MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE
SUMY STATE UNIVERSITY
ACADEMIC AND RESEARCH MEDICAL INSTITUTE

Eastern Ukrainian Medical Journal

2, M. Sumtsova st., Sumy 40007, Ukraine eumj.med.sumdu.edu.ua
e-mail: eumj@med.sumdu.edu.ua ISSN: 2663-5909 (print)/2664-4231 (online)

How to cite / Як цитувати статтю: Smiyan O, Taramak L, Smiian K, Vasilyeva O, Loboda A, Petrashenko V, Moshchych O, Vysotskyi I, Horbas V, Manko Yu, Holiuk K, Aleksakhina T. Modern view from Ukraine on etiology, pathogenesis and clinical-diagnostic aspects of community-acquired pneumonia in children. *East Ukr Med J*. 2023;11(4):360-374

DOI: https://doi.org/10.21272/eumj.2023;11(4):360-374

ABSTRACT

[1] Oleksandr I. Smiyan
https://orcid.org/0000-0001-8225-0975

[1] Liudmyla V. Taramak
https://orcid.org/0009-0005-1802-892X

[1] Kateryna O. Smiian
https://orcid.org/0000-0002-8030-6418

[1] Olena H. Vasilyeva
https://orcid.org/0000-0003-4470-8740

[1] Andriy M. Loboda
https://orcid.org/0000-0002-5400-773X

[1] Viktoriia O. Petrashenko
https://orcid.org/0000-0002-4648-8916

[2] Olexandr P. Moshchych
https://orcid.org/0000-0003-3505-6250

[3] Ihor Y. Vysotskyi
https://orcid.org/0000-0002-6357-3362

[1] Victoria A. Horbas
https://orcid.org/0000-0002-7455-6875

[1] Yuliia A. Manko
https://orcid.org/0000-0003-3348-2862

MODERN VIEW FROM UKRAINE ON ETIOLOGY, PATHOGENESIS AND CLINICAL-DIAGNOSTIC ASPECTS OF COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN

Pneumonia is a disease characterized by lung tissue inflammation and the development of respiratory failure. Pneumonia is the most common infectious cause of childhood mortality, occurring every 43 seconds worldwide. Despite advancements in medicine and the use of cutting-edge diagnostic, treatment, and preventive technologies, the incidence of pneumonia remains relatively high, especially in resource-poor countries, adversely affecting the socio-economic life of society.

Objective: To summarize contemporary scientific perspectives on the classification, etiology, pathogenesis, and clinical-diagnostic aspects of community-acquired pneumonia in children.

Materials and Methods: The literature search was conducted using PubMed, Scopus, Web of Science, WHO, UNICEF databases, international protocols, as well as domestic scientific manuals and professional publications, and medical care standards. Search terms included "community-acquired pneumonia," "pneumonia in childhood," and "pneumonia in children." The analysis utilized methods such as a systemic approach, epidemiological analysis, bibliosemantic analysis, and graphical representation.

Results: It was conducted the search and analysis of modern scientific medical literature on community-acquired pneumonia in childhood. Pneumonia is a leading infectious cause of illness and hospitalization in children worldwide. Bacteria, viruses, and mixed infections are identified among the main etiological agents, with cases of non-specific pathogens also observed. The variation in pathogens is presented based on age groups. It is discussed major risk factors for community-acquired pneumonia and pathways of

[1] Kateryna O. Holiuk
https://orcid.org/0000-0002-5298-9389

[4] Tetiana O. Aleksakhina
https://orcid.org/0000-0002-9905-330X

[1] *Department of Pediatrics, Sumy State University, Sumy, Ukraine;*

[2] *Department of Pediatric Otorhinolaryngology, Audiology and Phoniatrics, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine;*

[3] *Department of Biophysics, Biochemistry, Pharmacology and Biomolecular Engineering, Sumy State University, Sumy, Ukraine;*

[4] *Department of Foreing Languages and Linguodidactics, Sumy State University, Sumy, Ukraine*

pathogen penetration. Modern insights into the disease's pathogenesis are analyzed, involving a complex process with stages characterized by the development of infectious toxemia, respiratory failure, and disturbances in water-electrolyte balance. The main clinical symptoms are described according to the child's age, along with contemporary methods of laboratory and instrumental diagnostics of community-acquired pneumonia.

Conclusions: Information from scientific literature is provided on the contemporary definition, classification, epidemiology, etiology, pathogenesis, clinical presentation, and diagnostics of community-acquired pneumonia in childhood. Currently, severe and non-severe forms of pneumonia are distinguished based on respiratory rate and additional threatening symptoms. The increasing incidence of viral-bacterial pneumonia is noted, with bacteria remaining the primary etiological factor. Pneumococcus and Haemophilus influenzae type B predominate among bacteria. It is also observed an increase in cases of viral pneumonia, attributed to respiratory syncytial and coronavirus infections. The disease's pathogenesis involves multiple phases with the involvement of other organ systems. Clinical features of community-acquired pneumonia include fever, respiratory failure, and cough. Laboratory diagnostic methods include a complete blood count, determination of C-reactive protein levels, and procalcitonin. Among diagnostic methods, chest X-ray, computed tomography, and ultrasound diagnostics of the chest organs are considered the most conclusive.

Keywords: community-acquired pneumonia, children, inflammation.

Corresponding author: *Liudmyla Taramak. Department of Pediatrics, Sumy State University, Sumy, Ukraine*
e-mail: l.taramak@med.sumdu.edu.ua

РЕЗЮМЕ

[1] Олександр І. Сміян
https://orcid.org/0000-0001-8225-0975

[1] Людмила В. Тарамак
https://orcid.org/0009-0005-1802-892X

[1] Катерина О. Сміян
https://orcid.org/0000-0002-8030-6418

[1] Олена Г. Васильєва
https://orcid.org/0000-0003-4470-8740

[1] Андрій М. Лобода
https://orcid.org/0000-0002-5400-773X

[1] Вікторія О. Петрашенко
https://orcid.org/0000-0002-4648-8916

[2] Олександр П. Мощич
https://orcid.org/0000-0003-3505-6250

СУЧАСНИЙ ПОГЛЯД З УКРАЇНИ НА ЕТІОЛОГІЧНІ, ПАТОГЕНЕТИЧНІ ТА КЛІНІКО-ДІАГНОСТИЧНІ АСПЕКТИ ПОЗАГОСПІТАЛЬНОЇ ПНЕВМОНІЇ У ДІТЕЙ

Пневмонія – це захворювання, що характеризується ураженням легеневої тканини та розвитком дихальної недостатності. Запалення легень є найчастішою інфекційною причиною дитячих смертей, кожні 43 секунди у світі. І незважаючи на сучасний розвиток медицини та використання новітніх технологій діагностики, лікування і профілактики, рівень захворюваності на пневмонію залишається доволі високий, особливо у країнах з бідними ресурсами, що негативно відображується на соціально-економічному житті суспільства.

Мета – узагальнення сучасних наукових поглядів щодо класифікації, етіології, патогенезу та клініко-діагностичних аспектів позагоспітальної пневмонії у дітей.

Матеріали та методи. Пошук наукової літератури проводився на базі даних PubMed, Scopus, Web of Science, даних ВООЗ, ЮНІСЕФ, міжнародних протоколів та у вітчизняних наукових посібниках і фахових виданнях, стандартах медичної допомоги. Для пошуку використовувались пошукові терміни "позагоспітальна пневмонія", "пневмонія у дитячому віці",

[3] Ігор Ю. Висоцький
https://orcid.org/0000-0002-6357-3362

[1] Вікторія А. Горбась
https://orcid.org/0000-0002-7455-6875

[1] Юлія А. Манько
https://orcid.org/0000-0003-3348-2862

[1] Катерина О. Голюк
https://orcid.org/0000-0002-5298-9389

[4] Тетяна О. Алексахіна
https://orcid.org/0000-0002-9905-330X

[1] *Кафедра педіатрії, Сумський державний університет, м. Суми, Україна;*

[2] *Кафедра дитячої отоларингології, аудіології та фоніатрії, Національна медична академія післядипломної освіти імені П. Л. Шупика, м. Київ, Україна;*

[3] *Кафедра біофізики, біохімії, фармакології та біомолекулярної інженерії, Сумський державний університет, м. Суми, Україна;*

[4] *Кафедра іноземних мов та лінгводидактики, Сумський державний університет, м. Суми, Україна*

"запалення легень у дітей". У ході аналізу застосовано методи: системного підходу, епідеміологічний, бібліосемантичний, графічного зображення.

