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# ETIOLOGICAL STRUCTURE AND ECOLOGICAL SIGNIFICANCE OF OPPORTUNISTIC PATHOGENS IN BRONCHITIS

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The study of microecological indices of the microflora in patients with bronchitis revealed the spread of endogenous bacteria of the nasal pharynx in the bronchi biocenosis, which was confirmed by constancy index and Berger-Parker index of dominance. The etiological spectrum of infectious factors was dominated by *viridans* group streptococci and fungi of the genus *Candida*, which had a high colony-forming level. Microorganisms were inoculated in both monocultural and communities form, which numbered from two to four species. The most common were combinations of bacteria and fungi of the genus *Candida*, which were recorded in 62.7% (64/102). The communities included not only autochthonous bacteria, but also such uncharacteristic for biotope as K. pneumoniae, P. aeruginosa, E. coli, E. cloacae, E. aerogenes, E. faecalis, E. faecium.

**Key words:** opportunistic pathogens, bronchitis.

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## ЕТІОЛОГІЧНА СТРУКТУРА ТА ЕКОЛОГІЧНА ЗНАЧИМІСТЬ УМОВНО-ПАТОГЕННИХ МІКРООРГАНІЗМІВ ПРИ БРОНХІТАХ

У ході дослідження мікроекологічних показників мікрофлори хворих на бронхіт виявлено поширення ендогенних мікроорганізмів носоглотки у біоценозі бронхів, що підтверджувалося індексами постійності та домінування Бергера-Паркера. В етіологічному спектрі інфекційних чинників переважали стрептококи групи *viridans* та гриби роду *Candida,* які мали високий колонізаційний рівень. Мікроорганізми висівалися як у монокультурній, так і асоціативній формі, яка налічувала від двох до чотирьох видів. Найпоширенішими були комбінації бактерій і грибів роду *Candida,* які реєструвалися у 62,7 % (64/102). До складу асоціацій входили не лише автохтонні бактерії, а й нехарактерні для біотопу, такі як K. pneumoniae, P. aeruginosa, E. coli, E. cloacae, E. aerogenes, E. faecalis, E. faecium.

**Ключові слова:** умовно-патогенні мікроорганізми, бронхіти.

*The work is a fragment of the research project "Improvement of methods for diagnosis and treatment of purulent-inflammatory diseases caused by opportunistic pathogens", state registration No. 0118U000930.*

Currently, acute bronchitis is one of the most common reasons for patients to seek medical attention. The incidence of acute bronchitis varies widely – from 20 to 40% depending on the season and epidemiological situation [8, 12].

Effective treatment of bronchitis of bacterial etiology is impossible without accurate interpretation of the etiological factor. The trend of recent years indicates changes in the microflora in purulent-inflammatory processes of the bronchi. In the structure of etiologically significant agents in bronchitis, along with pathogenic ones, opportunistic pathogens are increasingly common. These are different representatives of the normal flora of the human upper respiratory tract.

Respiratory sinuses and lower respiratory tract (trachea, bronchi, lungs) in healthy people are sterile, which depends on the effective operation of the mucociliary apparatus. Usually respiratory infections of the lower respiratory tract are caused by viruses and bacteria such as: Respiratory syncytial virus, Influenza virus, Parainfluenza virus, C. pneumoniae, M. pneumoniae [5].

The mucociliary apparatus of the mucous membrane of the respiratory tract, which is primarily responsible for the sterility of the lower respiratory tract, is damaged by viral infections or other harmful effects. As a result, microorganisms that infect the nasal pharynx begin to colonize the lower respiratory tract, multiply rapidly and cause the development of bronchitis. The microflora of the upper respiratory tract is an ecological niche for many microorganisms. The formation of qualitative and quantitative microflora composition is regulated by complex relationships between its individual representatives within the biocenosis. The predominance of one microorganism in the microbiocenosis may have clinical significance, even if it is a representative of the endogenous microflora. Active reproduction of this microorganism against the background of suppression of other species can cause infectious disease [10].

Therefore, microbial flora of the trachea and bronchi contents in infectious diseases is nonspecific and in most cases comes from the nasal pharynx.

