage. In COVID-19, as in other infectious diseases, the virus multiplies briefly. So we have a very short therapeutic window."

DR HAB. N. MED. JERZY JAROSZEWICZ

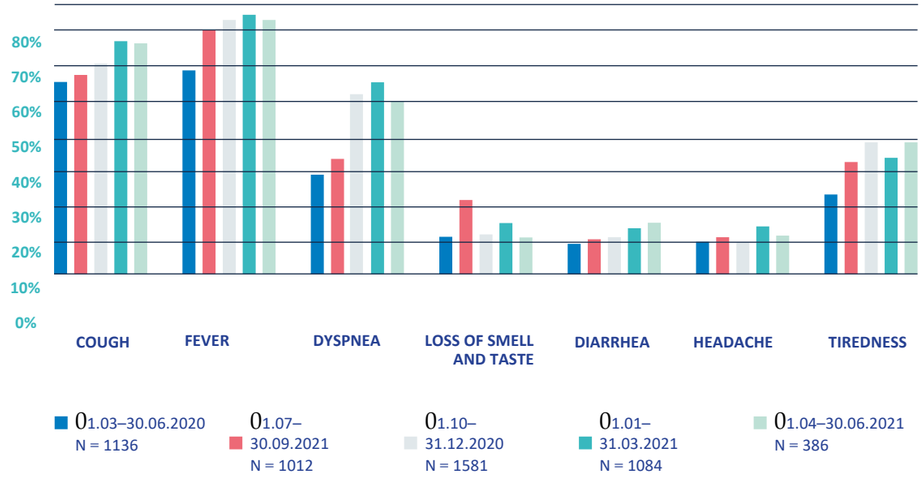
EXTRAPULMONARY SYMPTOMS COVID-19, DISEASE SPECTRUM:



COVID-19 has surprised us many times, which is why it is very important to validate international knowledge into Polish conditions based on local data. It means that we cannot transfer Chinese, British or American data directly to the Polish population. We know genetic factors can vary, let alone healthcare organization issues. The observations that I will present today are based on the SARSTer database, which includes over 11,000 patients hospitalized for COVID-19 in 31 Polish clinical centres (including 10 paediatric centres). It is a database created by the Polish Society of Epidemiologists and Infectious Diseases Specialists and co- financed by the Medical Research Agency.

Diagnosis and treatment pathway for COVID-19 patient starts of course with the first symptoms. Nevertheless, the symptomatology of COVID-19 is so complex that it is difficult to say that this or that constellation of symptoms allows the patient to be automatically considered infected. We recorded a different frequency of symptoms in individual waves of the pandemic. Fever occurred in 60–75% of patients, cough in 50–70%, and dyspnea in 30–50% of patients. The loss of smell and taste concerned only about 10% of patients.

TABLE: FREQUENCY OF CLINICAL SYMPTOMS AMONG HOSPITALIZED WITH COVID-19 IN PARTICULAR TIME RANGES

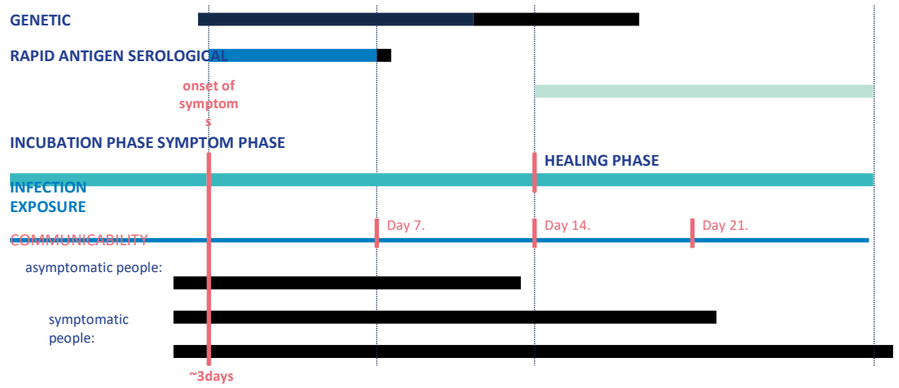


SOURCE: Flisiak R., Zjazd PTEiLChZ 2021, and Flisiak i wsp., J Clin Med. 2022 Jan, 11(1): 117

The variety and often atypicality of symptoms means that every patient showing symptoms however attributable to COVID-19 should be tested. The patient's diagnostic pathway is described in the guidelines of the Agency for Health Technology Assessment and Tariffs in the field of COVID-19 diagnostics[17].

17 Diagnostyka laboratoryjna SARS-CoV-2, Aktualizacja Zaleceń, wersja 2.0, data ukończenia – 7.04.2021 r., AOTMiT, https://www.aotm.gov.pl/media/2021/04/Diagnostyka-laboratoryjna-SARS-CoV-2-%E2%80%93-aktualizacja-Zalecen-wersja-2.0-7-kwietnia-2021-r..pdf .

PICTURE: APPLICATION OF DIAGNOSTIC TESTS DEPENDING ON THE PHASE OF THE DISEASE (ACCORDING TO THE COLOR INTENSITY)



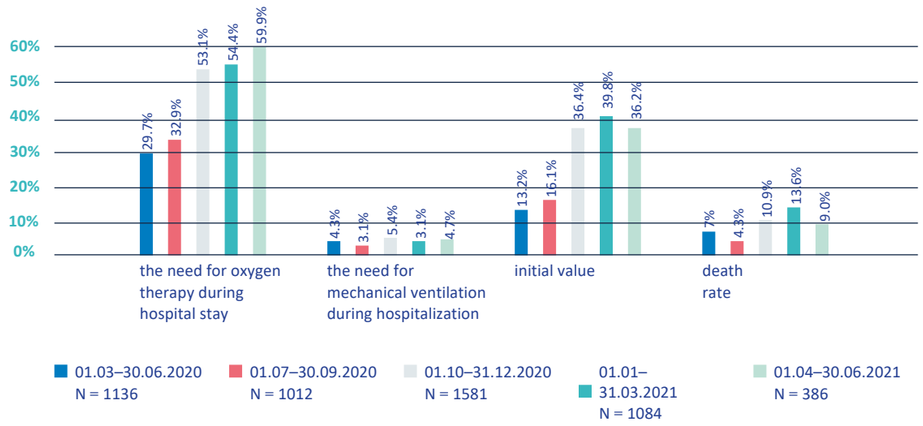
* People immunocompromised and treated with immunosuppressants may be infectious for longer.

PCR genetic tests are the most sensitive tests. This is the gold diagnostic standard. These are the tests that detect the virus at the earliest - even before the first symptoms appear. Genetic testing detects the coronavirus even in asymptomatic or subclinical patients. On the other hand, genetic tests have one drawback - the PCR test remains positive also after the end of the viremia period, i.e. the period of virus multiplication. Positive result of a PCR test may persist for several weeks. Thus, a positive PCR test does not necessarily correspond to communicability and the presence of a virus in the patient's body.

The introduction of rapid antigen tests was certainly a major breakthrough in COVID-19 diagnostics. Antigen tests, unlike PCR tests, show less clinical utility and are generally not recommended for the diagnosis of asymptomatic patients, i.e. testing before symptoms develop. However, in symptomatic patients, antigen tests are very sensitive and specific. Antigen tests give positive result for a short time - for five to seven days in the peak period of
infectiousness. Therefore, they are very helpful only in symptomatic patients. The third
type of tests - serological tests - are not suitable for the diagnosis of the acute phase of the disease. They are used to confirm whether the patient has had a history of COVID-19 or
has been vaccinated. These tests should be used wisely.

COVID-19 has a different severity depending on the pandemic wave and the virus variant. According to SARSTer, mortality among patients who were hospitalized reached 7% in the first wave, 4% in the second wave, and 11% in the third wave. In the fourth wave of the pandemic caused by the delta virus, the death rate was as high as 14%. It shows that the mortality rate depends on the SARS-CoV-2 coronavirus variant. Currently, during the dominance of the omicron variant, it is much lower.