Результати. Було здійснено пошук та обробку сучасної наукової медичної літератури з теми позагоспітальна пневмонія у дитячому віці. Запалення легень – одна з головних інфекційних причин захворюваності та госпіталізацій дітей усього світу. Серед основних етіологічних збудників виявляють бактерії, віруси та мікс-інфекції, також є випадки, в яких виявляються неспецифічні патогени. Поряд з тим представлені дані щодо варіювання збудників залежно від вікової групи. Наведені основні фактори ризику розвитку позагоспітальної пневмонії та шляхи проникнення збудників. Проаналізовано сучасні дані з питання патогенезу захворювання, який є доволі складним процесом, проходить у декілька етапів та характеризується розвитком інфекційного токсикозу, дихальної недостатності, порушенням водно-електролітного балансу. Описано та охарактеризовано основні клінічні симптоми залежно від віку дитини та наведені сучасні методи лабораторної та інструментальної діагностики позагоспітальної пневмонії.

Висновки. За даними наукової літератури наведено інформацію щодо сучасного визначення, класифікації, епідеміології, етіології, патогенезу, клініки та діагностики позагоспітальної пневмонії у дитячому віці. Наразі виділяють тяжку та нетяжку форму запалення легень, залежно від частоти дихання та додаткових загрозливих симптомів. Встановлено, що зростає кількість випадків поєднаної вірусно-бактеріальної пневмонії. Патогенез захворювання проходить у декілька фаз із залученням інших систем організму. Для клінічної картини позагоспітальної пневмонії характерні: лихоманка, дихальна недостатність, кашель. З лабораторних методів діагностики використовуються клінічний аналіз крові, визначення рівня С – реактивного білка, прокальцитоніну. Серед діагностичних методів найбільш доказовими є рентгенографія, комп'ютерна томографія та ультразвукова діагностика органів грудної клітки.

Ключові слова: позагоспітальна пневмонія, діти, запалення.

Автор, відповідальний за листування: *Людмила Тарамак, кафедра педіатрії, Сумський державний університет, м. Суми, Україна, e-mail: l.taramak@med.sumdu.edu.ua*

ABBREVIATIONS:
AP – arterial pressure
ARI – acute respiratory infections
CAP – community-acquired pneumonia
Chest Organs – organs of the thoracic cavity
CT – computed tomography
ECG – electrocardiography
ECHO – echocardiography
ESR – erythrocyte sedimentation rate
Min – minute
MOH – Ministry of Health

PCR – polymerase chain reaction
P/R – pulse/respiration
RF – respiratory failure
RR – respiratory rate
TLC – total lung capacity
TV – tidal volume
UNICEF – United Nations International Children's Emergency Fund Introduction
US – ultrasonography
WHO – World Health Organization

INTRODUCTION / ВСТУП

One of the indicators of overall well-being and a marker of social and environmental issues in society is the health of the child population. Respiratory organ diseases in children pose a significant medical and social problem, as they determine the level of childhood morbidity and mortality. Despite the achievements of modern medicine, community-acquired pneumonia (CAP) remains the most common reason for seeking medical care and hospitalizations. In recent years, the number of hospitalizations related to bronchopulmonary diseases in children has increased 3.6 times, mainly due to inflammatory processes in the upper and lower respiratory tract [1, 2, 3]. Each year, approximately 155 million cases of pneumonia are recorded among the child population worldwide, especially in countries with limited resources [1, 4, 5, 6, 7]. According to researchers, the incidence of pneumonia in young children in economically developed regions does not exceed 3–4% [8]. In Europe, approximately 300 children per 100,000 population aged 0 to 16 years fall ill with pneumonia annually [5]. Between 7 and 13% of children require hospitalization for pneumonia [9]. While there has been a decrease in pneumonia incidence worldwide (due to vaccine use and improved diagnostics), the number of child hospitalizations has increased 2.9 times, particularly due to severe and complicated cases, especially during the Covid-19 pandemic, placing a significant burden on the healthcare system [4, 10]. In Ukraine, more than 60,000 cases of community-acquired pneumonia are registered annually [11].

The problem of pneumonia is relevant not only due to high morbidity and hospitalizations but also because of a significant mortality rate [2, 4, 6, 7, 12]. According to UNICEF and WHO experts, pneumonia accounts for about 15% of child mortality cases, nearly 2 million children annually. In 2019, pneumonia claimed the lives of 921,000 children under the age of 5, accounting for 14% of total deaths in this age group [1, 2, 3, 4, 6, 7, 12]. In industrially developed countries, the child mortality rate from pneumonia is no more than 8–9% of all causes of mortality. However, in countries with low cultural, socio-economic levels, and unstable political situations, the frequency of pneumonia in similar age groups exceeds 10–20%, and its proportion in the structure of child mortality exceeds 25% [1, 2, 4, 7]. The mortality rate among hospitalized children under 5 years of age in developed countries is approximately 1%, with economically poor countries having a higher rate [7, 8]. In Ukraine, the average mortality from pneumonia is 13.1 per 10,000, and respiratory tract diseases rank third in the structure of early childhood mortality after perinatal pathology and congenital malformations [6, 11, 13].

Pneumonia is one of the most common indications for prescribing antibiotic therapy, posing a significant issue given the global rise in antibiotic resistance [3, 5, 14]. Therefore, prevention, timely diagnosis, and appropriately prescribed treatment considering etiological and pathogenetic factors expedite recovery and prevent unwanted complications.

Objective: To analyze contemporary scientific data from various sources regarding the peculiarities of the etiopathogenesis, clinical course, and diagnosis of community-acquired pneumonia in children.

Materials and Methods: The scientific search was conducted using the databases PubMed, Scopus, Web of Science, WHO, UNICEF, international protocols, domestic scientific manuals, professional publications, and medical care standards. Search terms included "community-acquired pneumonia," "pneumonia in childhood," "pneumonia in children." The methods used were a systemic approach, epidemiological analysis, bibliosemantic analysis, and graphical representation.

Results: Pneumonia is an acute infectious-inflammatory disease of the lung parenchyma characterized by infiltrative changes in lung tissue

and respiratory failure. The disease in children manifests as infectious damage to alveoli, accompanied by inflammatory infiltration of the parenchyma (neutrophils, macrophages, lymphocytes, etc.) and its exudation, water-electrolyte, and other metabolic disturbances with pathological shifts in all organs and systems of the child's body [10, 11, 12]. According to other definitions, pneumonia is considered a group of different etiology, pathogenesis, and morphological characteristics of acute focal infectious-inflammatory lung diseases with mandatory presence of intra-alveolar inflammatory exudation or invasion of the lower respiratory tract located below the larynx, caused by pathogenic microorganisms through inhalation, aspiration, invasion of the respiratory tract epithelium, or hematogenous spread [13, 14]. According to V. Nelson, pneumonia is considered an infection of the lower respiratory tract affecting the airways and lung parenchyma, leading to the consolidation of alveolar spaces [15]. According to the appendices to the order of the Ministry of Health of Ukraine (2022), pneumonia is an infection of infectious origin caused by microorganisms with subsequent development of an inflammatory reaction in alveoli with or without bronchial or bronchiolar involvement [6].

In 2014, the latest classification of pneumonia was reviewed by WHO. According to this clinically recommended classification, only "pneumonia with accelerated breathing and/or refractoriness/ retraction of the intercostal spaces of the chest" ("non-severe pneumonia") and "severe pneumonia with additional danger signs" should be distinguished [3]. In other words, non-severe pneumonia is defined by the respiratory rate:

≥ 50 / min for children aged 2–11 months,

≥ 40 / min for children aged 12–59 months,

> 20 / min for children aged 5 years and older, plus chest retraction or without it.