**The purpose** of the study was to research the species composition of the microflora in bronchitis and to determine the share of participation of various species in biocenosis structure.

**Materials and methods.** The study was performed on the basis of Non-Profit Municipal Enterprise of the Kharkiv Regional Council "Regional Clinical Hospital". The results of bacteriological researches of various clinical materials from 247 patients with bronchitis are used in the study. Bronchial lavage and sputum were used as clinical material.

Microbiological study included the isolation of pathogens, identification of morphological, cultural and biochemical properties of cultures in accordance with the Order of the Ministry of Health of the USSR No. 535 from 22.04.1985. [6].

Ecological analysis of microflora in the clinical material was carried out by studying its structure and functional characteristics using such indices: constancy index [7], Berger-Parker dominance index [4].

The constancy index was calculated by the formula: $C\% = p \cdot 100/P$, where C% is the Constancy Index, P is the number of samples in which the studied species are detected, and P is the total number of analyzed samples. Depending on the obtained values, all species were divided into dominant or constant (C > 50%), rare or additional (25%< C < 50%) and random ones (C < 25%).

Determination of the colony-forming level or quantification of the microbial population density was performed by counting viable colony-forming units of bacteria in 1 ml of a clinical sample and expressed by the decimal logarithm (lg CFU/ml).

The Berger-Parker dominance index, which means the relative significance of the most common species, was calculated by the formula: $d = N_{max}/N$, where d is the dominance index, $N_{max}$ is the number of organisms of the most common species, N is the number of organisms of the studied species.

**Results of the study and their discussion.** A total of 363 strains of microorganisms were isolated, which were classified into 9 genera and 11 species. The population composition of microflora of the studied clinical material was represented by facultative anaerobic and aerobic bacteria and fungi. According to the constancy index, only viridans group streptococci were classified as rare or additional, and all other species were classified as random.

When studying the etiological structure of bronchitis pathogens, it was found that streptococci of the viridans group were isolated most often – in 37.5 % (136/363) and fungi of the genus Candida – 22.6 % (82/363) (table. 1). Staphylococci (from 4.3 to 10.7%), Klebsiella – 8.3% (30/363) and Pseudomonas aeruginosa – 7.2% (26/363) were significantly inferior to them. Other types of microorganisms were isolated in isolated cases and were characterized by low constancy indices (from 0.3 to 4.3%), which allowed to classify them as random. Moreover, microorganisms with a higher frequency of occurrence were characterized by a higher colony-forming density (table 2). Thus, streptococci of the viridans group had a colony-forming level of $10^7$ CFU/ml, and fungi of the genus Candida –$10^6$ CFU/ml. S. pyogenes was identified in only 1.7% of patients, but the colony-forming density was $10^5$ CFU/ml, which may be significant in the development of the pathological process. Staphylococci were detected in the amount of $10^4$–$10^{4.5}$ CFU/ml. The level of colony-forming density of random microorganisms ranged from $10^2$–$10^3$ CFU/ml for enterococci and Enterobacter to $10^{4.5}$ CFU/ml for Penicillium spp.

The polymicrobial nature of respiratory pathogens is noted in the studies of various authors. In particular, bacteria were identified in the lower respiratory tract of 30-50% of sick children [11], and an association with bacterial infection was found in almost half of community-acquired acute bronchitis [14].

Isolated microorganisms were representatives of the microflora of the upper respiratory tract of healthy people, and their detection in the sputum of patients may indicate both colony-forming and participation in the infectious process. The significance of a particular pathogen depends on the patient's age, the presence of other chronic pathology, vaccination, and so on. Thus, the significant density of the microbial population of potential bacterial pathogens can complicate the course of the disease [13].

Bacterial microflora is activated in acute bronchitis of viral etiology against the background of reduced airway barrier function and immune protection, which can lead to superinfection [3]. The development of superinfection can be facilitated by the presence of chronic diseases of the upper respiratory tract in patients [2].

According to J.V. Park et al., mixed viral-bacterial communities were found in 18.9% of patients and the most common bacterial pathogens were found in patients with chronic respiratory diseases and in the elderly ones [14]. Joining a bacterial infection causes a more severe form of the disease and prolongs the duration of the disease [2]. In particular, staphylococci and pseudomonads may be important in the etiology of bronchitis when the mechanism of bronchial self-cleansing is disturbed (presence of tracheostoma, tracheal intubation, cystic fibrosis, etc.).