CLINICAL OUTPUT PARAMETERS CHARACTERIZING PATIENTS WITH SEVERE COVID-19 COVID-19 IN PARTICULAR TIMES



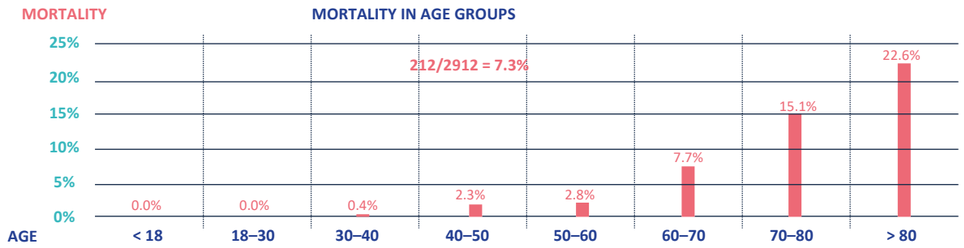
SOURCE: Flisiak R., Zjazd PTEiLChZ 2021, oraz Flisiak i wsp., J Clin Med. 2022 Jan; 11(1): 117

The most important task of a physician is to find out who may be at high risk and which patient should therefore be under special supervision. We know, of course, that the elderly are the main burden of poor prognosis. Already the first SARSTer data showed that the risk of death affects people over 60 in approx. 8%, after 70 - 15%, and over 80

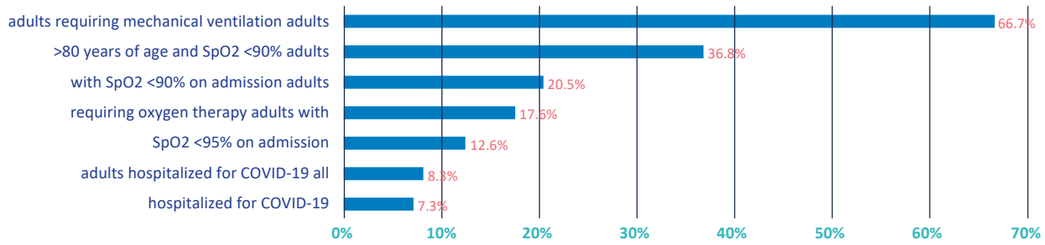
– approx. 23%. Saturation is a very important criterion for the severity of the disease. In the case of patients admitted to the hospital with saturation below 95%, mortality

was 12%, and among patients with saturation below 90% - as much as 20%.

SARSTer – MORTALITY



MORTALITY IN SUBPOPULATIONS

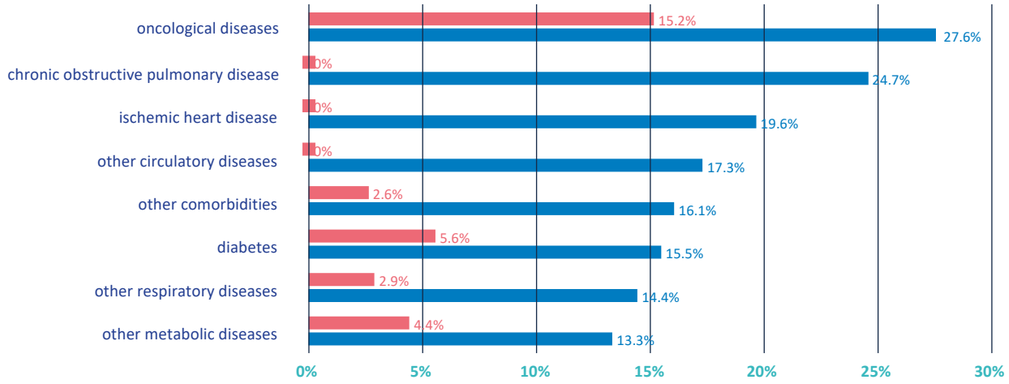


SOURCE: SARSTer – database, 20.01.2021

Apart from these two factors, multi-morbidity, i.e. comorbidities, is also very important. Among oncological patients, especially older than

60, the death rate due to COVID-19 reached approx. 30%. The increased risk of death - approx. 15%, also applies to oncological patients under 60 years of age. Chronic obstructive pulmonary disease (COPD) increased the risk of death of an infected patient over 60 years of age by approx. 25%, ischemic heart disease - by approx. 20%, other cardiovascular diseases - by approx. 17%, diabetes - by approx. 15% , diseases of the respiratory system - by approx. 14%.

MORTALITY DEPENDING ON COMORBIDITIES AND AGE



We know the whole range of diseases that worsen the prognosis in COVID-19. We

tried to also look at it statistically to group these factors - which are more and which are less important. This is critical for the referral of the patient to the hospital, but is also critical for the use of oral growth inhibitory medications inhibiting development of COVID-19.

In multivariate regression analysis, it seems that, apart from age and low saturation on admission, the most important factor is decreased renal filtration - that is, deterioration of kidney function. And we do not distinguish here whether it is acute nephritis,

or chronic, is it because the patient has a fever, drinks too little and hydrates not enough. Hydration at home is crucial. A reduction in glomerular filtration is a very poor prognostic factor. With eGFR below 30 ml / min, mortality can be as high as 80%. Cancer and chronic heart disease contribute to poor prognosis. A high CRP, high levels of neutrophils, low levels of platelets indicate that these patients, also in our population, will have a more severe course of the disease[18].

18 Dorota Zarębska-Michaluk i wsp., J Clin Med. 2021 May 10, 10(9): 2042.

DEATH RISK FACTORS DURING HOSPITALIZATION ACCORDING TO THE SARSTer DATABASE

Older age
Low oxygen saturation on
admission Reduced renal
filtration Cancer Chronic heart
disease
High CRP and neutrophils, low platelets

This data has also been validated in many other databases. High post mortality among patients with heart disease and COVID-19 at the level of approx. 42% was found in the Silesian Cardiovascular Database collecting data from the Silesian Centre for Heart Diseases in Zabrze and other Silesian cardiological units. This study had a slightly longer follow-up - not 28 days, but 72 days. This means that 20% of patients, unfortunately, die after discharge, not in the hospital, and not within 28 days, but in follow-up. Again, we see the same risk factors for the severe course of COVID-19, such as heart failure, diabetes, chronic kidney disease, and COPD[19].

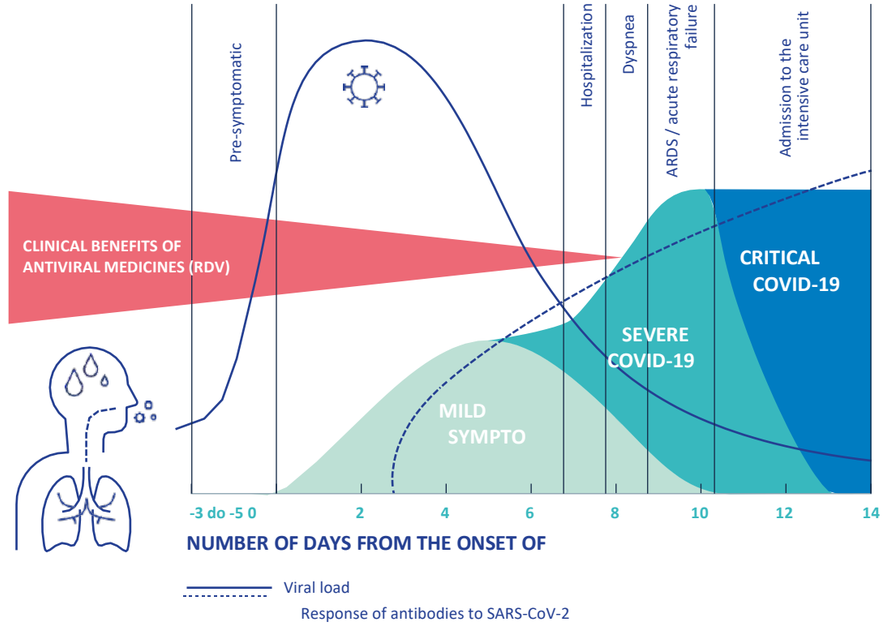
Remember that antiviral drugs only work when the SARS-CoV-2 coronavirus is multiplying, so at a very early stage. In COVID-19, as in other infectious diseases, the virus multiplies briefly. We have a very short therapeutic window – this is very important. So, if we were to use antiviral treatment, it is best as early as possible, optimally before symptoms appear, preferably very shortly after infection. This may be the latest within four or five days of the onset of symptoms. Later, the virus is gone, this drug will not work, there is no point in administering it, of course, except for some exceptions, mainly in case of severely immunocompromised patients, e.g. with immune deficiencies. This is very important and affects the drug distribution, as the patient has to be reached within the first five days.

"COVID-19 has surprised us many times, which is why it is very important to validate international knowledge into Polish conditions based on local data. "

DR HAB. N. MED. JERZY JAROSZEWICZ

19 Gąsior M. i wsp., Pol Arch Intern Med. 2021, Aug 30, 131(7-8): 749-751.

PICTURE. ROLE OF ANTIVIRAL DRUGS IN COVID-19



SOURCE: Dolken L. et al., Viruses 2021, 13: 963

The first edition of "Management of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists" was published on March 31, 2020 – at the very beginning of the pandemic. The newest "Management of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists" was published on February 23, 2022[20]. According to the recommendations, the choice of drugs used in COVID-19 must be determined by the phase of the disease, the patient's clinical condition and the assessment of risk factors for the severe course of COVID-19. For the purposes of this report, the recommended treatment modalities based on stage 1 and stage 2 disease are detailed below and additionally in the table below.

20 Management of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists. Robert Flisiak, Andrzej Horban, Jerzy Jaroszewicz, Dorota Kozielewicz, Agnieszka Mastalerz-Migas, Radosław Owczuk, Miłosz Parczewski, Małgorzata Pawłowska, Anna Piekarska, Krzysztof Simon, Krzysztof Tomasiewicz, Dorota Zarębska-Michaluk, 23 February 2022, http://www.pteilchz.org.pl/wp-content/uploads/2022/02/REKOMENDACJE-pl-w-C19-2022-23-02-2022pl.pdf.