Severe pneumonia manifests with symptoms similar to non-severe pneumonia but includes additional threatening symptoms such as refusal to eat, sudden deterioration of the general condition, drowsiness, unconsciousness, dehydration, and cerebral seizures [3, 6]. The classification according to Ukrainian authors is presented in Table 1 [12].

Table 1 – Classification of pneumonia

By origin	According to the clinical and X-ray form	By localization	By degree of severity	According to the presence of complications	According to the course of the disease
community-acquired; hospital-acquired; ventilation; aspiration; intrauterine; with immunodeficiency	focal; segmental; lobar; interstitial pneumonia	right-sided; left sided; bilateral	mild; moderate; severe	not complicated; complicated	acute pneumonia (up to 6 weeks); prolonged pneumonia (6 weeks or more)

According to epidemiological studies in recent decades, it has been identified a significant correlation between age and the frequency of pneumonia [16, 17, 18]. It is established that pneumonia is diagnosed in approximately 20 out of 1000 infants and 40 out of 1000 preschool children [2, 5]. In Ukraine, the incidence of pneumonia in children ranges from 4 cases per 1,000 infants aged 1 month to 20 cases per 1,000 children aged 15 years [10, 11]. The highest percentage of pneumonia cases occurs among children under 6 years old, accounting for 54.5% of all cases, followed by children aged 7–14 years (35.9%), and 9.45% in those older than 15 years [8]. According to the statistics of the Ministry of Health of Ukraine, annually, 90,000 to 140,000 children in Ukraine suffer from pneumonia, with hospitalization rates of 25–30% for those under 1 year, 50% for those aged 1 to 5 years, and 10–20% for those older than 5 years. Over the past 10 years, pneumonia incidence in Ukraine has increased by 33.7–40% [6, 8].

The infectious agents causing community-acquired pneumonia (CAP) vary depending on the child's age [11, 15, 21, 22, 23, 24, 25]. S. pneumoniae is the most common bacterial agent of CAP in children of all age groups (18–28%) [5, 12, 13, 15, 16, 19, 23, 24]. This rate has somewhat decreased with the introduction of vaccination [26]. In newborns in the early neonatal period (up to 7 days of life), the main agents are E. coli, S. agalactiae, Listeria monocytogenes [15]. Among infants aged up to 6 months, the etiological factors of CAP include E. coli, group B streptococci, other gram-negative bacilli, respiratory syncytial viruses,

coronaviruses, and rarely Moraxella catarrhalis [12, 16, 18, 25, 27]. In the age group of 6 months to 5 years, the etiological agents of CAP are S. pneumoniae (70–88%), H. influenzae type b (up to 10%), M. pneumoniae (15%), C. pneumoniae (3–7%), and viruses [12, 13, 15, 16, 23, 27]. Among viruses, respiratory syncytial virus, influenza viruses, parainfluenza viruses, rhino- and adenoviruses, and coronaviruses are common [12, 16, 18, 21, 23, 28, 29]. In school-age children, the etiological agents of CAP are S. pneumoniae (35–40%), M. pneumoniae (23–44%), C. pneumoniae (15–30%), and H. influenzae type b (rarely) [12, 16, 23, 29].

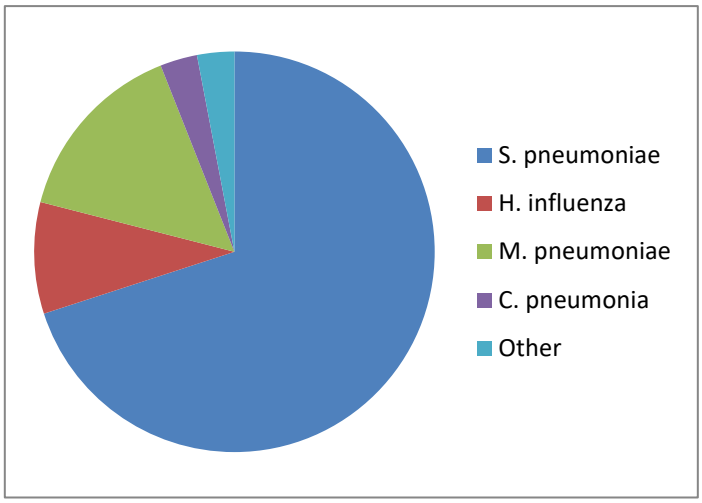

Figure 1 – The structure of etiological bacterial pathogens of community-acquired pneumonia in children aged 6 months to 5 years

Other etiological agents may be considered depending on specific contacts and include Staphylococcus aureus, Streptococcus pyogenes (especially after the flu), Mycobacterium tuberculosis, Francisella tularensis, Brucella spp, Coxiella burnetii, Chlamydophila psittaci, Legionella pneumophila, Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis, and oral flora or gram-negative bacilli (after aspiration) [15, 25, 24, 26, 28, 29, 30]. It should be noted that some authors emphasize the high frequency of detection of viral-bacterial associations, ranging from 21 to 33% of cases. The most common causes of mixed infection are mycoplasma and viruses. It is also established that the frequency of co-infection is higher in severe M. pneumoniae infection than in non-severe pneumonia [30, 31, 32]. Pneumonia caused by rubella, chickenpox, measles, as well as Pneumocystis jiroveci and fungi such as Candida albicans, Aspergillus niger, and Variotii Zaaminelli, has been described [15, 24, 29].

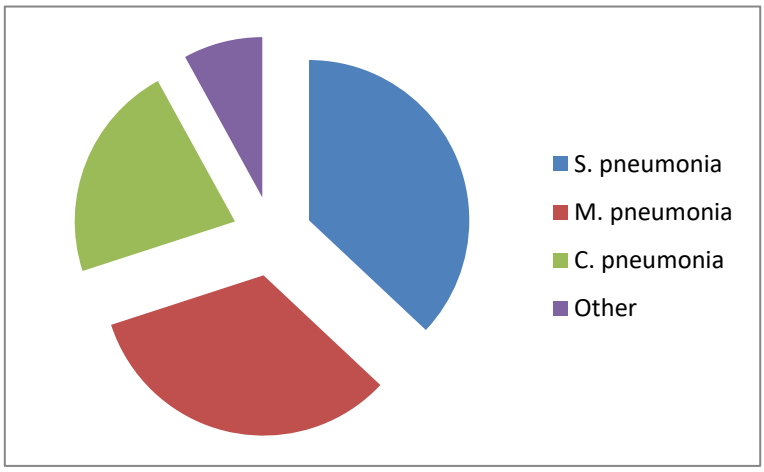

Figure 2 – Etiological structure of bacterial pathogens of nosocomial pneumonia in children aged 6 to 18 years

In the absence of humoral immunity and immunodeficiency, pneumonia in children can be caused by pneumococci, staphylococci, enterobacteria. In children with primary cellular immunodeficiencies, HIV-infected, and those with AIDS, as well as in cases of prolonged corticosteroid therapy, pneumonia is more often caused by P. carinii, Candida fungi, and rarely by cytomegalovirus, Mycobacterium avium [15, 16, 29]. In patients with acute leukemia and lymphomas with neutropenia, pneumonia can be caused by both bacteria and viruses and fungi [12, 15, 29]. Pneumonia in patients with cystic fibrosis is usually caused by S. aureus in infants and Pseudomonas aeruginosa or Burkholderia cepacia in older patients [25, 26].

Risk factors for pneumonia in childhood include weakened immune systems often associated with malnutrition, congenital pathologies, low birth weight, incomplete immunization, a history of antibiotic therapy, frequent acute respiratory infections (ARI), and environmental factors. The latter includes environmental pollution and indoor air quality, smoking in the patient's family, and living in densely populated buildings [15, 25, 30, 33, 34, 35, 36].