Determination of microecological indices of the microflora showed the spread of endogenous microorganisms of the nasal pharynx in the biocenosis of the bronchi, which was confirmed by indices of consistency and dominance (table 2). Thus, the Berger-Parker index confirms the importance of streptococci and staphylococci, but isolation of opportunistic pathogens indicates the development of allochthonous microbiocenosis, which is formed against the background of mucosal dysbiosis in bronchitis caused by a weakening of local immunity and, possibly, irrational antibiotic therapy.

Table 1

**Species composition of the microflora isolated from clinical material in bronchitis**

| Pathogen | Frequency of pathogen isolation (absolute value/%) | | | | |
|---|---|---|---|---|---|
| | Total | In monoculture | In communities | | |
| | | | Two-component | Three-component | Four-component |
| Viridans group streptococci | 136/37.5 | 72/52.9 | 55/40.4 | 8/5.9 | 1/0.7 |
| S. aureus | 39/10.7 | 8/20.5 | 22/56.4 | 8/20.5 | 1/2.6 |
| K. pneumoniae | 30/8.3 | 6/20 | 13/43.3 | 10/33.3 | 1/3.3 |
| P. aeruginosa | 26/7.2 | 17/65.4 | 6/23.1 | 3/11.5 | - |
| S. epidermidis | 15/4.0 | 11/73.3 | 3/20 | 1/6.7 | - |
| S. anhaemolyticus | 16/4.3 | 7/43.7 | 8/50 | 1/6.3 | - |
| S. pyogenes | 6/1.7 | 2/33.3 | 3/50 | 1/16.7 | - |
| E. coli | 4/1.1 | 2/50 | 1/25 | 1/25 | - |
| E. faecalis | 3/0.8 | 1/33.3 | 2/66.7 | - | - |
| E. cloacae | 2/0.6 | 2/100 | - | - | - |
| E. faecium | 1/0.3 | 1/100 | - | - | - |
| E. aerogenes | 1/0.3 | - | 1/100 | - | - |
| Candida spp. | 82/22.6 | 16/19.5 | 49/59.8 | 16/19.5 | 1/12.2 |
| Penicillium spp. | 2/0.6 | - | 2/100 | - | - |

Table 2

**Ecological characteristics of the microflora isolated from clinical material in bronchitis**

| Pathogen | Constancy index, % | Berger-Parker dominance index | Colony-forming level, lg CFU/g (M±m) |
|---|---|---|---|
| Viridans group streptococci | 37.5 | 1.0 | 6.7±0.6 |
| S. aureus | 10.7 | 3.5 | 4.0±0.4 |
| K. pneumoniae | 8.3 | 4.5 | 3.6±0.3 |
| P. aeruginosa | 7.2 | 5.2 | 4.8±0.5 |
| S. anhaemolyticus | 4.3 | 8.5 | 4.3±0.4 |
| S. epidermidis | 4.0 | 9.1 | 4.5±0.5 |
| S. pyogenes | 1.7 | 22.7 | 5.0±0.6 |
| E. coli | 1.1 | 34.0 | 3.7±0.4 |
| E. faecalis | 0.8 | 45.3 | 2.0±0.3 |
| E. cloacae | 0.6 | 68.0 | 3.0±0.2 |
| E. faecium | 0.3 | 136 | 3.0±0.3 |
| E. aerogenes | 0.3 | 136 | 3.0±0.2 |
| Candida spp. | 22.6 | 1.7 | 6.5±0.6 |
| Penicillium spp. | 0.6 | 68 | 4.5±0.4 |

The presence of numerous microbial communities, which were isolated in 41.3% (102/247) of patients (table 3), is noteworthy. In 33.6% (83/247) cases, these were two-component communities, which included the majority of isolated bacteria (165 strains out of 363 or 45.5%). In 18 patients out of 247 (7.3%) three-component communities were isolated, in 1 patient (0.4%) 4 types of microorganisms were isolated. The most common were combinations of bacteria and fungi of the genus Candida, which were recorded in 62.7% (64/102) (table 4). Gram-positive bacteria and combinations of gram-positive and gram-negative bacteria were isolated in 19.6% (20/102) and 13.7% (14/102) of cases, respectively. Only 2% (2/102) of patients had a combination of gram-negative bacteria and an association of fungi of the genera Candida and Penicillium.