TABLE. RECOMMENDED PHARMACOLOGICAL MANAGEMENT IN ADULTS AT CLINICAL STAGE 1 AND 2 OF SARS-COV-2 INFECTION, INCLUDING PRIMARY AND SUPPORTIVE TREATMENT. DETAILS ON DOSAGE AND USE RESTRICTIONS ARE CONTAINED IN THE SUMMARY OF THE MEDICINAL PRODUCTS (SPC) FOR THE EU / POLAND

DISEASE STAGE	PRIMARY TREATMENT	SUPPORTIVE TREATMENT
Stage 1 **mildly symptomatic** • $SpO_2 \geq 94\%$ • no hospitalization is necessary	The commencement of antiviral therapy is recommended up to 5 days after the onset of symptoms (up to 10 days in immunosuppressed patients), with particular emphasis on patients at risk of a severe course of COVID-19* and under direct medical supervision during the qualification and monitoring of treatment. These drugs should not be used in pregnant and lactating women. • Molnupiravir used orally twice daily 800 mg for 5 days. or • **Nirmatrelvir/ritonavir** used orally twice daily 300/100 mg for 5 days. Contraindicated in patients with: – severe hepatic failure, – eGFR < 30 ml/min (in patients with eGFR 30–60 ml/min) the dose should be reduced to 150/100 mg) or • **Remdesivir** administered intravenously once daily for 3 days, a loading dose of on day 1: 200 mg, then a maintenance dose of 100 mg for 2 days. Contraindicated in patients with: – eGFR < 30 ml/min – ALT activity ≥ 5 times the upper limit of normal. or • **Sotrovimab** used as a single intravenous infusion of 500 mg. or • Casirivimab /imdevimab used intravenously or subcutaneously as a single dose of 1200 mg (600/600 mg) provided the locally dominant viral variant is not a resistant variant (eg. Omicron).	• Inhaled budesonide at a dose of 2 x 800 μg daily, • antipyretic drugs (paracetamol, ibuprofen, etc.), • rest, • Oral hydration, • LMWH in chronically bedridden patients and in those with indications for thromboprophylaxis unrelated to COVID-19 • Antitussive drugs for persistent cough • Systemic glucocorticosteroids are contraindicated, • Antibiotics and anti-influenza medications are contraindicated, unless there is a bacterial coinfection or concomitant influenza, • Oxygen saturation control using the Pulsocare remote alarm system (using pulse oximeters).
Stage 2 **fully symptomatic** • $SpO_2 < 94\%$ • Usually week 1 after disease onset • hospitalization is required	The initiation of antiviral therapy with each of the following drugs is recommended up to 5 days after the onset of symptoms (up to 10 days in immunosuppressed patients). These drugs should not be used in pregnant and lactating women. • Molnupiravir used orally twice daily 800 mg for 5 days. or • **Nirmatrelvir/ritonavir** used orally twice daily 300/100 mg for 5 days. Contraindicated in patients with: – severe hepatic failure, eGFR <30 ml/min (in patients with eGFR 30–60 ml/min the dose should be reduced to 150/100 mg) or • **Remdesivir** administered intravenously once daily for 5 days, a loading dose of on day 1: 200 mg, then a maintenance dose of 100 mg for 4 days. Contraindicated in patients with: – eGFR < 30 ml/min – ALT activity ≥5 times the upper limit of normal [63]. or • **Sotrovimab** used as a single intravenous infusion of 500 mg. or • **Casirivimab /imdevimab** used intravenously or subcutaneously as a single dose of 1200 mg (600/600 mg) provided the locally dominant viral variant is not a resistant variant (eg. Omicron).	• LMWH in a prophylactic dose, which can be increased in justified cases, • Dexamethasone can be considered but only in patients receiving antiviral drugs and oxygen therapy, orally or intravenously 4–8 mg/d; should not be used in the first week of the disease if antiviral drugs are not used. • Antibiotic therapy in the case of secondary bacterial infections, • Symptomatic treatment, • Oxygen therapy, • Oral or intravenous hydration.

Stage 1. COVID-19

The vast majority of patients (80%) infected with SARS-CoV-2 has an asymptomatic or oligosymptomatic course of the infection that does not require hospitalization. This percentage increased significantly with the predominance of the omicron variant, which mainly caused symptoms of upper respiratory tract infection. However, it should be remembered that in some cases the appearance of these mild symptoms may precede progression to diagnosed pneumonia usually in stage 2 of the disease. Patients in stage 1 (Sp02 ≥ 94%), usually under the care of a primary health care physician, require, first of all, the assessment of general condition and monitoring of SpO2 as well as the assessment of risk factors for the development of severe COVID-19, which include, among others: age> 60 years, obesity, diabetes, cancer , chronic heart failure, chronic respiratory failure, chronic renal failure, immunodeficiency, or immunosuppressive therapy. Obviously, this list is not complete and each case must be evaluated individually be a phycisian.

Currently, we have drugs that inhibit the replication of SARS-CoV-2 and monoclonal antibodies that neutralize the virus, the use of which, however, is limited by the variable sensitivity of virus variants. Drugs that inhibit viral replication, such as molnupiravir, nirmatrelvir (PF-07321332)/ritonavir or remdesivir, should generally be applied up to five days after the onset of symptoms in patients who meet the criteria for developing severe disease (as above). In patients with documented immunosuppression as a result of disease or therapy, the duration of antiviral therapy may be extended to 10 days, assuming a longer duration of viral replication activity.

These drugs should be used prescribed and under the supervision of a physician due to the limitations of each of them. According to the Summary of Product Characteristics (SPC), none of the antiviral drugs can be used in pregnant or lactating women due to the lack of clinical trials in these groups of patients. Molnupiravir and nirmatrelvir/ritonavir are orally administered drugs used twice a day for five days (detailed dosage in the stage 2 treatment description).

According to the latest modification of the SPC, remdesivir can be administered as intravenous infusions for three days also in patients who do not need oxygen therapy. The use of all the above-mentioned antiviral drugs significantly reduces the risk of hospitalization and the severe course of COVID-19 in people suffering from the above-mentioned risk factors. An alternative to the outpatient antiviral drugs listed above is neutralizing monoclonal antibodies.

Casirivimab/imdevimab, which is currently available in Poland, should be used in a single intravenous infusion of 1200 mg. However, due to the predominance of the omicron variant, which is not neutralized by

casirivimab/imdevimab in vitro studies, its use is currently not recommended. On the contrary, sotrovimab administered up to five days after the onset of symptoms in a single intravenous infusion of 500 mg is still active against the omicron variant, significantly reduces the risk of disease progression to severe and critical form, hospitalization or death, and shortens recovery time.

Patients with mild symptoms of respiratory tract infections (mild or short-term fever, sore throat, headache, muscle pain, rhinitis) without signs of lung involvement and no comorbidities affecting the prognosis usually do not require pharmacological therapy, but only clinical monitoring. It is advisable to register all adult patients staying at home in the DOM/PulsoCare (Home Medical Care) system for SpO2 monitoring, which should remain at least 94%. All patients covered by the DOM system reporting measurements are under the care of consultants and physicians who assess indications for hospitalization on an ongoing basis, and in the event of emergency values, they can call a medical emergency team. It is worth remembering that in patients with chronic respiratory diseases, the baseline oxygen saturation may be lowered and does not necessarily mean that respiratory failure caused by SARS-CoV-2 is worsening, but when it is clearly decreasing, immediate action should be taken. As symptomatic treatment, patients may require treatment with antipyretics in the event of fever (non-steroidal anti-inflammatory drugs or paracetamol).

Antitussive drugs are recommended for patients with severe, dry cough (making it difficult to speak and sleep). In adult patients with symptomatic, mild to moderate COVID-19 inhalation of budezonid in a daily dose twice a day of 800 μg may be considered. However, it should be underlined that systemic corticosteroids should not be administered in patients at this stage due to their immunosuppressive effects, which may increase and prolong the viral replication time, and thus worsen the prognosis. Based on the results of studies indicating the risk of a more severe course of COVID-19 in people with vitamin D3 deficiency, its supplementation is advisable if the deficit is documented, in accordance with the recommendations for the Polish population. However, one should bear in mind the consequences of overdosing, which may be associated with long-term health consequences. There is insufficient data to support the routine use of antiplatelet drugs in COVID-19. Prophylactic dose of low molecular weight heparin is recommended in chronically immobilized patients and with other indications for thromboprophylaxis unrelated to COVID-19, especially in patients with risk factors for deep vein thrombosis and / or pulmonary embolism. Antibiotics should be introduced only in case of justified suspicion of the development of a bacterial infection, because their effectiveness in COVID-19 treatment has not been proven. Home oxygen therapy in the acute phase of the disease is also not recommended. This is mainly due to the fact that

the necessity of oxygen therapy associated with a rapid deterioration of the clinical condition is an absolute indication for hospitalization. The course of the disease can be very quick and often hours can determine the fate of patients.

Stage 2. COVID-19

Increasing dyspnoea, accompanied by SpO2 below 94%, requires inpatient oxygen therapy. Usually, in this phase of the disease, low-flow oxygen therapy, not exceeding 15 l/min, is sufficient. Prophylactic doses of low molecular weight heparin are part of standard treatment in hospitalized patients, and their doses may be increased in justified cases. Antiviral therapy should be started no later than within 5 days after the onset of symptoms. In immunosuppressed individuals, this period may be extended up to 10 days. It is pointless to start treatment after this time due to the loss of viral replication. Due to the limitations resulting from the characteristics, these drugs should be used under medical supervision, excluding their use mainly in pregnant and lactating women.

