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## CLINICAL AND EPIDEMIOLOGICAL FEATURES OF THE COURSE OF CORONAVIRUS INFECTION DEPENDING ON THE PERIOD OF ILLNESS

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*After the COVID-19 pandemic, the persistence of Long COVID symptoms is of particular concern, which significantly affects the quality of life and ability to work.*

**The aim of the study** is to establish the peculiarities of clinical and epidemiological data in patients infected with SARS-CoV-2 depending on the period of illness.

**Patients and methods.** We examined 108 patients divided into three groups: those with confirmed COVID-19, those with Long COVID, and practically healthy persons. The epidemiological and clinical features of the course were determined based on the analysis of medical records and the developed questionnaire.

**Results.** Women predominated among the study subjects (56 %) with an average age of 41.44 years. The main symptoms that characterized the clinical picture of COVID-19 were generalized weakness/fatigue (94 %), headache (74 %), fever/body aches and cough in 71 % of patients ( $p < 0.05$ ). In the Long COVID group, compared to the COVID-19 group, generalized weakness/fatigue (40 %), headache (29 %), fever/body aches (3 %), and cough (9 %) were significantly less common, sleep disorders / insomnia (17 %), muscle pain (11 %), shortness of breath (17 %), runny nose / sneezing (6 %), loss (worsening) of appetite (3 %), sore throat (6 %), difficulty concentrating (6 %), abdominal pain (3 %) ( $p < 0.05$ ).

**Conclusions.** Reduced access to healthcare services leads to delayed hospitalization, prolonged treatment, and complications.

*The level of vaccination does not affect the risk of Long COVID.*

*Clinical signs of Long COVID: generalized weakness/fatigue, anxiety, mood disturbance, headache are detected in one third of patients and cause a decrease in overall quality of life. The most persistent are general weakness/fatigue, headache, shortness of breath, sleep disorders/insomnia and persist in 34-42 % of patients from the moment COVID-19 is confirmed.*

**Key words:** COVID-19; Long COVID; SARS-CoV-2; features; epidemiology; good health.

Despite the fact that the COVID-19 pandemic has led to the loss of a large number of lives and significant social and financial consequences, new cases of SARS-CoV-2 are gradually decreasing in severity. The decrease in pathogenic properties with the emergence of new strains, the accumulation of knowledge on approaches to therapy, rehabilitation, prognosis, the growth of herd immunity, and the high level of vaccination contributed to this trend [1-4].

The steady decline in mortality from SARS-CoV-2 infection is shifting the focus to patients who have survived COVID-19 and have lasting Long COVID (LC) symptoms. Decreased quality of life, physical endurance, psycho-emotional instability, and asthenic syndrome, combined with high prevalence (up to 10 % of infected people, which is about 76 million cases worldwide), pose a new threat to the healthcare system [5, 6].

According to meta-analyses and systematic reviews, the main risk factors for LC are female gender, older age, high body mass index, smoking, history of comorbidities, including mental illness, inpatient treatment, and intensive care unit treatment [7]. The data on the impact of immunization on the duration and severity of symptoms are mixed, but all the literature we studied indicates a reduced risk of developing LC among those vaccinated. According to a survey of people with LC who were vaccinated after COVID-19, 61.9 % reported no changes, 16.7 % reported improvement, and 21.4 % reported worsening, which indicates a dubious result from active immunization as secondary prevention among affected individuals [8-11].

The clinical picture of LC is extremely diverse due to the involvement of all organs and systems. Generalized weakness and fatigue are predominant in all previous studies. Signs of the asthenic syndrome, such as arthralgia/myalgia, and sleep disorders, have been frequently reported. Symptoms related to the respiratory system: cough, shortness of breath during exercise or at rest, chest tightness; upper respiratory tract: voice change, hoarseness, rhinorrhea, hearing loss, ague, anosmia; cardiovascular system (exercise intolerance, chest pain, palpitations,

thrombotic complications). Among all the signs of LC, neuropsychiatric disorders are particularly prominent: "brain fog" (decreased concentration, mental fatigue, inability to concentrate, memory loss), anxiety, depression, post-traumatic stress disorder [6, 12-14].