The infection in CAP enters the body through various pathways: airborne (viruses, chlamydia, mycoplasma, legionella); microaspiration (from the naso- and oropharynx) – (streptococci, oral anaerobes, pneumococci, Haemophilus influenzae); contact (streptococci, pneumococci, chlamydia, blue pus bacillus, mycobacteria); aspiration (anaerobes and gram-negative bacilli); hematogenous (Staphylococcus aureus, gram-negative bacilli). The lymphatic route is possible only if the barrier function of the lymphatic ring is compromised [10, 13, 16, 34, 36]. The development of CAP in children is often preceded by ARI, which can be complicated by bacterial infection or its association with viruses. Additionally, respiratory diseases decrease the immunological reactivity of the child's body and alter the state of the respiratory tract epithelium, opening the way for bacterial flora [15, 17, 30]. Additionally, the body has barriers that prevent the entry of pathogens. These include anatomical structures such as nasal hair, nasal conchae, tonsils, cilia, humoral, and cellular immunity. Disruption of the functioning of these protective mechanisms contributes to the development of the disease. In the absence of protective mechanisms, infection through droplet transmission (mainly for viral etiology) or colonization of the nasopharynx (for bacteria) leads to inflammation [14, 34, 37, 38]. The pathogenesis of CAP is multifaceted, which determines the variety of the clinical picture of the inflammatory process with disturbances in numerous biochemical and physiological processes, the functional state of organs and systems of the body [12, 16, 18, 29, 30, 37].

In the pathogenesis of pneumonia, several consecutive phases of the development of the pathological process are distinguished:

• Phase I – penetration of the pathogen and primary alteration;

• Phase II – activation of non-specific inflammatory processes;

• Phase III – activation of free radical oxidation processes;

• Phase IV – disruption of the pathophysiological mechanisms of respiratory regulation;

• Phase V – respiratory failure and impairment of non-respiratory lung functions;

• Phase VI – metabolic and functional disorders of organs and systems [12, 13, 16, 29].

Therefore, the development of pneumonia is a dynamic interaction process between the microorganism and the anti-infective defense system.

The first phase of the pathogenesis of pneumonia is characterized by the penetration of the etiological agent into the lung tissue through inhalation, bronchogenic, hematogenous, or lymphogenic pathways. Pathogens that have penetrated the bronchial epithelium induce primary alterations in goblet and ciliated cells. As a result, the clearance mechanism and mucociliary clearance are disrupted, leading to bronchial obstruction. Additionally, the functioning of neutrophils, macrophages, and T-lymphocytes is disturbed, causing suppression of local immune defense. These mechanisms facilitate the penetration of pathogens into the focus of inflammation [12, 16, 29, 36, 39].

In the second phase of pneumonia pathogenesis, primary alteration activates the complement system through the alternative pathway, resulting in partial lysis of the pathogen, increased capillary permeability, and active migration of polymorphonuclear leukocytes and neutrophils to the focus of inflammation. Furthermore, chemotaxis and the production of pro-inflammatory cytokines are induced by activated phagocytes. Activation of the Hageman factor triggers the hemocoagulation system and the kallikrein-kinin system. Bradykinin, along with other basic peptides, increases vessel permeability and induces smooth muscle contraction, especially in the smooth interalveolar

muscles, enhancing obstruction. Infiltration of polymorphonuclear leukocytes causes the release of a significant amount of lysosomal enzymes (elastase, collagenase, proteases, and superoxide anion), which destroy phagocytized microorganisms that have penetrated the epithelial cell. These processes and the activation of trigger systems (kallikrein-kinin, hemocoagulation, complement, etc.) lead to secondary alterations in lung tissue and the expansion of the damage zone. Exudation with inflammatory changes in bronchi, alveolar, and interstitial tissues develops as a result of alteration. Due to the damage to the walls of pulmonary capillaries, exudate with a high protein and blood cell content enters the alveoli, leading to inflammatory exudation of lung parenchyma. Inflammation is an important element in neutralizing the pathogen, producing local and general immunity, and eliminating breakdown products [10, 12, 13, 29, 37, 39].

The third phase involves the activation of lipid peroxidation, causing the oxidation of unsaturated fatty acids in cell membranes and surfactant phospholipids lining the inner surface of the alveoli. Surfactant deficiency increases fluid transudation into the alveoli, reduces alveolar surface tension, and disrupts gas exchange [12, 13, 16, 36].

In the fourth phase of pathogenesis, further progression of the disease occurs, associated with disturbances in central respiratory regulation, oxygen transport through the alveolar-capillary barrier, lung ventilation, and tissue respiration. These processes lead to dyspnea, hypoxia, and hypoxemia, ultimately resulting in the development of respiratory failure [12, 13, 16, 29, 36].

Four forms of hypoxia are distinguished:

- Hypoxic – the result of physiological disorders of the lung apparatus, the main feature is low oxygen tension in arterial blood;

- Circulatory – develops with impaired oxygen transport by blood flow, characterized by an increase in arteriovenous oxygen content difference;

- Hemical – develops as a result of a small amount of hemoglobin or its loss for oxygen binding, the main feature is high PCO_2 tension with low oxygen content;

- Histotoxic – caused by the inability of tissues to utilize oxygen due to damage to enzymatic or energy systems, characterized by a rapid decrease in arteriovenous oxygen content difference [12, 13, 30, 36].

The fifth phase of pneumonia development is characterized by the development of respiratory failure as a result of previously developed airway obstruction, alteration and alveolar exudation, disruption of gas diffusion and hemodynamics in the lungs. There is impairment of non-respiratory lung functions (cleansing, immune, excretory, metabolic, hemodynamic, secretory, water-electrolyte balance regulation, etc.) [12, 13, 16, 29, 36].

The sixth phase of pneumonia pathogenesis is also called the phase of metabolic and functional disorders of organs and systems. It is characterized by an extensive clinical picture of the disease with disturbances in numerous biochemical and physiological processes, the functional state of organs, and the body's systems [12, 13, 16, 36].

The basis of pathogenesis includes infectious toxemia, respiratory failure, electrolyte and water imbalance involving all organs and systems. Its complexity and multistage nature determine the variety of the clinical picture of the disease [16, 18, 30, 39, 40].

Initial symptoms of the disease are often associated with intoxication and manifest as behavioral disturbances such as excitement, crying, and restlessness [16]. Pneumonia in newborns may be manifested only by fever and hypoxia, and sometimes the first sign may be apnea. The child becomes lethargic and refuses to breastfeed [15]. In preterm infants and children in the first months of life, there may be disturbances in trophic functions: hypovitaminosis, characteristic changes in tissue turgor, muscle function disorders, and the appearance of pallor [22, 25, 36, 39].

In children aged 1 month and older, a typical symptom is cough, which can vary in character: from irritant, infrequent to persistent, without relief, frequent, and muffled [13, 16, 41, 42].

Older children may also complain of pain in the chest associated with pleurisy. One of the main symptoms is fever. Fever without cough and respiratory distress can also be a manifestation of pneumonia. In infants, afebrile pneumonia caused by bacteria can occur [43]. Other symptoms include worsening well-being, decreased appetite, vomiting, and bowel disorders [25, 41].

Viral pneumonias are often characterized by cough, wheezing, and stridor. Fever is less characteristic for them compared to bacterial pneumonia. Bacterial pneumonia typically presents with high temperature, chills, cough, and dyspnea [15, 16]. Atypical pneumonia is characterized by a gradual onset of the disease, moderate intoxication syndrome, dry cough, and nonspecific respiratory symptoms (dry wheezing, mild shortness of breath) [12, 16, 25, 30].

The clinical picture of pneumonia is characterized by dyspnea in the absence of broncho-obstructive syndrome. In the acute phase of the disease, breathing becomes superficial, accelerated, and pathological types of breathing appear [13, 41]. Indicators of respiratory distress in premature newborns and infants in the first months of life include froth near the mouth, rhythmic movement of the lips, head nodding in time with breathing, and chest wall retraction [12, 13, 16, 41].

Pneumonia due to obstruction of the airways, alteration and alveolar exudation, disturbance of gas diffusion, and hemodynamics in the lungs lead to respiratory failure [12, 16, 41]. Respiratory failure (RF) is a condition in which either the lungs cannot maintain the normal gas composition of the blood, or it is achieved through abnormal operation of the external respiratory apparatus, leading to a decrease in the body's functional capabilities [10]. According to other authors, RF is a condition in which the lungs' ability to maintain the normal gas composition of arterial blood during breathing with air is limited [12, 13, 16].