The first registered antiviral drug with proven efficacy against SARS-CoV-2 in adults and children over 12 years of age was remdesivir, which should be given to hospitalised patients as an intravenous infusion of 200 mg on the first day and 100 mg on the following four days. The main contraindication to the use of remdesivir is renal failure with GFR < 30 ml/min. Treatment with remdesivir should be discontinued if alanine aminotransferase activity exceeds five times the upper limit of normal.

Alternatively to remdesivir, oral molnupiravir may be used twice daily 800 mg for five days or oral nirmatrelvir (PF-07321332)/ritonavir twice daily at 300/100 mg for five days. It should be remembered that nirmatrelvir/ritonavir is contraindicated in patients with severe hepatic impairment and in patients with renal insufficiency and creatinine clearance (eGFR) < 30 ml/min. In patients with eGFR 30–60 ml/min the drug can be used in a dose reduced to 150/100 mg. This drug is an inhibitor of CYP3A and therefore the risk of drug interactions needs to be assessed. None of the three antiviral medicines are approved for use in pregnant or lactating women. Due to relatively low clinical experience in the use of antiviral drugs anti-SARS-Cov-2, particular attention should be paid to patients in procreative age. If a patient is pregnant, may be pregnant, or is planning to have a baby, she should ask her doctor for advice before taking this medicine. Women of childbearing potential should use effective contraception during treatment with this medicine and for four days after the last dose. Instead of drugs that inhibit replication, it is also possible to use monoclonal antibodies with neutralising activity against SARS-CoV-2

in hospital conditions. The hopes associated with this form of treatment have been cooled with the predominance of the omicron variant, which is currently only neutralised by sotrowimab used in a single intravenous infusion containing 500 mg of the drug.

Other medications of this group, including casirivimab/imdevimab available in Poland, used intravenously or subcutaneously at a single dose of 1 200 mg (600/600 mg), which are known to have limited activity against the omicron variant, may be used in the future, provided that the predominant SARS-CoV-2 variant is sensitive to them.

Due to the lack of evidence from clinical trials, the combination of the above-mentioned drugs with different mechanisms of action is currently not recommended. The use of glucocorticoids in the first week of the disease may be potentially unfavourable due to the risk of severity or prolongation of viral replication. However, in the absence of clinical improvement, despite antiviral therapy, the addition of 4-8 mg daily dexamethasone at the end of the first week of the disease may be considered. Antibiotics may be considered where there is a high probability of bacterial superinfection.

"The most important task of a physician is to find out who may be severely affected and which patient should therefore be under special supervision. We obviously know that the elderly are mainly burdened with poor prognosis."

DR HAB. N. MED. JERZY JAROSZEWICZ

CURRENTLY AVAILABLE ANTIVIRAL THERAPIES IN COVID-19

PROF. DR HAB. MARCIN DRĄG

My laboratory works on proteolytic enzymes. They are proteins that perform catalytic functions and are found in all living organisms. These proteins can be also found in virus, so we started to study them immediately after the outbreak of the current epidemic. The research is conducted in collaboration with a group of prof. Rolf Hilgenfeld from the University of Lübeck, who already promised us at the beginning of January that if only this protein, this enzyme is available, he would deliver it to my laboratory. And so it was – in early February this enzyme was delivered to the laboratory. It is important because it processes immature proteins that are in the middle of the virus, i.e. it performs a very important function. Without it a virus cannot survive. So it's a great drug candidate. What we do in the laboratory is to profile such enzymes thanks to the available technology, which here in Poland we developed, and determine the so-called substrate specificity.

After we focused our interest on SARS (Severe Acute Respiratory Syndrome), we knew pretty quickly that the main problem was that if we had another epidemic or pandemic, we were completely defenceless due to the lack of antiviral therapies available. We spoke about it many years before the outbreak of COVID-19. Already then we were looking for antiviral drugs that can be

used in the form of pills, and therefore they can be taken by patients at home.

The search for these therapies was abandoned very shortly after the end of the SARS epidemic in 2003–2004. The total number of cases at that time amounted to about eight thousand cases, approx. 800 people died — so neither the pharmaceutical industry nor the governments were particularly interested in it. Meanwhile we never lost interest in it, also working on MERS (Middle East Respiratory Syndrome).

From the very beginning, from January 2020 really, I suggested that the only effective solution in the treatment of COVID-19 would be an antiviral medicine taken at home (such as oseltamivir for the flu). But there was no such drug then. From the very beginning, there were some indications towards the use of remdesivir. The problem with remdesivir is that it must be administered intravenously. There have been studies on oral formulation, but for now without success. Research has also been carried out on the "retargeting" well known drugs. Thousands of these studies have been carried out, but nothing has been found towards antiviral drugs. Dexamethasone and many other drugs for the later phases of COVID-19 have been found.

My research group was convinced from the beginning that one of the surest targets would be proteases. In March 2020, so at the beginning of the pandemic, we were the first in the world, in free access, to publish the results of our research. We described the substrate specificity of SARS-CoV-2-Mpro protease, which is key to stopping the replication of the virus. Here we were also the first to show that the active center Mpro with SARS-2 is identical to SARS-1. At least two types of medicines are needed to treat COVID-19 and its complications: antiviral drug and a drug that fights the cytokine storm. An antiviral medicine should be given at an early stage of infection to extinguish the replication of the virus.

We currently have three types of antiviral drugs: monoclonal antibodies, allosteric drugs, and proteases. Antibodies make sense if we have a virus that is not mutating strongly on the surface, because the antibodies hit the whole virus. If the virus mutates, these drugs will become less effective. Therefore, monoclonal antibodies are practically ineffective against the coronavirus omicron variant. The second type of drugs are allosteric drugs, which are also supposed to interact on the surface of proteins, and many of such variations have also been developed. However, these are also drugs that are completely mutation-dependent. If mutations occur, allosteric drugs become ineffective. The third group of drugs - proteases, in addition to being proteins, are also enzymes and are necessary for the processing of the virus and for its replication. So when this S protein begins to form inside a human viral cell, it has to be cut. A protease is used in order for it to be cut selectively and to be able to create new copies. This protease in the active centre cannot mutate if no mutation is possible there (and while there can be a lot of mutations on the surface of this protein,

in the active centre there must be no mutations at all, because in such case the virus will kill itself immediately).

And here we would see a chance for a drug which, if created, will be effective both for the first variant and for subsequent variants. What we were waiting for was actually a drug in the form of a pill that could be given to the patient very quickly and could be taken at home — not like remdesivir only in the hospital. We know that remdesivir works, but is given too late. The idea is that the antiviral drug is given as soon as possible — practically immediately, reduce replication as much as possible and prevent subsequent severe COVID-19 symptoms, including death. We have two such drugs, which are currently recommended by the Food and Drug Administration, FDA. On January 28, 2022 nirmatrelvir/ritonavir was registered by the European Medicines Agency, EMA, indicated for use in the treatment of coronavirus-induced disease 2019 (COVID-19) in adult patients who do not require oxygen therapy and who have an increased risk of progression to severe COVID-19[21]. According to the European Medicines Agency recommendation as of November 22, 2021 despite the lack of authorisation in the European Union, molnupiravir can be used to treat adults with COVID-19 who do not require oxygen therapy and are at increased risk of developing severe COVID-19[22]. Molnupiravir is an old drug. It was developed in the United States, first at Emory University in Atlanta, as a drug against coronaviruses of colds long before the current coronavirus SARS-CoV-2 appeared. The drug has been somewhat retargeted, tested by Merck and has now been used in COVID-19 therapy. The second drug, nirmatrelvir, is a drug targeting the active centre of the Mpro protease. It is extremely selective. My research group has been working on it from the very beginning of the pandemic, it can be said that we even had a little contribution to the development of this drug, because we were the first to show that there are mutations in proteases between SARS1 then and SARS2 now and between SARS2 variants that are not in the active centre. First of all, nirmatrelvir will work on all possible variants of the coronavirus. Second, current studies show that nirmatrelvir will work on all human coronaviruses. Proteases are generally found in human coronaviruses, and this major protease is also there. Reasearch published in "Science" show that nirmatrelvir is selective to MERS, the previous SARS1, but also known other human coronaviruses, which is why this drug is so brilliant. In addition to the fact that it is very selective towards this protease, i.e. does not interact with other human proteases, which is very important, it works very quickly,

21 https://www.pfizerpro.com.pl/sites/default/files/paxlovid_chpl_28.01.2022.pdf.

22 https://www.gov.pl/web/zdrowie/komunikat-ministra-zdrowia-w-sprawie-produktu-leczniczego-lagevrio-molnupiravir.

demonstrating high efficiency, inhibiting replication within 89–90%, and proving to be a very safe drug. Nirmatrelvir is administered with ritonavir to increase stability. Ritonavir has been used in HIV therapy for several years. The drug therefore consists of two elements: nirmatrelvir, which targets Mpro protease, and it is generally intended to inhibit the replication of the virus, and ritonavir, which enhances the action of nirmatrelvir.