The diversity and unspecificity of clinical symptoms make it difficult to systematize and combine them into a single syndrome, however, the distribution of symptoms by individual groups (central neurological, cardiorespiratory, systemic/inflammatory, abdominal) will reveal the relationship with epidemiological features and pathogenetic mechanisms of infection. Determining the dependence of the clinical picture of LC on the characteristics of the course of COVID-19 will make it possible to predict and prevent long-term consequences at the stage of primary disease.

### Patients and methods

The study involved 108 patients and was divided into three groups: group A (n – 31) – patients who were inpatients at the Krasovitsky Medical Clinical Center for Infectious Diseases and Dermatology with confirmed COVID-19 at the time of the study (positive PCR result for SARS-CoV-2 or rapid COVID-19 test); group B (n – 35) – patients with LC (symptoms after COVID-19 for more than 3 months, which last for 2 months or more and cannot be explained by other causes); Group C (n – 42) consisted of clinically and anamnestic healthy persons (comparison group) who underwent a routine medical examination at the University Clinic of Sumy State University and had no confirmatory data on the presence or history of COVID-19.

In conducting this study, ethical standards were observed, and each participant gave written informed consent to be involved in the study and to process personal data in accordance with the Helsinki Declaration.

Recruitment to the study was randomized based on the exclusion criteria: age under 18 years and over 60 years, treatment with artificial lung ventilation, including CPAP, high-flow oxygen and high doses of corticosteroids, hepatitis, type 2 diabetes mellitus, obesity above grade 2 inclusive, autoimmune diseases (psoriasis, thyroid disease, rheumatic heart disease, rheumatoid arthritis, glomerulonephritis, etc.)

Patients were examined using generally accepted clinical objective research methods. A questionnaire consisting of three main blocks was developed for a thorough collection of epidemiological, life and medical history: anamnesis before COVID-19, complaints at the time of the interview and changes after SARS-CoV-2 infection.

Data collection, systematization, and correction were carried out using Microsoft Office Excel 2016 spreadsheets. Statistical data processing was performed using the licensed Stata/SE 18 software by StataCorp (Texas, USA).

To compare qualitative indicators, the Pearson's test was used in the statistical processing of the data. The Kolmogorov-Smirnov and Shapiro-Wilk criteria were used to check for compliance with the normal distribution. Non-parametric variables were analyzed using the Mann-Whitney U test, and Student's t-test was used for variables that corresponded to normal distribution. The mean value (M) and 25th and 75th quartiles were used to describe the data. The criteria were recognized as significantly significant at  $p < 0.05$ .

### Research results and discussion

Women predominated in the study groups – 56 %. According to the gender distribution, the groups did not differ from each other: group A – 55 % of men and 45 % of women; B – 41 % and 59 %, respectively; C – 40 % and 60 %, respectively ( $p > 0.05$ ). This distribution is in line with current literature, when COVID-19 has a higher incidence among men, and LC – among women [1]. The age of patients in the groups also did not differ: in group A, the mean age was 43.42 (34.00-52.00) years, in group B – 43.20 (34.00-53.00), in group C – 38.52 (32.00-45.00) ( $p > 0.05$ ). The average age of patients was 41.44 (32.25-50.00) years.

Hospitalization of patients with COVID-19 occurred on 5.58 (3.00-9.00) days of illness with a hospital stay of 10.23 (8.00-11.00) days, due to the low level of diagnosis at the pre-hospital stage and reduced availability of medical services due to the war. Among patients with LC, 3 % reported having a history of heart disease before COVID-19, 7 % had a history of coagulation system pathology, 17 % had dizziness or loss of consciousness, 7 % were seen by a neurologist with degenerative disc disease, and these data did not differ from the comparison group ( $p > 0.05$ ).

74 % of patients were vaccinated, mostly with the Pfizer vaccine (46 %) (Fig. 1). Among conditionally healthy individuals, the percentage of unvaccinated was the highest (38 %). The level of vaccination did not affect the risk of developing Long COVID (in groups A and B, 20 % of unvaccinated persons were unvaccinated). Literature data on the effect of immunization on the duration and severity of symptoms are mixed, but indicate a reduced risk of developing it among the vaccinated [8-11].