Three degrees of respiratory failure are distinguished. The first degree is dyspnea during physical exertion. Oral cyanosis, which intensifies during rest. The pulse/respiration (P/R) ratio = 2.5:1, tachycardia, normal blood pressure. Spirometric indicators show an increased minute ventilation (MV), decreased lung vital capacity (LVC), and decreased tidal volume (TV). The blood gas composition is minimally changed. The second degree is dyspnea at rest, tachycardia, increased blood pressure. Oral and facial cyanosis. P/R = 2–1.5:1, increased MV, decreased LVC by more than 25–30%. The Sa O_2 level is 70–85%. The third degree of RF involves significant dyspnea (respiratory rate more than 150% of the norm), decreased blood pressure, generalized cyanosis. P/R varies, MV is reduced, LVC and TV are reduced by more than 50%. Blood gas composition - Sa O_2 is below 70%. The development of decompensated mixed acidosis occurs [12, 13, 36, 44].

For successful pneumonia diagnosis, a correctly and thoroughly collected medical history is important. The main clinical manifestations that allow suspicion of pneumonia in a child are symptoms of intoxication, RF, and physical data [12, 16, 25, 30, 40, 41, 42].

Literary data indicates that typical pneumonia cases are characterized by: febrile temperature lasting more than 3 days; cyanosis and the presence of the following signs of respiratory distress: respiratory rate over 40/minute in children from 1 to 5 years old, over 30/minute in children older than 5 years in the absence of signs of bronchial obstruction; tachypnea; cough, which may be absent in 15–25% of children [12, 20].

Typical signs of pneumonia inflammation include: cough, fever, abdominal or chest pain, dyspnea, wheezing, general malaise, decreased appetite, headache, and fatigue - these are nonspecific symptoms and individually may indicate another illness [30, 40, 46]. Viral and bacterial pneumonia have almost identical clinical and diagnostic criteria. Therefore, to definitively diagnose pneumonia, the combination of symptoms, clinical presentation, and examination data is assessed [27, 32, 33, 40].

When examining a child, attention is paid to signs of RF without pronounced obstruction - dyspnea, cyanosis, involvement of auxiliary muscles in the act of breathing, tachycardia, sweating, dryness of mucous membranes [10, 25, 30]. Late symptoms of RF include severe dyspnea, hypotension, cyanosis, and impaired consciousness [25]. Palpation reveals chest wall retraction, increased vocal fremitus over the fremitus zone. Percussion - at the beginning of the disease, the data are not very informative, later localized sound attenuation is determined; auscultation - weakened breath sounds; local crepitation or asymmetry of fine bubbling sonorous rales. The nature of wheezing changes during the course of the disease: initially, there are few of them, they are delicate, later they become coarse, diverse, and their number increases [9, 18, 25, 29, 30, 43].

The generally accepted standard for pneumonia diagnosis is laboratory diagnostics, which includes counting the number of leukocytes and their formula: leukocytosis over 10–12x10^9/L, a shift in the leukocyte formula to the left (>10% of stab neutrophils), accelerated ESR indicate a high probability of bacterial infection. Indicators of a severe course of the inflammatory process in the lungs are a decrease in leukocytes below <3x10^9/l or an increase above 25x10^9/l [25, 41]. With viral community-acquired pneumonia, the number of leukocytes can be normal or increased due to an increase in the number of lymphocytes in the blood. [13, 15, 38, 42, 45].In addition, an increase in the concentration of C-reactive protein and other acute-phase proteins is determined in the blood. However, there are recommendations according to which blood proteins should not be determined since these tests are not informative enough [44].

Other researchers point out the importance of determining the procalcitonin level, as according to the results of recent studies, it is one of the markers distinguishing bacterial and viral pneumonia and contributes to the reduction of the duration of antimicrobial therapy [21, 46, 47]. Studies on the determination of the lectin level (a protein that binds to mannose) indicate the interdependence of the protein level and the clinical picture, the development of complications, and the duration of non-hospital pneumonia treatment [48].

Determining the etiology of community-acquired pneumonia (CAP) is a rather complex process [12, 20, 36, 33, 42]. Bacteriological analysis involves using secretions from the upper respiratory tract or tracheal aspirates, but the microorganisms identified are not always identical to the flora in the lower respiratory tract. Moreover, pathogens found in the nasopharyngeal pathways in children with pneumonia are also present in healthy individuals [28]. Immunological or molecular methods are employed for diagnosing mycoplasmal and chlamydial etiology of CAP [12, 13, 15, 25, 44]. Gram staining and sputum cultures are infrequently performed since obtaining material for these studies in children is challenging [31, 33]. Blood cultures yield positive results in 10–20% of cases, more commonly in children with pneumonia complicated by pleuritis [13, 42]. Respiratory viruses are typically diagnosed using polymerase chain reaction (PCR) or rapid testing for viral antigens in nasopharyngeal material, but these methods cannot exclude a concomitant bacterial cause of the disease [15, 22, 31, 44]. Multiplex PCR technology in children with pneumonia identifies multiple viral agents in 30–40% of cases [49, 50]. Isolating the pathogen should be done before commencing antibiotic therapy, as subsequent analyses are not informative [22, 50, 51].

Establishing an etiological diagnosis is aided by the analysis of pleural fluid. However, significant pleural fluid is not characteristic of most community-acquired pneumonias for aspiration, and pleural puncture is an invasive method that can lead to complications [22, 33, 37].

In everyday practice, determination of the etiological agent is rarely carried out, only in certain cases [13, 22], since antiviral therapy has limited application in respiratory diseases, and no definitive method has been established for accurate identification of the etiological cause of CAP [28]. However, rapid identification of the pathogen contributes to reducing the use of radiographic examination and antimicrobial drugs in treatment [50, 51, 52].

Among the instrumental methods used for CAP diagnosis is pulse oximetry. It is performed in all children with suspected pneumonia and hypoxemia. The hypoxemia indicator is crucial for hospitalization, further examination, and treatment [12, 25, 27, 30, 44].

Children with clinical signs of CAP are recommended to undergo chest X-ray (CXR) [12, 15, 20, 41, 53, 54]. This examination confirms the clinical diagnosis and specifies the form of pneumonia. Radiographic signs of CAP include enhanced lung pattern in the affected area due to increased vascular filling and inflammatory tissue swelling, as well as widening of the root of the lung. On the 2nd to 3rd day from the onset of the disease, homogeneous intensive darkening appears - the focus of infiltration. Pleural effusion and cavities may join later [12, 13, 25, 54, 55, 56, 57].

CXR of the chest in two projections (posteroanterior and lateral) should be performed in patients with CAP with suspicion or documented hypoxemia, or significant respiratory distress [44, 54, 55]. Repeat CXR is done only in the absence of positive dynamics against the background of antibiotic therapy for 48–72 hours, as well as in case of suspicion of complications [6, 39, 41, 53, 56].

Some researchers believe that the results of radiographic studies cannot be used to determine the etiological factor of pneumonia, and chest X-ray is not obligatory for uncomplicated CAP in outpatient treatment [6, 44].

Computed tomography (CT) of the lungs is justified only for differential diagnosis if the routine radiograph is uninformative and for a more accurate assessment of possible complications [6, 10, 12, 15, 27]. The study allows for the detection of early infiltrative and interstitial changes when the X-ray is still not informative, as well as cavities, lymphadenopathy, pleural effusion, focal inflammation in case of ineffective antibiotic therapy [12, 13, 25]. CT allows for a detailed study of the morphology of lung tissue (evaluate the condition of lobes, segments, and lung tissue, detect bronchiectasis, areas of bronchiolar emphysema, tumors, foci of inflammation). CT is necessary to determine the relationship of the detected lung formation to the parietal pleura, pericardium, ribs, and major blood vessels. More often, several slices (5–10) at a distance of 5–10 mm from each other are made during lung CT. No special preparation of patients is required for this study [6, 12, 42].