To sum up, currently we have oral COVID-19 treatment available in Poland, which should be administered as soon as possible. That is, if COVID-19 is diagnosed and the patient is at risk, the oral medicine should be given immediately. This is a safe therapy for patients. These drugs are not very stable, so their clearance is quite fast, they are non-toxic, and the therapy is very short - up to five days. I can give you examples of similar drugs already used in the clinic in the treatment of HCV and HIV. These are slightly different, long-term therapies, but also based on this technology. We have been waiting for such medicines since the very beginning of the COVID-19 pandemic: a drug that the patient can take orally at home. A drug that with very high effectiveness reduces the replication of the virus, preventing serious symptoms. This is a drug that, according to all indications, will be effective on all variants of the coronavirus, i.e. a panviral drug.

“From the very beginning, from January 2020 really, I suggested that the only effective solution in the treatment of COVID-19 would be an antiviral medicine taken at home. But there was no such drug then.

PROF. DR HAB. MARCIN DRĄG

“We have currently available oral COVID-19 treatment in Poland, which should be administered as soon as possible. That is, if COVID-19 is diagnosed and the patient is at risk, the oral medicine should be given immediately.

PROF. DR HAB. MARCIN DRĄG

DIAGNOSIS AND TREATMENT PATHWAY FOR PATIENT WITH COVID-19

FROM THE PRIMARY HEALTHCARE PERSPECTIVE

DR N. MED. MICHAŁ SUTKOWSKI

The standard of treatment of a patient infected with SARS-CoV-2 coronavirus for the primary healthcare (POZ) doctor is the “Statement of a national consultant in the field of family medicine dated 22.12.2021 on the treatment of patients infected with SARS-CoV-2 during isolation in domestic conditions”[23]. The course of COVID-19, a disease caused by SARS-CoV-2 infection, is in almost 85% cases mild and does not require hospitalisation. A patient in home isolation requires constant monitoring of his health due to the nature of the disease - his condition may deteriorate rapidly, or a gradually increasing respiratory failure may occur, which is an absolute indication for hospitalization. Any suspicion of COVID-19 should result in the patient being referred for a test (antigenic or PCR). If the result is positive - the place of treatment should be determined: home or hospital (or isolation room). Saturation <94% (in COPD <88%) is an indication for hospitalization, other indications should be assessed individually. In outpatient treatment,

23 Stanowisko konsultanta krajowego w dziedzinie medycyny rodzinnej z dnia 22.12.2021 dotyczące postępowania z pacjentami zakażonymi SARS-CoV-2 w trakcie izolacji w warunkach domowych, https://ptmr.info.pl/wp-content/uploads/2021/12/Stanowisko_KK_med_rodz_ws_covid-19_pozaszpitalnie.pdf.

the following shall be used: budesonide 800 mcg twice a day in adults, antipyretic/anti-inflammatory drugs — paracetamol or NSAIDs, antibody drugs, non-pharmacological treatment: hydration, respiratory exercises, rest.

Attention should be paid to the uninterrupted treatment of chronic diseases. The patient who is chronically burdened with risk factors should be more closely monitored. Systemic steroids and home oxygen therapy — except for indications in conditions other than COVID-19 — are not recommended. Antibiotics are not recommended if there are no bacterial overinfections. Each patient during home isolation should have at least two medical checkups (online, or, if the patient's medical condition so requires, personal visits to the clinic or at home).

Doctors and nurses should inform, encourage and include patients in the Home Medical Care programme, which allows for continuous monitoring of health, including saturation. As doctors, we are very happy that the expected oral antiviral drugs have appeared in COVID-19. At the same time, we are proposing to change the distribution system of these medicines. They should be reimbursed, prescribed on prescription in a general pharmacy. In Poland, retailing of medicinal products is lawfully operated by general pharmacies, pharmacy centres and hospital pharmacies. To burden the health care centre with such a task is a dramatically wrong solution. In addition to all the logistical nuisance, this reconciles the relationship between the doctor and the patient. It creates unnecessary conflicts and moral-ethical dilemmas on both sides.

Diagnosis and treatment pathway for COVID-19 patient varies in Poland. This protocol is sometimes a path that leads, unfortunately, to the death of the patient, and sometimes to full recovery. This happens for many reasons. These reasons are both on the side of the patient and health care system. Sometimes the patient does not vaccinate. Let us not forget that vaccines against COVID-19 are crucial. Medications are very important, but thanks to vaccinations you will not get sick, or the infection course will be less severe. The patient's pathway should be based on the responsibility of the patient, his family, every physician and other medical professionals. The patient's pathway should start from a phone call to a family doctor. Sometimes online counselling is enough, but very often in patients with concomitant chronic diseases, an online consultation is not enough. You have to reach the patient, you have to invite him to the clinic, you also have to do it according to the standards that prevailed in 2019, but under the full sanitary regime. In the primary care clinic, patients should be divided into those who are infected and those who are not. We hope that strategic actions will be taken in relation to primary health care, outpatient specialist care and hospital treatment in the implementation of the COVID-19 patient pathway.

"Diagnosis and treatment pathway for COVID-19 patient varies in Poland. This protocol is sometimes a path that leads, unfortunately, to the death of the patient, and sometimes to full recovery.
This happens for many reasons. These reasons are both on the side of the patient and health care system.

DR N. MED. MICHAŁ SUTKOWSKI

DIAGNOSIS AND TREATMENT PATHWAY FOR PATIENT WITH COVID-19

FROM CARDIOLOGIST AND CLINICAL PHARMACOLOGIST PERSPECTIVE

PROF. DR HAB. MED. KRZYSZTOF J. FILIPIAK

I am very glad that in February 2022 we have published new recommendations for the management of SARS-CoV-2 infections. In the diagnosis and treatment pathway for COVID-19 patient, the first contact of the patient should always refer to

the competence of the primary care physician. This is also important because the contact of these patients through the emergency medical team and HED will make hospitals inefficient. The idea that a primary care physician should personally examine each patient over 60 is also unrealistic. The mere use of a "magic" stethoscope will probably not change the prognosis of this patient, but will only paralyse the health care system. However, it is real and justified in the context of examining an infected patient after the age of 60 and prescribing an oral antiviral drug by a GP.

Two oral medications are currently approved. As a clinical pharmacologist, I realise that we don't have a prospective randomised head-to-head trial comparing the effects of both drugs. Fortunately, we have studies with an identically defined endpoint, i.e. a reduction in the risk of hospitalisation and death, an almost identical protocol and the same regimen of administration. It shows that molnupiravir guarantees approx. 30% reduction in the risk of hospitalisation and death, while nirmatrelvir/ritonavir a 90%. This is a very big, threefold difference. So we see a very big difference in the clinical effectiveness and efficiency of both drugs. Given the similar costs of five-day therapy, this translates into a higher cost-effectiveness of nirmatrelvir/ritonavir. The summary of product characteristics of nirmatrelvir/ritonavir is also slightly broader compared to malnupiravir. First of all, the age of a patient over 60 years of age will be an indication for the inclusion of nirmatrelvir/ritonavir in the SPC. There is no hypertension in the recommendations, and in the SPC it is listed, which would mean that every patient infected with SARS-CoV-2 with hypertension has an indication for this drug. Heart failure was also removed in the recommendations. Other elements of the SPC have been also removed, eg. active cancer and smoking.

So I can imagine that if someone is 18 years old, has a positive SARS-CoV-2 and smokes cigarettes, theoretically, according to the SPC, has indications for treatment with nirmatrelvir/ritonavir.

Therefore, I perfectly understand the intentions of the authors of the recommendations to act in SARS-CoV-2 infections, because for practical use it is necessary to synthesise and select the most burdened patients for oral therapy. Polish databases — such as SARSTer — reafirm us in this. Once again, I will emphasise that oral therapies should be prescribed by GP, because they have the fastest and first contact with a COVID-19 patient. They may issue an e-prescription for an oral medicine when they have confirmation that the patient is infected, belongs to the risk group, and the symptoms are present for a maximum of five days. Distribution by the Government Strategic Reserve Agency (RARS) delays the time of administration of the drug and introduces deviations from the standard distribution of the drug in Poland. Since we only have five days to start antiviral therapy with oral antiviral drugs, and the Agency informs that you have to order the drug on the website and wait for delivery, it will be worse than with vaccines against

COVID-19. I know that molnupiravir is distributed to specific clinical centres, e.g. dialysis stations, heamatooncological departments, etc.

On the other hand, in the standard use of oral drugs in COVID-19 therapy, the diagnosis and prescription of the drug by a primary healthcare doctor and the implementation of a prescription by the patient in a general pharmacy are crucial. In addition, it would be good that in addition to publicly reimbursed oral medicines for COVID-19 patients at risk, oral medicines are available in a general pharmacy on a full-paying basis, based on a prescription from a physician. As physicians, we want to be able to direct such therapy to anyone over the age of 18 when they want to actively treat themselves. Denying the possibility of access to an effective antiviral drug, of course after medical regulation, should not take place. The legislation in force in Poland stipulates that every phycisian, regardless of specialisation, has the right to write a prescription for a drug available in a general pharmacy.