The most common early complications in the COVID-19 group were respiratory failure (RF) – 71 % (35 % were on oxygen support), acute bronchitis – 52 %, and pneumonia – 48 % (auscultation in 61 % – decreased breathing, 42 % – rigid breathing, 42 % – crepitation). Frequent bacterial complications are due to a decrease in nonspecific immunity due to the persistence of SARS-CoV-2 and the development of local inflammation [14, 15]. In this group, 58 % of patients had no concomitant pathology, but 23 % of subjects had grade 1 obesity, 35 % had arterial hypertension, and 16 %

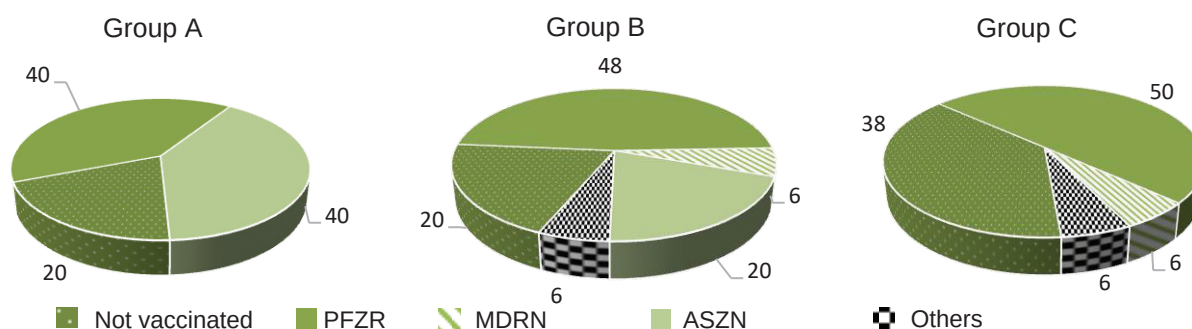


Fig. 1. Distribution of vaccines among study groups (%).

had coronary heart disease. The data was collected during inpatient treatment and did not include long-term consequences of the disease.

According to the questionnaire, heart disease after COVID-19 was unevenly distributed: 6 % of patients reported arrhythmias, 9 % – progression of hypertension.

Among the respondents, 74 % had no history of smoking (distribution in the groups was even: group A – 80 %, B – 74 %, C – 67 %). Regarding smoking, in group A, the remaining patients answered “not often”; in group B – 9 % “often”, 6 % “not often” and “rarely”, 3 % “very rarely”; in group C – 6 % “often” and 22 % “rarely”.

After suffering from COVID-19, patients began to notice a decline in their quality of life. For example, in the LC group, 11 % of patients reported a slight decrease in quality of life compared to the group of conditionally healthy persons (0 %) and no change – 49 % (94 % in the comparison group). Physical endurance decreased: 6 % of patients in the LC group had to give up the physical activity they had been doing before the disease, 20 % had to reduce the amount of physical activity, and 74 % did not notice any changes (in the comparison group, this response was received from 100 % of the subjects).

The course of the disease in 42 % of patients with COVID-19 was moderate, 58 % – severe. The level of saturation during hospitalization was 95.97 (94.00-97.00) %, the temperature was 37.44 (37.00-38.00) °C, which decreased to the physiological norm within 3.65 (1.00-4.00) days. The heart rate was 95.57 (87.75-107.00) beats per minute, systolic blood pressure was 124.35 (120.00-135.00) mm Hg, diastolic blood pressure was 80.97 (80.00-85.00). In this group, 58 % of patients had no concomitant pathology, but 23 % of the subjects had grade 1 obesity, 35 % had arterial hypertension, and 16 % had coronary heart disease.

The main symptoms that characterized the clinical picture of COVID-19 were generalized weakness/fatigue (94 %) (in the LC group it was 2.35 times lower, occurred

most often and amounted to 40 %), headache (74 %) (in the LC group it was 2.55 times lower and amounted to 29 %), fever/body aches and cough were observed in 71 % of patients (in the LC group these symptoms were rarely detected – 3 % and 9 %, respectively) ( $p < 0.05$ ).

Half of the subjects reported mood deterioration (29 % in LC patients), sleep disorders/insomnia (17 % in group B), and muscle pain (11 % in group B). Shortness of breath (48 %), sneezing/runny nose (43 %), loss of appetite (40 %), and sore throat (39 %) were reported in more than a third of patients with COVID-19. Other symptoms were less common (Fig. 2).