Table 3

**Microbial communities found in clinical material in bronchitis**

| | Monoculture | Communities | | |
|---|---|---|---|---|
| | | Two-component | Three-component | Four-component |
| Number of patients = 247 | 145 | 83 | 18 | 1 |
| Relative amount of communities, % | 58.7 | 33.6 | 7.3 | 0.4 |
| Amount of isolated strains = 363 | 145 | 165 | 49 | 4 |

Table 4

**Composition of microbial communities detected in the clinical material in bronchitis**

| Pathogen | Frequency of communities isolation | |
|---|---|---|
| | Absolute amount | Relative amount, % |
| Bacteria + fungi of the genus Candida | 64 | 62.7 |
| Gram-positive bacteria | 20 | 19.6 |
| Gram-positive bacteria + gram-negative bacteria | 14 | 13.7 |
| Gram-negative bacteria | 2 | 2.0 |
| Fungi of the genera Candida + Penicillium | 2 | 2.0 |

When analyzing the species composition of two-component communities, it was found that combinations of viridans group streptococci with fungi of the genus Candida (36%, 30/83), S. aureus (21%, 17/83) and Klebsiella (8.4%, 7/83) were predominant. All other communities included fungi of the genus Candida in combination with Klebsiella and streptococci of the viridans group (26.3%, 5/19), as well as staphylococci (52.6%, 10/19) and Pseudomonas aeruginosa and Escherichia coli in isolated cases.

It should be noted that the most frequently isolated microorganisms, namely streptococci of the viridans group, were slightly more represented in monoculture (52.9%, 72/136), and fungi of the genus Candida, on the contrary, more actively formed colonies in the studied biotope in communities (77.4%, 66/82). Despite the predominance of streptococci in the studied material, they were not dominant, according to the constancy index, which led to a more intensive population of gram-negative and gram-positive microorganisms that are not characteristic of this biotope. These were K. pneumoniae, P. aeruginosa, E. coli, E. cloacae, E. aerogenes, E. faecalis, E. faecium. In addition, the microbiocenosis was characterized by the appearance of transient species, namely S. pyogenes, S. aureus, S. epidermidis and S. anhaemolyticus.

The composition of the microbiome of the lower respiratory tract is determined by microbial immigration from the oral cavity and nasal pharynx, which is common in healthy people [1, 15]. With chronic respiratory diseases or recurrences, drastic changes in the microbiome occur. Disease recurrence cause respiratory dysbiosis – a violation of the microbial ecosystem, which has a negative impact on the biology of the host. Respiratory dysbiosis causes dysregulation of the immune response, which in turn alters the growth conditions of bacteria in the respiratory tract, contributing to further dysbiosis and supporting inflammation [9]. Identifying the difference in the composition of the original airway microbiota will be able to help explain the so-called phenotype of frequent recurrences, which is observed in diseases, and to determine the therapeutic regimen. The study of the respiratory microbiome organization in the respiratory tract diseases reveals the mechanisms of its interaction with external pathogens and the immune system, deepens the understanding of its basic physiological functions in relation to human health and diseases. Numerous scientific studies indicate the importance of preserving the microecosystem of compensatory, symbiotic and opportunistic pathogens of the respiratory system. Further studies should highlight the role of members of the microbiome in the development of pathology to determine the group of patients who should be prescribed antibiotic therapy to reduce the risk of complications.

Thus, studies have shown that in patients with bronchitis there is active colony-formation of the bronchi by representatives of the nasal pharyngeal microflora with certain qualitative and quantitative changes in the microbiocenosis. This is manifested in an increase in colony-forming density, as well as in the appearance of transient opportunistic pathogens against the background of reduced dominance of the autochthonous microflora of the nasal pharynx.