"As physicians, we want to be able to direct such therapy to anyone over the age of 18 when they want to actively treat themselves. Denying the possibility of access to an effective antiviral drug, of course after medical regulation, should not take place. The legislation in force in Poland stipulates that every physician, regardless of specialisation, has the right to write a prescription for a drug available in a general pharmacy."

PROF. DR HAB. MED. KRZYSZTOF J. FILIPIAK

DIAGNOSIS AND TREATMENT PATHWAY FOR A HEART PATIENT WITH COVID-19

FROM CARDIOLOGIST AND OBESITOLOGIST PERSPECTIVE

PROF. DR HAB. N. MED. ARTUR MAMCARZ

In 2020, in Poland, there were 67,000 more deaths than in 2019. Of this number, deaths due to cardiovascular diseases account for approx. 17%, i.e. about 11,000 people more died. Let's not forget that because of cardiovascular diseases 200,000 people died in 2020. Therefore, patients with cardiovascular diseases should be in risk groups, with priority reimbursement access to oral medications in COVID-19 therapy. We are learning this disease all the time, we do not know everything, and we will learn many things on a regular basis. Of course, the availability of new antiviral therapies in oral form is a very positive thing.

In this context, I would like to draw attention to the consistency of communication from the point of view of preventing a severe disease. Physicians already know who is more vulnerable to more severe COVID-19. I have several months of experience of running a general COVID-19 unit where cardiac patients, obese patients and the elderly have been treated. I am pleased that attention has been drawn to obesity as a risk factor that clearly determines the severe and unfavourable course of COVID-19 in hospitalised patients. Again, as far as outpatient patients are concerned - because this is what we are dealing with today - I think that the consistency of messages should include the entire area of chronic diseases. Currently, this

communication is not consistent and there is a lot of misinformation in the public space about both the disease and the severity of COVID-19.

We need to do a lot together to make message clear: that the treatment of chronic diseases should be in line with the guidelines, and patients should vaccinate and regularly take medications. Lack of adherence will determine the severe course of COVID-19 and the need to hospitalise these patients. I would like to point out that we are facing not only the issue of access to modern oral therapies, but also the need to assure patients that all chronic diseases should be treated in accordance with the guidelines. The availability of patients for this information, also to the health care system, whether it be a primary healthcare physician or a specialist, should be ensured universally. Each of us tries to do as much as possible in the field of health education and communication. We take part in webinars, workshops, discussions and conferences, we also give interviews in the media. With this message, we must reach a group of not entirely convinced and sceptical about vaccination and the COVID-19 disease itself. We need to repeat that we have modern vaccines and excellent therapies that cause patient prognosis to be improved. I think oral therapies should be widely available. In a situation where we have evidence that they reduce the risk of death by 30-90 %, it is difficult from a medical point of view to think that we have to do a ranking that patients more or less deserve these therapies.

"We need to do a lot together to make message clear: that the treatment of chronic diseases should be in line with the guidelines, and patients should vaccinate and regularly take medications. Lack Lack of adherence will determine the severe course of COVID-19 and the need to hospitalise these patients."

PROF. ARTUR MAMCARZ

DIAGNOSIS AND TREATMENT PATHWAY FOR COVID-19 PATIENT

FROM PATIENT ORGANIZATION PERSPECTIVE

AGNIESZKA WOŁCZENKO

Diagnosis and treatment pathway for a COVID-19 patient with cardiovascular disease is extremely important. As patients, from the very beginning, since the COVID-19 pandemic began, we reported the need for clear diagnostic and therapeutic guidelines – easy to understand for John Doe. Unfortunately, we still receive numerous reports from cardiac patients from various regions of the country regarding problems with access to primary care doctors and cardiologists. If a patient is older, lonely, lives somewhere on the outskirts of Poland, calls the primary health care clinic and says that he most likely has SARS-CoV-2, the primary health care doctor will not be able to verify it because he will not do a home visit, or refuse to write a referral for the test.

We are very happy that effective oral therapies are emerging. It is a rescue especially for patients with multiple diseases, i.e. patients who are simply more vulnerable to the severe course of COVID-19. We shall, of course, promote vaccination against COVID-19. It is very important to define the beginning of the patient's pathway: what a person with a suspected SARS-CoV-2 infection should do and who to contact. Reality shows that we do not have this well organized from the very beginning. I believe that we should also pay attention to the key information for

patients: who is to write prescriptions for oral medications, where it is to take place, how to obtain it, whether it can be a cardiologist, diabetologist, or just the primary healthcare doctor. Let's send a clear message to patients that if they suspect infection, they should contact their GP as soon as possible. If they are infected and have cardiovascular disease, we are talking about five key days for administration of an oral medicine that significantly reduces the risk of COVID-19 complications.

DIAGNOSIS AND TREATMENT PATHWAY FOR A DIABETIC PATIENT WITH COVID-19

FROM DIABETOLOGIST AND INTERNIST PERSPECTIVE

PROF. DR HAB. N. MED. LESZEK CZUPRYNIAK

According to the Ministry of Health report, the increase in deaths among people with diabetes and COVID-19 was roughly 16% in 2020. Diabetes mellitus is the second disease, after cardiovascular disease, that increases the risk of severe COVID-19. Fortunately, oral medications are emerging for these patients that are effective in the early stages of COVID-19 in preventing the development of severe complications. Approximately 60% of our society was vaccinated against COVID-19. We know that vaccinated

people have much milder course of infection. The development of a drug for a disease such as COVID-19 is perhaps an even greater breakthrough than the development of vaccines.

Such drugs should be available by prescription in general pharmacies. Every physician in Poland has the right to prescribe any medicine, so there is no reason why one doctor should be able to do it and the other should not. However, we currently have a certain reimbursement restriction. Free of charge medicines for seniors can be prescribed by family doctors, and not by geriatricians, which I don't think is logical, but that's how it was agreed. However, what if an oral antiviral drug for COVID-19 becomes generally available? Everyone will buy it, whether they are sick or not, to have it at home just in case. Remember that when there was an avian flu epidemic everyone was buying oseltamivir. There is some way to control the prescription and distribution of oral medications in COVID-19 therapy. At the same time, restricting prescription is unethical.

The secret of COVID-19 is that you really don't know who will develop a serious course of the disease. Admittedly, there are known risk factors, but in our hospital wards, we see older people going through a mild disease and young people with a severe course and dying. Today we are discussing the diagnostic and therapeutic pathway for a patient with a viral infection, which is more severe than a seasonal infection or even flu, and a patient who is not seriously ill has to sit at home and wait for it to pass, and can be treated or consulted by family doctor, and if he is more seriously ill - he is to be referred to the hospital. Simply, the patient with COVID-19 needs to be secured. So, up to a certain level, the care of a family doctor is enough, and in more severe cases, the exacerbation of a chronic disease requires intravenous treatment, treatment with oxygen and the patient should be hospitalized. In this context, the health care system should be thoroughly remodelled. This requires strengthening primary health care not only with money, but also with competence. The primary health care doctor should have the right to direct any broad diagnostics — of course, after appropriate training. If it's possible, it should be treated on an outpatient basis.

At the moment, hospitals play the role of clinics - especially in poviats. We are talking about the pathway for patients, but we are really talking about the obvious things. We are taught at the university what the primary health care (POZ) doctor does, until which moment he treats, when he refers to a specialist, when he refers to a hospital. And that's how it should be. It is worth noting that on 23 March 2020, the Polish Diabetes Association issued a guide for patients with diabetes "Coronavirus SARS-CoV-2 and diabetes". It was an official statement of the Polish Diabetes Association. It stated that COVID-19 is a serious threat, and that the elderly and those with severe chronic diseases, including diabetes, are at increased risk of developing complications and having a very severe course of infection. The risk of contracting COVID-19 in diabetic patients is not higher than in the general population, but they are more likely to develop severe COVID-19 complications. If diabetes is well controlled, the risk of developing a severe form of COVID-19 infection is similar

to that seen in the general population. In people with poor disease control and fluctuations in sugar levels, there is a greater risk of developing diabetic complications[24]. It is worth remembering that every year the Polish Diabetes Association publishes clinical recommendations for the treatment of diabetic patients, which also refers to the treatment of patients with diabetes and COVID-19[25].

The development of a drug for a disease such as COVID-19 is perhaps an even greater breakthrough than the development of vaccines. Such drugs should be available by prescription in general pharmacies. Every physician in Poland has the right to prescribe any medicine, so there is no reason why one doctor should be able to do it and the other should not.

PROF. LESZEK CZUPRYNIAK

24 Oficjalne wytyczne PTD w kwestii koronawirusa, PTD 23 marca 2020 r., https://www.pfed.org.pl/aktualno347ci/oficjalne-wytyczne-ptd-w-kwestii-koronawirusa.

25 Zalecenia kliniczne dotyczące postępowania u chorych na cukrzycę 2021, PTD, https://ptdiab.pl/zalecenia-ptd-test/2021-guidelines-on-the-management-of-patients-with-diabetes.