Recommended examination for community-acquired pneumonia (CAP) includes computerized phono-spirography. This study is based on the use of a computerized system for recording and analyzing respiratory sounds, followed by their three-dimensional visualization. Phono-spirography is based on the spectral-frequency-temporal characteristics of respiratory sounds. Phonographic criteria for segmental CAP include a reduction in the frequency characteristics of basic respiratory sounds by no less than 1.5–2 times and their intensity by no less than 1.3–1.7 times (weakened vesicular breathing); the presence at the end of each phase of inhalation of groups of high-intensity wide-band impulse spectral components with a frequency of 150–1200 Hz (crepitation). Phono-spirographic criteria for focal pneumonia include an increase in the frequency range of basic respiratory sounds by no less than 22% on inhalation and 83% on exhalation under conditions of the child's calm breathing (harsh breathing); the presence at the end of each phase of inhalation of groups of high-intensity wide-band impulse spectral components with a frequency of 90–1100 Hz (crepitation) [12, 13, 25, 30, 57].

Another instrumental method of examination for CAP is ultrasound study (US) [12, 25, 55, 58, 59, 60, 61]. This study allows visualization of changes in lung tissue, detection of the localization of the inflammatory process, its structure, possible complications, dynamic monitoring of the course of the disease, and the effectiveness of treatment [58, 59, 60, 61]. Ultrasound of the chest is recommended for children with severe CAP and pleuropneumonia upon hospitalization, immediately after performing standard X-ray examination of the lungs in 2 projections [12, 57, 59, 60, 61].

According to various authors, in focal CAP, an echogram visualizes an irregularly round-shaped focus of infiltration [59, 60, 61]. In the acute phase of focal-consolidative pneumonia, it is visualized an iso- or hypoechoic formation with clear contours, irregular or pyramidal in shape, with enhancement of the distal contour. Non-air areas of lung tissue in pneumonia, except for peribronchial localization, can be visualized in 100% of cases. In the acute phase of the disease, the "air bronchogram" phenomenon is detected in 50% of patients. The presence of this phenomenon is a positive prognostic sign and indicates a tendency to restore the transparency of lung tissue [55, 58, 61].

Based on the results of conducted studies, it has been established that comprehensive chest ultrasound is the method of choice in assessing pathological changes in the lungs and pleural cavities in children. The diagnostic efficiency indicators of this method for pneumonia are: sensitivity – 93.4–98%, specificity – 80–97.7% [25, 60, 61].

Electrocardiography (ECG), echocardiography (ECHO-KG) with Doppler mapping are used among other additional objective diagnostic criteria for CAP. [6, 12, 30, 41, 43, 55, 60, 61].

CONCLUSIONS / ВИСНОВКИ

Analyzing modern literary sources, it is established that the number of combined bacterial-viral community-acquired pneumonias is increasing, but bacteria remain the main etiological agent. The pathogenesis of the disease is a multifaceted process of interaction between micro- and macroorganisms. The main links of which are the penetration of the pathogen in the presence of bronchopulmonary protection, the development of a local inflammatory process, sensitization and the formation of immune-inflammatory reactions, a violation of the pulmonary microcirculation system, the metabolism of organs, and the participation of the immune system in the development of inflammation. Among the main clinical manifestations of community-acquired pneumonia, fever, cough, and respiratory failure are highlighted. Analyzing scientific databases, pneumonia is characterized by leukocytosis with a shift to the left, an accelerated ESR, an increase in the level of C-reactive protein and procalcitonin. The most informative diagnostic methods for verifying the diagnosis are X-ray, computed tomography, and ultrasound examination of the chest.

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

A promising direction for research will be the study of the impact of the course of community-acquired pneumonia on the hormonal level of the pituitary-adrenal system in children.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

FUNDING / ДЖЕРЕЛА ФІНАНСУВАННЯ

None.

AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

REFERENCES/СПИСОК ЛІТЕРАТУРИ

1. World Health Organization. Geneva. (2022). Pneumonia in children. Access mode: https://www.who.int/news-room/fact-sheets/detail/pneumonia.
2. United Nations International Children's Emergency Fund. NewYork. (2016). One is too many: Ending child deaths from pnemonia and diarrhea. Access mode: https://data.unicef.org/resources/one-many-ending-child-deaths-pneumonia-diarrhoea.
3. World Health Organization. Geneva. (2014). Revised WHO classification and treatment of pneumonia in children at health facilities: Evidence summaries. Access mode: http://apps.Who.int/iris/bitstream/10665/137319/1/9789241507813_eng.pdf.
4. McAllister DA et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. *Lancet Glob Health.* 2019;7:47–57. https://doi.org/10.1016/S2214-109X(18)30408-X.
5. Pro zatverdzhennia Standartiv medychnoi dopomohy «Pozalikarniani pnevmonii u ditei» ["Community-acquired pneumonia in children"]. Nakaz Ministerstva okhorony zdorovia Ukrainy № 1380. 2022 Aug 02. Retrieved from: https://moz.gov.ua/article/ministry-mandates/nakaz-moz-ukraini-vid-02082022--1380-pro-zatverdzhennja-standartiv-medichnoi-dopomogi-pozalikarnjani-pnevmonii-u-ditej. [In Ukrainian].
6. Marushko YV, Shef HH. Pnevmoniia [Pneumonia]. *Dytiachyi likar*. 2016;2(47):5-19. Retrieved from: https://d-l.com.ua/ua/archive/2016/2%2847%29/pages-5-19/pnevmoniya. [In Ukrainian].
7. Troeger C, Blacker BF, Khalil IA et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2018;11:1191–1210. doi:1016/S1473-3099(18)30310-4.
8. Madhi SA, De Wals P, Grijalva CG et al. The burden of childhood pneumonia in the developed world: a review of the literature. *Pediatr Infect Dis.* 2013;32:119–127. https://doi.org/10.1097/INF.0b013e3182784b26.
9. Wrotek A, Robakiewicz J, Pawlik K et al. The Etiology of Community-Acquired Pneumonia Correlates with Serum Inflammatory Markers in Children. *J. Clin. Med.* 2022;11:1–15. https://doi.org/10.3390/jcm11195506.
10. le Roux DM, Zar HJ. Community-acquired pneumonia in children – a changing spectrum of disease. *Pediatr Radiol*. 2017;47(11):1392–1398. https://doi.org/10.1007/s00247-017-3827-8.
11. Volosovets O, Bolbot Y, Abaturov O et al. Dynamics of the incidence rate of pneumonia in children in Ukraine over the past 20 years. *Med. perspekt*. 2020;25(4):174–181. Retrieved from: https://journals.uran.ua/index.php/2307-0404/article/view/221680.
12. Saux NL, Robinson JL. Uncomplicated pneumonia in healthy Canadian children and youth: Practice points for management. *Paediatrics & Child Health*. 2015;8:441–445. https://doi.org/10.1093/pch/20.8.441.
13. Melnyk PS, Dziuba OM, Kudrenko MV, Dudnyk SV, Chepelevska LA, Slabkyi HO, redaktory. Shchorichna dopovid pro stan zdorovia naselennia Ukrainy ta sanitarno-epidemiolohichnu sytuatsiiu ta rezultaty diialnosti systemy okhorony zdorovia Ukrainy [Annual report on the state of health of the population, the sanitary-epidemic situation and the results of the health care system of Ukraine]. Kyiv: MVTs «Medinform»; 2018. 458 p. Retrieved from: https://dspace.uzhnu.edu.ua/jspui/handle/lib/22919. [In Ukrainian].
14. Liu L, Oza S, Hogan D et al. Global, regional, and national causes of under-5 mortality in 2000–2015: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet.* 2016;388(10063):3027–3035. https://doi.org/10.1016/S0140-6736(16)31593-8.
15. Maidannyk VH, Yemchynska YO. Klinichni nastanovy z diahnostyky ta likuvannia pozalikarnianoi pnevmonii u ditei z pozytsii dokazovoi medytsyny [Clinical guidelines for the diagnosis and treatment of community-acquired pneumonia in children from the standpoint of evidence-based medicine]. *International Journal of Pediatrics, Obstetrics and Gynecology*. 2014;3:55-82. Retrieved from: http://ijpog.org/downloads/15/55-82.pdf. [In Ukrainian].
16. Berezhnyi VV. *Pediatriia : natsionalnyi pidruchnyk. 2 t. T. 1.* [*Pediatrics: a national textbook in 2 vols. Vol. 1.*]. Kyiv: Medytsyna; 2013. 1040 p. [In Ukrainian].
17. Bengoechea JA, Pessoa JA. Klebsiella pneumoniae infection biology: living to counteract host defences. *FEMS Microbiology Reviews*. 2019;43:123–144. https://doi.org/10.1093/femsre/fuy043.
18. Marcdante KJ, Kliegman RM. *Nelson Essentials of Pediatrics, 8th edition.* Philadelphia, PA: Elsivier, 2018. 840 p.