## Conclusions

1. The etiological spectrum of infectious factors in bronchitis is represented by opportunistic pathogenic microflora with a predominance of streptococci of the viridans group and fungi of the genus Candida, which had a high colony-forming level.

2. Microorganisms were inoculated in both monocultural and associative form, which numbered from two to four species of bacteria and fungi of the genus Candida. The communities included not only autochthonous nasal pharyngeal bacteria, but also such uncharacteristic for biotope as K. pneumoniae, P. aeruginosa, E. coli, E. cloacae, E. aerogenes, E. faecalis, E. faecium.

3. Isolation of a large number of bacterial communities from the clinical material of bronchi indicates a decrease in colony-forming resistance and the development of opportunistic pathogens, which affects the pathogenesis of the disease.

4. The identified features of the microbiocenosis in patients with bronchitis indicate the need for treatment regimens that contain broad-spectrum antibiotics, as well as contribute to the restoration of normal microflora.

*Prospects for further research are as follows. Determination of microecological indices in bronchitis will expand the understanding of pathogenetic changes in the affected areas due to dysbiotic processes, and optimize treatment regimens for bronchitis.*

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## ANALYSIS OF SUCCESSFUL RESUSSITATION IN PRE–HOSPITAL STAGE IN UKRAINE

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The article presents a retrospective analysis of 384 cases of successful cardiopulmonary resuscitation at the prehospital stage in Ukraine. The study was conducted in the period from 2017 to 2019. The patients' general group was divided into two subgroups depending on the initial rhythm of sudden circulatory arrest: defibrillation and non–defibrillation rhythms. In each of the subgroups studied: age of patients, causes of sudden cessation of blood circulation, location, home care, time of resuscitation, methods of restoring airway patency, the presence of self–breathing in the post–resuscitation period, and level of consciousness. The subgroup with non–defibrillation rhythms included 199 cases (51.8%), the subgroup with defibrillation rhythms – 185 cases (48.2%). It was determined that the main cause of circulatory arrest in both subgroups was an acute coronary syndrome.

**Keywords**: sudden cardiac arrest, cardiopulmonary resuscitation, pre–hospital stage, emergency medicine care.

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## АНАЛІЗ ВИПАДКІВ УСПІШНОГО ПРОВЕДЕННЯ СЕРЦЕВО–ЛЕГЕНЕВОЇ РЕАНІМАЦІЇ НА ДОГОСПІТАЛЬНОМУ ЕТАПІ В УКРАЇНІ

В статті наведено результати ретроспективного аналізу 384 випадків успішного проведення серцево–легеневої реанімації на догоспітальному етапі в Україні. Дослідження проводилось в період з 2017 по 2019 роки. Загальна група пацієнтів була розподілена на дві підгрупи залежно від початкового ритму раптової зупинки кровообігу: дефібриляційні та не дефібриляційні ритми. В кожній з підгруп вивчили: вік пацієнтів, причини зупинки раптової зупинки кровообігу, місце випадку, надання домедичної допомоги, час проведення реанімаційних заходів, методи відновлення прохідності дихальних шляхів, наявність самостійного дихання в післяреанімаційному періоді та рівень свідомості. В підгрупу з не дефібриляційними ритмами увійшло 199 випадків (51,8%), в підгрупу з дефібриляційними ритмами – 185 випадків (48,2 %). Визначено, що основною причиною зупинки кровообігу в обох підгрупах був гострий коронарний синдром.

**Ключові слова**: раптова зупинка кровообігу, серцево–легенева реанімація, догоспітальний етап, екстрена медична допомога.

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Sudden cardiac arrest (SCA) remains a pressing and significant problem in today's medicine. The number of cases of SCA remains consistently high worldwide and tends to increase steadily due to the prevalence of the cardiovascular disease in all age groups. Thus, the number of cases of SCA in the US is about 500 thousand every year. In England, 30 thousand, on average, in the EU, the number of cases is 51–55 per 100 thousand populations [1, 4]. For a detailed analysis of all cases of SCA in countries with developed EMD systems, "registers of cases of SCA" are widely introduced [7]. One of the crucial indicators, which is determining on their basis, is the level of successful CPR in the prehospital stage and the final results of the treatment this group of patients. On average, the number of discharged patients without severe neurological