DIAGNOSIS AND TREATMENT PATHWAY FOR A DIABETIC PATIENT WITH COVID-19

FROM PATIENT ORGANIZATION PERSPECTIVE

ANNA ŚLIWIŃSKA

As the Polish Diabetics Association, we educate patients in the field of COVID-19 vaccination. Thanks to this, we can boast of a very high immunisation of our patients. Now, knowledge about the availability of oral drugs, when they need to be given and what action they have, should be promoted. Unfortunately, people often think of COVID-19 in simple categories: either you are vaccinated or you are sick or you die. The fact is that currently many people are infected with COVID-19 during their stay in hospital. Therefore, there is a fear of hospitalisation, which can be a positive factor in early reporting to a primary health care doctor and willingness to take oral therapy.

According to data from the Ministry of Health, the mortality rate among people with diabetes increased by 16% in Poland in 2020. Not only did the COVID-19 disease contribute to this, but also the fact that patients out of fear of infection did not go to the appointments, or had difficulty getting one. Online visits are very helpful in leading a diabetic patient and supporting him in controlling the disease, but older patients prefer a personal contact with their doctor.

DIAGNOSIS AND TREATMENT PATHWAY FOR COVID-19 PATIENT WITH A RESPIRATORY DISEASE

FROM THE INTERNIST AND ALLERGOLOGIST :CTIVE

DR N. MED. PIOTR DĄBROWIECKI

In 2020, there was a relative increase in deaths of nearly 10% among people suffering from lung diseases and COVID-19. Patients with chronic respiratory diseases, including COPD, are at risk of more severe COVID-19. Of this group, patients suffering from chronic obstructive pulmonary disease have the highest risk of a severe course of COVID-19. It is six times higher than in other chronic patients and nearly 18 times higher in comparison with patients without COPD. Other lung diseases also have poor prognosis: pulmonary fibrosis, pulmonary hypertension and lung cancer. Fortunately, we do not observe this, in the case of bronchial asthma and other allergic diseases, in most cases patients with asthma had less disease than the average population. The clinical course of pneumonia in COVID-19 can be mild, scarcely symptomatic, with relatively rapidly resolving lesions, or severe, with pneumonia meeting diagnostic criteria of acute respiratory distress syndrome (ARDS). Dedicated, early treatment can improve the prognosis among these patients and reduce the risk of developing or exacerbating the comorbidities of COVID-19 (myopathy, cardiological and neurological complications, chronic fatigue syndrome, depression, etc.).

Therefore, oral antiviral therapies are an excellent solution for pulmonary patients suffering from COVID-19. Unfortunately, currently getting to a pulmonologist or allergist within five days of infection is almost a miracle. For this reason, the role of the primary care (POZ) physician is extremely important and we will not replace this link of care in any way. We cannot predict the use of these drugs only by specialists in AOS.

In the case of patients with COPD, it is certainly necessary to start oral therapy as soon as possible. In the case of patients with COPD, it is certainly necessary to start oral therapy as soon as possible. There must be cooperation with the family doctor. He is the one to initiate the administration of the drug and a specialist can continue to care for a patient whose course of COVID-19 is extremely severe despite oral treatment. Patients treated for COPD who take their inhalers correctly will certainly have a milder disease progression than patients with COPD and COVID-19 symptoms who do not have diagnosis and appropriate treatment. As specialists, we try to diagnose and implement appropriate treatment in the group of patients with COPD as soon as possible in order to protect the patient from complications of the untreated disease. It is a group of over 2,000,000 patients, over 1,400,000 of whom are not diagnosed. These patients are at particular risk of an unfavourable course of Covid-19 and the occurrence of complications. It is also worth recalling that the Polish Association of Lung Diseases and the Polish Allergology Society published the "Standard on the treatment of pulmonary complications in patients after SARS-CoV-2 infection."[26]. The guidelines take into account the latest reports and aim to ensure optimal standards of care for patients with pulmonary complications following COVID-19. Every medical doctor should read it.

"Of the group of patients with chronic respiratory diseases, people suffering from chronic obstructive pulmonary disease (COPD) have the highest risk of a severe course of COVID-19. It is six times higher than in other chronic patients and nearly 18 times higher in comparison with patients without COPD. Oral therapy for COVID-19 is able to reduce complications and possibly reduce the number of deaths among these patients."

DR N. MED. PIOTR DĄBROWIECKI

26 Stanowisko Polskiego Towarzystwa Chorób Płuc i Polskiego Towarzystwa Alergologicznego dotyczące leczenia powikłań płucnych u chorych po przebytym zakażeniu SARS-CoV-2, Pneumonologia Polska, tom 2, nr 1-2 (2021) #85004, http://ptchp.org/content/uploads/2021/05/Stanowisko-PTChP-i-PTA-dotyczace-leczenia-powiklan-plucnych-u-chorych-po-przebytym-zakazeniu-SARS-CoV-2_v2.pdf.

DIAGNOSIS AND TREATMENT PATHWAY FOR ONCOLOGICAL PATIENT WITH COVID-19

FROM ONCOLOGIST AND HEAMATOLOGIST PERSPECTIVE

PROF. DR HAB. N. MED. WIESŁAW JĘDRZEJCZAK

Cancer and COVID-19 accounted for a 5% increase in mortality in 2020. Cancer patients are a group that has been hit twice. It was hit by COVID-19 and at the same time unfortunately it lost access to oncologist and hematologist care. There is a delay in oncological and haematological treatment. It must be said that the DILO card improves access to care, however, when it comes to the outpatient side of managing chronic patients who are in the process of treatment, they are, of course, under the care of the hematological or oncological centres. The patients who are being treated in these centres were eager to vaccinate against COVID-19. The problem here, however, is that now even three vaccination scheme does not always develop sufficient immunity in these patients. That is why we recommend them more boosters.

Another issue is to ensure environmental vaccination, i.e. all people potentially in contact should be vaccinated against COVID-19. Our postulate is that the physician leading such patients should have the possibility of individual prescription of vaccines. There are huge differences and in fact it should be subject to the individual assessment of the

physician who leads such patients, and these are usually very highly qualified specialists. Another issue is the issue of COVID-19 oral treatment, which has been registered in the European Union. Unfortunately, this treatment is not yet fully available to doctors and patients in Poland. We currently have a lot of patients who are infected with SARS-CoV-2 coronavirus in the hospital, so we should be able to prescribe these oral drugs not only outside the hospital, but also in the hospital. Outside of the hospital, they should be prescribed not only by primary health care physicians, because a person with a chronic haematological disease, as a rule, remains under the care of a haematologist for the rest of his life. This patient should be able to receive an oral medicine either directly in a hospital pharmacy, the same as in case of many other drugs, or receive a prescription from a haematologist or oncologist and purchase it in a general pharmacy. However, reimbursement indications should be limited to risk groups in order not to prescribe these drugs to everyone. The groups of our patients are not that numerous, so this is not a problem of scale. The problem is primarily the current availability of these drugs and the processing capacity of their manufacturers in the context of deliveries to Poland. In other words, the best today would be distribution through hospital pharmacies. At the moment, many oral medicines are distributed by hospital pharmacies either as part of drug programmes or as part of the chemotherapy catalogue, and here also oral drugs in COVID-19 therapy could be distributed in this way.

Cancer patients are a group that has been hit twice. It was hit by COVID-19 and at the same time unfortunately it lost access to an oncologist and haematologist."

PROF. WIESŁAW JĘDRZEJCZAK

FROM PATIENT ORGANIZATION PERSPECTIVE

KRYSTYNA WECHMANN

COVID-19 is a disease that, although it has been targeting communities around the world for two years, is still questioned by some as to its existence in general. I am surprised how anyone can still not believe in COVID-19, given approx. 107,000 deaths from COVID-19 in Poland.

Big reliable data on oncological patients in the COVID-19 pandemic in Poland can be found in the "The impact of the COVID-19 pandemic on the oncological care system" report developed by experts and scientists, among others, from the Maria Skłodowska-Curie National Institute of Oncology of the National Research Institute in Warsaw, commissioned by the Ministry of Health and coordinated by prof. Piotr Rutkowski[27]. This is the first such comprehensive study of the impact of the COVID-19 pandemic on oncological care in Poland. It is worth noting that oncological facilities have vaccinated most of the medical staff very efficiently. Accelerating vaccination of patients with cancer, as well as other procedures, such as the requirement to test patients before hospital admission

27 Wpływ pandemii COVID-19 na system opieki onkologicznej, Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie Państwowy Instytut Badawczy w Warszawie, 2021, https://www.pib-nio.pl/wazne-wnioski-z-raportu-wplyw-pandemii-covid-19-na-system-opieki-onkologicznej/.

or reduced visits, guarantee almost 100% safety of patients treated or diagnosed in oncological facilities. During the pandemic, there was a similar increase in deaths of oncological patients as in the whole population. Unfortunately, there was a large decrease in the number of DILO rapid cancer diagnostic cards issued by doctors — depending on the type of cancer reaching 10-20%. The number of malignant cancer diagnoses decreased by about 20%. In April-May 2020, there was a collapse of the number of preventive examinations carried out. This was due to patients' fear of visits to hospitals and restrictions on the functioning of POZ and AOS facilities during this period. Due to the numerous transformations of hospitals into COVID-19 facilities, there has been a decrease of 10-15 % in the area of oncological surgery. Depending on the specific diagnosis, the decrease in the number of new cancer diagnoses (measured by the number of first-time contacts and first-time hospitalisations) was 10-20%. However, this relatively good situation in oncological care was occupied by a significant increase in the costs of, among others, personal protective equipment and tests for SARS-CoV-2 by oncology institutions, which may begin to face financial problems.