The clinical symptoms observed in COVID-19 and persisted in LC were: generalized weakness/fatigue – 94 % and 40 %, respectively (42 % of patients had this symptom since COVID-19 confirmation), headache – 74 % and 29 % (39 % of patients had it after SARS-CoV-2 infection confirmation), sleep disorders/insomnia – 50 % and 17 % (34 % had persistent symptoms), dyspnea – 48 % and 17 % (35 % of patients had it since COVID-19 confirmation).

In the LC group, compared to the COVID-19 group, the following were significantly less common: generalized weakness/fatigue (40 % and 94 %), headache (29 % and 74 %), fever/body aches (3 % and 71 %), cough (9 % and 71 %), sleep disorders/insomnia (17 % and 50 %), muscle pain (11 % and 50 %), shortness of breath (17 % and 48 %), runny nose/sneezing (6 % and 43 %), loss (worsening) of appetite (3 % and 40 %), sore throat (6 % and 39 %), difficulty concentrating (6 % and 30 %), abdominal pain (3 % and 20 %) ( $p < 0.05$ ).

Mood disturbances (50 % and 29 %), anxiety/concern (30 % and 31 %), memory loss or confusion (30 % and 11 %), dizziness (20 % and 9 %), weight loss (20 % and 9 %), voice changes (16 % and 6 %), anosmia (13 % and 11 %), chest pain (10 % and 0 %), diarrhea (10 % and 0 %), swallowing difficulties (10 % and 3 %), visual disturbances (10 % and 14 %), hearing loss/tinnitus (10 % and 11 %), ague (6 % each), nausea/vomiting (6 % and 0 %), postural