19. Reheda MS, Reheda MM, Furdychko LO. *Pnevmoniia: monohrafiia.[Pneumonia; Monograph.]*. 6 vyd., dop. ta pererob. Lviv, 2012. 162 p. [In Ukrainian].
20. Dean P, Florin TA. Factors Associated With Pneumonia Severity in Children: A Systematic Review. *J Pediatric Infect Dis Soc.* 2018;7(4):323–334. https://doi.org/10.1093/jpids/piy046.
21. Chi H, Huang Y, Liu C et al. Characteristics and etiology of hospitalized pediatric community-acquired pneumonia in Taiwan. *Journal of the Formosan Medical Association.* 2020;10:1490–1499. https://doi.org/10.1016/j.jfma.2020.07.014.
22. Rodrigues CMC, Groves H. Community-Acquired Pneumonia in Children: the Challenges of Microbiological Diagnosis. *J Clin Microbiol*. 2018;56(3):10–28. https://doi.org/10.1128/JCM.01318-17.
23. Lee E, Kim CH, Lee YJ et al. Pneumonia and Respiratory Disease Study Group of Korean Academy of Pediatric Allergy and Respiratory Disease. Annual and seasonal patterns in etiologies of pediatric community-acquired pneumonia due to respiratory viruses and Mycoplasma pneumoniae requiring hospitalization in South Korea. *BMC Infect Dis*. 2020;20(1):128–132. https://doi.org/10.1186/s12879-020-4810-9.
24. Zhang LN, Cao L, Meng LH. Pathogenic changes of community-acquired pneumonia in a children's hospital in Beijing, China before and after COVID-19 onset: a retrospective study. *World J Pediatr.* 2022;18(11):746–752. https://doi.org/10.1007/s12519-022-00592-8.
25. Katerynych KM, Lishchyshyna OM, Moisiienko MB, Pranik NB, Renchkovska SO, Rykov OA. Pozalikarniana pnevmoniia v ditei vikom vid 1 misiatsia: klinichna nastanova, zasnovana na dokazak [Community-acquired pneumonia in children 1 month of age and older: An evidence-based clinical guideline]. *Suchasna pediatriia. Ukraina.* 2020;8(112):68-108. [In Ukrainian].
26. Ordóñez JE, Ordóñez A. A cost-effectiveness analysis of pneumococcal conjugate vaccines in infants and herd protection in older adults in Colombia. *Expert Rev Vaccines*. 2023;22(1):216–225. https://doi.org/10.1080/14760584.2023.2184090.
27. Yun KW. Community-acquired pneumonia in children: an updated perspectives on its etiology, diagnosis, and treatment. *Clin Exp Pediatr*. 2023;1:1–26. https://doi.org/10.3345/cep.2022.01452.
28. Mathew JL. Etiology of Childhood Pneumonia: What We Know, and What We Need to Know! *Indian J Pediatr*. 2018;85:25–34. https://doi.org/10.1007/s12098-017-2486-y.
29. Das A, Patgiri SJ, Saikia L et al. Bacterial pathogens associated with community-acquired pneumonia in children aged below five years. *Indian Pediatr*. 2016;53(3):225–227. https://doi.org/10.1007/s13312-016-0825-0.
30. Torres A, Cilloniz C, Niederman MS et al. Pneumonia. *Nat Rev Dis Primers*. 2021;7(1):2–28. https://doi.org/10.1038/s41572-021-00259-0.
31. Roh EJ, Lee MH, Lee JY et al. Analysis of national surveillance of respiratory pathogens for community-acquired pneumonia in children and adolescents. *BMC Infect Dis.* 2022;22(1):330. https://doi.org/10.1186/s12879-022-07263-z.
32. Bhuiyan MU,Snelling TL,West R et al. Role of viral and bacterial pathogens in causing pneumonia among Western Australian children: a case–control study protocol. *BMJ Open.* 2018;8:1–10. https://doi.org/10.1136/bmjopen-2017-020646.
33. Yun KW, Wallihan R, Juergensen A et al. Community-Acquired Pneumonia in Children: Myths and Facts. *Am J Perinatol*. 2019;36:54–57. https://doi.org/10.1055/s-0039-1691801.
34. Sitaresmi MN, Wahab A. Risk factors for childhood pneumonia: a case-control study in a high prevalence area in Indonesia. *Clinical and Experimental Pediatrics.* 2021;64(11):588–595. https://doi.org/10.3345/cep.2020.0033925.
35. Goyal JP, Kumar P, Mukherjee A et al. Risk Factors for the Development of Pneumonia and Severe Pneumonia in Children. *Indian Pediatr*. 2021;58:1036–1039. https://doi.org/10.1007/s13312-021-2369-1.
36. Barson W. *Pneumonia in children: Epidemiology, pathogenesis and etiology.* Retrieved from: https://www.medilib.ir/uptodate/show/5986_2022_09_20.
37. Cillóniz, Catia, Cardozo et al. Epidemiology, pathophysiology, and microbiology of community-acquired pneumonia. *Annals of Research Hospitals*. 2018;2:1–10. https://doi.org/10.21037/arh.2017.12.03.
38. Zar HJ. Bacterial and viral pneumonia: New insights from the Drakenstein Child Health Study. *Paediatr Respir Rev.* 2017;24:8–10. https://doi.org/10.1016/j.prrv.2017.06.009.
39. Reshetar DV. Nehospitalni pnevmonii: deiaki aspekty patohenetychnykh mekhanizmiv rozvytku [Community-acquired pneumonia: some aspects of pathogenetic mechanisms of development]. *Naukovyi visnyk Uzhhorodskoho universytetu. Ceriia Medytsyna*. 2015;1:246-253. [In Ukrainian].
40. Rambaud-Althaus C, Althaus F, Genton B et al. Clinical features for diagnosis of pneumonia in children younger than 5 years: a systematic review and meta-analysis. *Lancet Infect Dis.* 2015;15(4):439–450. https://doi.org/10.1016/S1473-3099(15)70017-4.
41. Pro zatverdzhennia Unifikovanoho klinichnoho protokolu pervynnoi medychnoi dopomohy "Intehrovane vedennia khvorob dytiachoho viku" ["Integrated management of childhood diseases"]. Nakaz MOZ Ukrainy № 1945. 2021 Sept 14. Retrieved from: http://surl.li/okczq. [In Ukrainian].
42. Leung AKC, Wong AHC, Hon KL. Non Community-Acquired Pneumonia in Children. *Recent Patents on Inflammation & Allergy Drug Discovery.*