ROLE OF HEALTH EDUCATION IN COVID-19

IGOR GRZESIAK,
PATRYCJA RZUCIDŁO-ZAJĄC
Institute for Patients' Rights and Health Education

The importance of information has never been so crucial for the health of millions of people around the world as in the last two years. During the COVID-19 pandemic we have had to face many new challenges, including in the area of communication. In case of such a large health crisis, it turned out that the biggest challenge is not only to convince people to certain behaviour, but also to build a reliable message, coherent communication and matching the arguments to the audience. Information activities were also not conducive to phenomena that we have dealt with before — oversupply of information and the growing problem of disinformation about health. It also turned out that communication would not be effective without a prior analysis of the motivation and psychology of social behaviour, and the same message would not convince everyone, even if we put it in the mouth of a popular actor.

The role of health education will be of particular importance during the autumn wave of infections. New therapeutic options for the treatment of COVID-19 require building knowledge and awareness among patients particularly exposed to severe disease in the first place. The need for rapid diagnostic and therapeutic measures requires very precise information that will reach patients with cancer, diabetes, cardiac or people with asthma and COPD. These patients must be aware that in the event of symptoms of the disease, they will have to report to an POZ physician or a specialist doctor in their clinic as soon as possible. There are only five days from the onset of the first symptoms. Time is therefore of great importance in this case

and the information campaign should take into account the current challenges of the COVID-19 pandemic.

First of all, we must also be aware that with each subsequent season of the disease, it is increasingly difficult to draw public attention to this health problem. After two years of the pandemic, we are already tamed with the Sars-COV-2 virus, we are less and less afraid of the disease and are therefore more and more likely to risk the infection. Despite increasing diagnostic and therapeutic capabilities, this can still end tragically, especially for people from high-risk groups. The impact of COVID-19 on these groups will depend in part on the quality of communication, as well as on the ability to provide simple information answering the questions "what should I do?", "who should I go to?".

Secondly, it is of utmost importance to start communication early enough and to align the messages with key target groups. The educational campaign, in order to have a chance to work, must be carried out at a certain time and reach the audience at least several times. Therefore, assuming that in autumn we will have another wave of pandemics, educational activities concerning the management of SARS-COV-2 infection, taking into account new therapeutic possibilities, have to start today. The same message will not work for everyone, which is why outreach measures should first take into account people at risk and their families, as well as health professionals who make decisions on treatment.

Thirdly, we must remember that health issue is being discussed out of healthcare centres, and the conversation about health is also taking place in a cafe, at the family table, in a TV series, and most importantly — in social media. When choosing communication channels, it will be worth considering where it will be best to disseminate information to people at risk. The key role will be played by patient organisations that not only reach these groups very precisely (using their own channels or direct actions), but are also credible to them. In the case of this group, a costly billboard or TV campaign makes less sense, more effective will be platforms/applications used for daily monitoring of disease, support group or ambassadors representing risk groups. Communication plays a crucial role today in the process of managing the health of the community's data, and the "information saves lives" message has ceased to be an empty slogan. Reliable information, consistent health messages and an understandable, evidence-based argumentation may actually affect the final decision on specific health behaviour. Therefore, well-planned educational activities must be a key element of any health strategy. This is particularly important in the event of a COVID-19 challenge where inefficient communication could create information gaps in vulnerable groups and consequently additional difficulties in fighting the pandemic.

CONCLUSIONS

1. SARS-CoV-2 infection can cause severe COVID-19 systemic disease, potentially leading to patient death or serious long-term health consequences.

2. Vaccination against COVID-19 is the most effective form of prevention of infection with the SARS-CoV-2 virus, and in case of infection in a person already vaccinated — it gives a higher probability of a mild course of the disease.

3. COVID-19 oral therapy, applied as soon as possible after the diagnosis of SARS-CoV-2 coronavirus infection, allows for effective inhibition of the development of infection and general organ complications associated with it, including probably post-COVID/long-COVID syndromes, significantly affects the patient's clinical condition and further prognosis, the risk of hospitalisation and death. This is particularly true for patients at risk of severe COVID-19.

4. A well-developed diagnostic and therapeutic pathway for a patient with COVID-19 allows a quick diagnosis of the infection and physician's decision about the prescription of oral therapy used in home conditions. This will avoid costly hospitalisations, advanced healthcare and severe health consequences of COVID-19.

5. The optimal way of distributing oral therapy is the implementation of a medical prescription in a general pharmacy according to certain criteria of public refund for high-risk groups. Other patients infected with SARS-CoV-2 coronavirus should be able to complete such a medical prescription in full. Oral therapy should also be available in a hospital prescription.

RECOMMENDATIONS

1. Consistent and effective public campaigns on awareness of the importance of COVID-19 vaccination in the prevention of SARS-CoV-2 coronavirus infection should be carried out; it is still necessary to remind people about the need to vaccinate, to take a booster dose and in the populations most at risk for a second booster.

2. Extensive and coherent health education on COVID-19 prevention (vaccination, anti-epidemic behaviour) is needed, raising awareness of the benefits of vaccination and the importance of extensive testing, rapid diagnosis and the inclusion of oral therapy.

3. Public reimbursement of COVID-19 oral therapy is recommended according to certain criteria for patients from high-risk groups. Other patients infected with SARS-CoV-2 should be able to complete a full medical prescription. Oral therapy should also be available in a hospital prescription.

4. A specific diagnostic and therapeutic pathway for a COVID-19 patient in the Polish health system should be introduced and promoted. The basis of the patient's pathway is easily accessible and rapid testing for SARS-CoV-2 virus, which will enable the diagnosis and application of early oral antiviral therapy.

5. It is recommended to develop and implement the strategy before the next COVID-19 wave expected in autumn 2022.

PROPOSALS OF KEY ELEMENTS OF THE STRATEGY FOR AUTUMN 2022

– SUMMARY

The experts agreed that the experience of the two years of the COVID-19 pandemic and the progress made in COVID-19 diagnosis and therapy allow for key strategy recommendations ahead of the expected next COVID-19 wave in autumn 2022. The following ten key elements of the strategy have been developed.

1. Further promotion of COVID-19 vaccinations
   a) Full vaccination — still significant number of unvaccinated
   b) Booster — only 30% of Poles have taken a booster dose
   c) Vaccination of children and adolescents 5-17 years — still low vaccination rate
   d) Second booster — the need to change the accepted Polish criteria (only 80+ in Poland vs all 55+ in the USA)
2. Vaccination of refugees from Ukraine
3. Education and counteracting anti-vaccine movements
4. Rebuilding the testing system
   a) Introducing other ways to settle tests in POZ and hospitals
   b) Equipping family doctors with rapid COVID-19/influenza tests
5. Educational action pointing to the current state of the pandemic in the world based on the premises:
   a) The pandemic is still ongoing, but current knowledge and data indicate that we are now moving from a pandemic state to a dangerous seasonal infection phase.
   b) A large part of the population has acquired immunity, but it depends on vaccination and disease, and it is likely to last 6-12 months.
   c) A significant part of the population has acquired immunity, but this has come at the cost of around 116,000 deaths from COVID-19, as well as at the cost of more than 200,000 redundant deaths, partly due to restrictions on access to healthcare.

d) COVID-19 is a much more dangerous disease than seasonal colds and even flu.

e) Educational activities to raise awareness about COVID19, based on up-to-date data (new mutations, need for further vaccinations)

6. Determination of the patient's diagnostic pathway

7. Implementation of recommendations on managing SARS-CoV-2 infections of the Polish Society of Epidemiologists and Infectious Diseases in all institutions of the health care system

8. Education campaign on medicines registered against COVID-19 in the European Union

a) In April 2022, in the European Union 8 medicines were registered in COVID-19 therapy: anakinra, kasiriwimab/imdewimab, regdanwimab, remde- sivir, sotrowimab, tiksagewimab/cilgawimab, tocilizumab, and one oral medicine: nirmatrelvir/ritonavir[28]

9. Widespread availability of oral antiviral drugs necessary to be taken for five days, with the start of taking by the fifth day of symptoms:

a) Oral medicaments in hospital treatment — available in a hospital prescription

b) Oral medicines fully reimbursed within the framework of the list open to specific risk groups — issued on the basis of a medical prescription

c) Full-paid oral drugs as part of the open list for all other patients wishing to take an antiviral medicine — issued on the basis of a medical prescription

10. Create a framework for the functioning of specialised care and rehabilitation of patients with long COVID and post-COVID.

The above recommendations do not cover all the issues and challenges for the COVID-19 strategy for autumn 2022, but should certainly be addressed. Experts also emphasise the need to adapt strategies, recommendations and actions to the changing genotype of SARS-CoV-2 virus and the external environment (social, geopolitical and other conditions).

28 https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-treatments.

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PFIZER POLAND SP. Z O.O.
Żwirki i Wigury Street 16B, 02-092 Warsaw