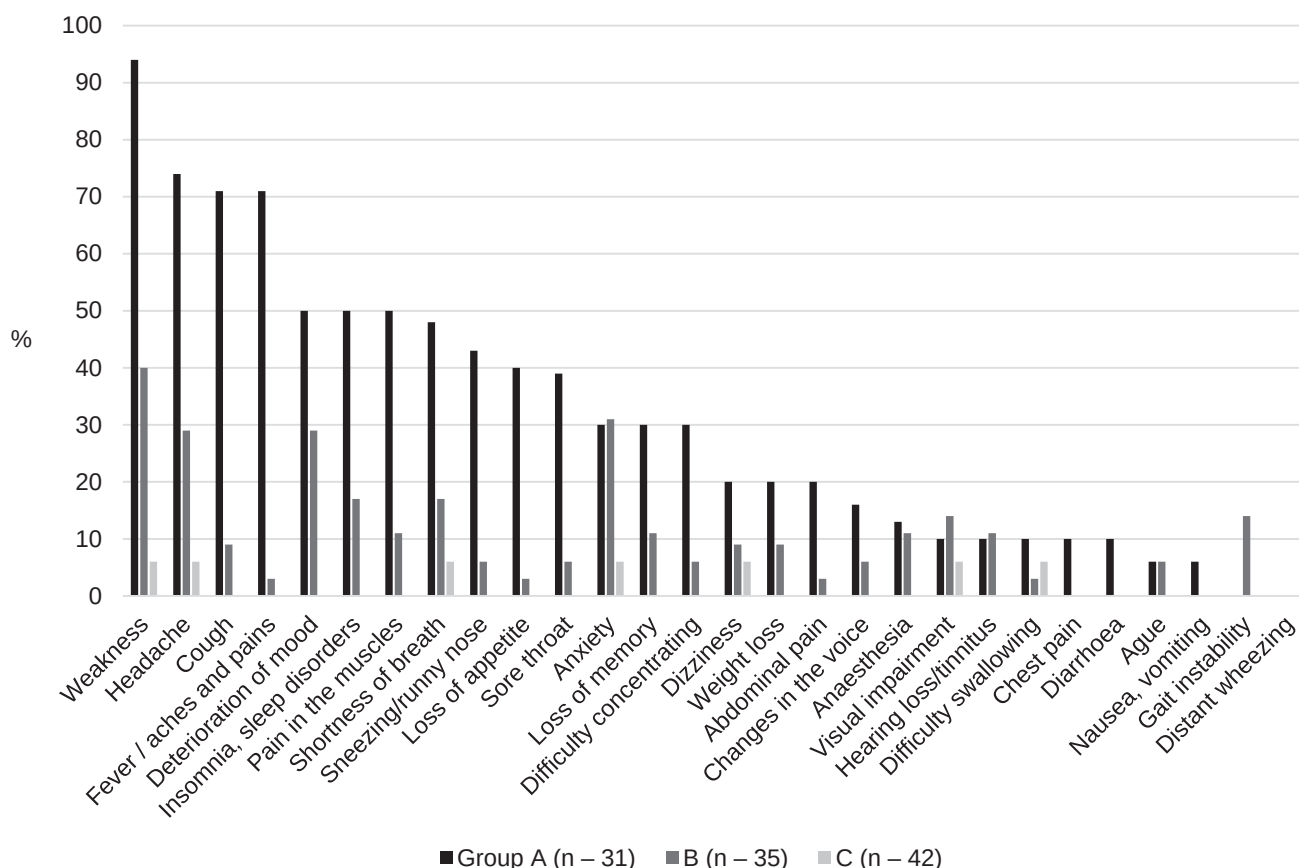


Fig. 2. Distribution of symptoms in the study groups.

and/or gait instability (0 % and 14 %) were evenly distributed in groups A and B ( $p > 0.05$ ) (Table 1).

The increase in the number of symptoms in both acute and long-term COVID has a significant negative impact on

the level of quality of life. Identifying these relationships may provide a new perspective for the treatment of LC [16].

Table 1

Frequency of symptoms in the study groups

Symptom	Group			p
	A (n – 31), %	B (n – 35), %	C (n – 42), %	
1	2	3	4	5
Fever / aches and pains	71	3	0	$p_1=0.000$ ; $p_2=0.000$ ; $p_3=0.469$
Weakness	94	40	6	$p_1=0.000$ ; $p_2=0.000$ ; $p_3=0.008$
Dizziness	20	9	6	$p_1=0.310$ ; $p_2=0.236$ ; $p_3=0.694$
Deterioration of mood	50	29	0	$p_1=0.205$ ; $p_2=0.001$ ; $p_3=0.012$
Headache	74	29	6	$p_1=0.000$ ; $p_2=0.000$ ; $p_3=0.050$
Insomnia, sleep disorders	50	17	0	$p_1=0.033$ ; $p_2=0.001$ ; $p_3=0.062$
Alert	30	31	6	$p_1=0.931$ ; $p_2=0.077$ ; $p_3=0.033$

1	2	3	4	5
Memory loss	30	11	0	$p_1=0.153$ ; $p_2=0.014$ ; $p_3=0.136$
Gait instability	0	14	0	$p_1=0.205$ ; $p_3=0.092$
Weight reduction	20	9	0	$p_1=0.310$ ; $p_2=0.049$ ; $p_3=0.201$
Pain in the abdomen	20	3	0	$p_1=0.005$ ; $p_2=0.049$ ; $p_3=0.469$
Sore throat	39	6	0	$p_1=0.001$ ; $p_2=0.002$ ; $p_3=0.301$
Pain in the chest	10	0	0	$p_1=0.060$ ; $p_2=0.173$
Anosmia	13	11	0	$p_1=0.855$ ; $p_2=0.112$ ; $p_3=0.136$
Ageusia	6	6	0	$p_1=0.900$ ; $p_2=0.271$ ; $p_3=0.301$
Nausea, vomiting	6	0	0	$p_1=0.127$ ; $p_2=0.271$
Diarrhea	10	0	0	$p_1=0.060$ ; $p_2=0.173$
Difficulty swallowing	10	3	6	$p_1=0.334$ ; $p_2=0.662$ ; $p_3=0.625$
Loss of appetite	40	3	0	$p_1=0.001$ ; $p_2=0.004$ ; $p_3=0.469$
Distant wheezing	0	0	0	
Visual impairment	10	14	6	$p_1=0.725$ ; $p_2=0.662$ ; $p_3=0.342$
Sneezing/running nose	43	6	0	$p_1=0.000$ ; $p_2=0.001$ ; $p_3=0.301$
Pain in the muscles	50	11	0	$p_1=0.007$ ; $p_2=0.001$ ; $p_3=0.136$
Hearing loss/tinnitus	10	11	0	$p_1=0.899$ ; $p_2=0.172$ ; $p_3=0.136$
Difficulty concentrating	30	6	0	$p_1=0.031$ ; $p_2=0.014$ ; $p_3=0.301$
Voice changes	16	6	0	$p_1=0.170$ ; $p_2=0.072$ ; $p_3=0.301$
Shortness of breath	48	17	6	$p_1=0.007$ ; $p_2=0.002$ ; $p_3=0.238$
Cough	71	9	0	$p_1=0.000$ ; $p_2=0.000$ ; $p_3=0.201$