2018;12:136–144. https://doi.org/10.2174/1872213X12666180621163821.
43. Keitel K, Samaka J, Masimba J et al. Safety and Efficacy of C-reactive Protein–guided Antibiotic Use to Treat Acute Respiratory Infections in Tanzanian Children: A Planned Subgroup Analysis of a Randomized Controlled Noninferiority Trial Evaluating a Novel Electronic Clinical Decision Algorithm. *Clinical Infectious Diseases*. 2019;11:1926–1934. https://doi.org/10.1093/cid/ciz080.
44. Bradley JS, Byington CL, Shah SS et al. The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis.* 2011;53(7):617–630. https://doi.org/10.1093/cid/cir625.
45. Esposito S. et al. Procalcitonin measurements for guiding antibiotic treatment in pediatric pneumonia. *Respiratory medicine.* 2011;12:1939–1945. https://doi.org/10.1016/j.rmed.2011.09.003.
46. Hevkaliuk NO. Leikohrama yak pokaznyk reaktyvnosti orhanizmu ditei, khvorykh na hostri respiratorni virusni infektsii [Leukogram as an indicator of reactivity in children with acute respiratory viral infections]. *Aktualni pytannia pediatrii, akusherstva ta hinekolohii*. 2013;1:22-25. [In Ukrainian].
47. Ratageri VH, Panigatti P, Mukherjee A et al. Role of procalcitonin in diagnosis of community acquired pneumonia in Children. *BMC Pediatr*. 2022;22(1):217. https://doi.org/10.1186/s12887-022-03286-2.
48. Taras R, Capitanescu G, Ionescu M et al. The Prognostic Value of Mannose-Binding Lectin in Community-Acquired Pneumonia. *Maedica (Bucur).* 2020;15(1):11–17. https://doi.org/10.26574/maedica.2020.15.1.11.
49. El Kholy AA, Mostafa NA, Ali AA et al. The use of multiplex PCR for the diagnosis of viral severe acute respiratory infection in children: a high rate of co-detection during the winter season. *Eur J Clin Microbiol Infect Dis.* 2016;35(10):1607–1613. https://doi.org/10.1007/s10096-016-2698-5.
50. Driscoll AJ, Deloria Knoll M, Hammitt LL et al. The Effect of Antibiotic Exposure and Specimen Volume on the Detection of Bacterial Pathogens in Children With Pneumonia. *Clin Infect Dis.* 2017;64:368–377. https://doi.org/10.1093/cid/cix101.
51. Ginocchio CC. Strengths and weaknesses of FDA-approved/cleared diagnostic devices for the molecular detection of respiratory pathogens. *Clin Infect Dis.* 2011;52(4):312–325. https://doi.org/10.1093/cid/cir046.
52. Subramony A, Zachariah P, Krones A et al. Impact of Multiplex Polymerase Chain Reaction Testing for Respiratory Pathogens on Healthcare Resource Utilization for Pediatric Inpatients. *J Pediatr*. 2016;173:196–201. https://doi.org/10.1016/j.jpeds.2016.02.050.
53. Shalom BS and others, Use of Chest Radiography Examination as a Probe for Pneumococcal Conjugate Vaccine Impact on Lower Respiratory Tract Infections in Young Children. *Clinical Infectious Diseases.* 2020;1:177–187. https://doi.org/10.1093/cid/ciz768.
54. Wrotek A, Czajkowska M, Jackowska T. Chest Radiography in Children Hospitalized with Bronchiolitis. *Adv Exp Med Biol.* 2019;1222:55–62. https://doi.org/10.1007/5584_2019_435.
55. Zar HJ, Moore DP, Itzikowitz G et al. Diagnosis and management of community-acquired pneumonia in children: South African Thoracic Society guidelines. *Afr J Thorac Crit Care Med.* 2020;26(3):95–116. https://doi.org/10.7196/AJTCCM.2020.v26i3.104.
56. Lukrafka JL, Fuchs SC, Fischer GB et al. Chest physiotherapy in paediatric patients hospitalised with community-acquired pneumonia: A randomised clinical trial. *Arch Dis Child.* 2012; 97(11):967–971. https://doi.org/10.1136/archdischild-2012-302279.
57. Harris M, Clark J, Coote N et al. British Thoracic Society Standards of Care Committee. British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. *Thorax.* 2011;66:2–23. https://doi.org/10.1136/thoraxjnl-2011-200598.
58. Urbankowska E, Krenke K, Drobczyński Ł et al. Lung ultrasound in the diagnosis and monitoring of community acquired pneumonia in children. *Respir Med*. 2015;109(9):1207–1212. https://doi.org/10.1016/j.rmed.2015.06.011.
59. Reissig A, Copetti R. Lung Ultrasound in Community Acquired Pneumonia and in Interstitial Lung Diseases. *Respiration.* 2014;87(3):179–189. https://doi.org/10.1159/000357449.
60. Shah VP, Tunik MG, Tsung JW. Prospective evaluation of point-of-care ultrasonography for the diagnosis of pneumonia in children and young adults. *JAMA Pediatr.* 2013;167(2):119–125. https://doi.org/10.1001/2013.jamapediatrics.107.
61. Boursiani C, Tsolia M, Koumanidou C, Malagari A, Vakaki M, Karapostolakis G et al. Lung ultrasound as first-line examination for the diagnosis of community-acquired pneumonia in children. *Pediatr Emerg Care.* 2017;33(1):62–66. https://doi.org/10.1097/PEC.0000000000000969.

Received 29.11.2023
Accepted 07.12.2023

Одержано 29.11.2023
Затверджено до друку 07.12.2023

INFORMATION ABOUT THE AUTHORS / ВІДОМОСТІ ПРО АВТОРІВ

Oleksandr I. Smiyan, Doctor of Medical Sciences, Professor, Head of department Pediatrics, Sumy State University.

E-mail: ped@med.sumdu.edu.ua, tel: +380542662318.

ORCID ID: https://orcid.org/0000-0001-8225-0975

Liudmyla V. Taramak, Medical Institute, Sumy State University.

E-mail: l.taramak@med.sumdu.edu.ua, tel. 0993023249.

ORCID ID: https://orcid.org/0009-0005-1802-892X

Kateryna O. Smiian, PhD in Medical Science, Associate professor of Sumy State University.

E-mail: smiyan-gorbunova@med.sumdu.edu.ua, tel. 0509585557.

ORCID ID: https://orcid.org/0000-0002-8030-6418

Olena H. Vasilyeva, PhD in Medical Science, Associate professor of Sumy State University.

E-mail: ol.vasilyeva@med.sumdu.edu.ua, tel. 0667342308.

ORCID ID: https://orcid.org/0000-0003-4470-8740

Andriy M. Loboda, MD, Professor of Sumy State University.

E-mail: kafedrapediatrii@med.sumdu.edu.ua, tel. +380542662156.

ORCID ID: https://orcid.org/0000-0002-5400-773X

Viktoriia O. Petrashenko, PhD in Medical Science, Associate professor of Sumy State University.

E-mail: kafedrapediatrii@med.sumdu.edu.ua, tel. +380542662156.

ORCID ID: https://orcid.org/0000-0002-4648-8916

Olexandr P. Moshchych, MD, PhD, D. Sc., Full Professor of Shupyk National Healthcare University of Ukraine.

E-mail: medrodyn@gmail.com, tel. +380442013293.

ORCID ID: https://orcid.org/0000-0003-3505-6250

Ihor Y. Vysotskyi, Professor, Doctor of medical Sciences, Head of Biochemistry, Pharmacology Course of Sumy State University.

E-mail: y.vysotsky@med.sumdu.edu.ua, tel. +38 0542660941.

ORCID ID: https://orcid.org/0000-0002-6357-3362

Victoria A. Horbas, Docent, Candidate of Medical Sciences of Sumy State University.

E-mail: v.gorbays@med.sumdu.edu.ua, tel. 095595426.

ORCID ID: https://orcid.org/0000-0002-7455-6875

Yuliia A. Manko, PhD in Medical Science, Assistant of Sumy State University.

E-mail: yuly2005@ukr.net, tel. 0955372454.

ORCID ID: https://orcid.org/0000-0003-3348-2862

Kateryna O. Holiuk, PhD in Medical Science, Assistant of Sumy State University.

E-mail: k.holiuk@med.sumdu.edu.ua, tel. 0509315816.

ORCID ID: https://orcid.org/0000-0002-5298-9389

Tetiana O. Aleksakhina, PhD in Philology in Specialty “General linguistics”, Instructor of the Department Foreign Languages and Linguodidactics of Sumy State University.

E-mail: t.aleksakhina@el.sumdu.edu.ua, tel. 0503015627.

ORCID ID: https://orcid.org/0000-0002-9905-330X