Notes: \* – significant difference according to Pearson's test ( $p < 0.05$ );  $p_1$  – (group A/group B),  $p_2$  – (group A/group C),  $p_3$  – (group B/group C).

### Conclusions

Women predominate among the study population – 56 %, aged 41.44 years. Reduced access to healthcare services leads to delayed hospitalization, prolonged treatment, and complications.

The level of vaccination does not affect the risk of developing Long COVID.

The main symptoms that characterize the clinical picture of COVID-19 are: general weakness/fatigue, headache, fever/body aches, and cough. Half of the patients reported mood deterioration, sleep disorders/insomnia, and muscle

pain. Shortness of breath, sneezing/runny nose, loss of appetite, sore throat occurred in more than a third of patients.

The clinical signs of Long COVID are generalized weakness/fatigue, anxiety, mood disturbance, and headache, which are detected in one third of patients and lead to a decrease in overall quality of life.

The most persistent symptoms since the confirmation of COVID-19, which persist in 34 % to 42 % of patients, are generalized weakness/fatigue, headache, shortness of breath, and sleep disorders/insomnia.

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## КЛІНІКО-ЕПІДЕМІОЛОГІЧНІ ОСОБЛИВОСТІ ПЕРЕБІГУ КОРОНАВІРУСНОЇ ІНФЕКЦІЇ ЗАЛЕЖНО ВІД ПЕРІОДУ ХВОРОБИ

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**РЕЗЮМЕ.** Після пандемії COVID-19 особливе занепокоєння викликає довготривале збереження симптомів Long COVID, що значно порушує якість життя та працездатність населення.

**Мета роботи** – встановити особливості клінічних та епідеміологічних даних у пацієнтів, інфікованих SARS-CoV-2, залежно від періоду хвороби.

**Пацієнти і методи.** Обстежено 108 осіб, які поділено на три групи: із підтвердженням COVID-19, із Long COVID та практично здорові особи. Встановлювалися епідеміологічні та клінічні особливості перебігу на підставі аналізу медичних карток і розробленого опитувальника.

**Результати.** Серед досліджуваних переважали жінки – 56 % із середнім віком 41,44 року. Основними симптомами що характеризували клінічну картину COVID-19, були загальна слабкість (94 %), головний біль (74 %), гарячка (ломота в тілі) та кашель (71,0 % пацієнтів). У групі з Long COVID порівняно із групою з COVID-19 достовірно рідше реєстрували загальну слабкість (втому) (40 %), головний біль

(29 %), гарячку (ломоту в тілі) (3 %), кашель (9 %), розлади сну (17 %), біль у м'язах (11 %), задишку (17 %), нежить (чхання) (6 %), втрату чи погіршення апетиту (3 %), біль у горлі (6 %), труднощі з концентрацією уваги (6 %), біль у животі (3 %) ( $p < 0,05$ ).

**Висновки.** Знижена доступність до отримання медичних послуг призводить до запізнілої госпіталізації, тривалого лікування та наявності ускладнень. Рівень вакцинації не впливає на ризик виникнення Long COVID. Клінічні ознаки Long COVID (загальна слабкість, тривога, погіршення настрою, головний біль) виявляються у третини хворих і обумовлюють зниження загальної якості життя. Найстійкішими є загальна слабкість, головний біль, задишка, розлади сну і які зберігаються у 34-42 % пацієнтів з моменту підтвердження COVID-19.

**Ключові слова:** COVID-19; Long COVID; SARS-CoV-2; особливості; клініка; епідеміологія; міцне здоров'я.

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