# ENGLISH VERSION: THE ROLE OF SOME INFLAMMATORY CYTOKINES IN THE DEVELOPMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON THE BACKGROUND OF OBESITY*.

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*Systemic inflammation is a common link in the pathogenesis of chronic obstructive pulmonary disease and obesity. During inflammation all cellular elements are activated and secrete cytokines - factors chemotaxis of inflammatory cells or mediators of inflammation. Cytokines induce acute inflammatory response, may have immunopathological effects on cells and tissues, providing consistency, harmony and completeness of the immune response. Of particular interest is foreign and domestic researchers is to study the role of interleukin-26 (IL-26) in the development and maintenance of inflammation in the body in various diseases. IL-26 (AK-155), is a homodimer protein, which belongs to the family of cytokines IL-10. Expressed by T cells, mononuclear cells, natural killer (NK). Biological activity of IL-26 is poorly understood. However, there is evidence that despite the similarity of IL-10, IL-26 does not inhibit production of inflammatory cytokines such as TNF-α, and IL-1 in monocytes or macrophages. In response to invading infectious agent alveolar macrophages produce increased amounts of IL-26. It is believed that in the lung tissue it increases the pool of immune cells and stimulates neutrophils receptor apparatus, causing the latter to focus on bacterial invasion. All the above-mentioned shows that IL-26 is actively involved in the inflammatory process as proinflammatory cytokines. However, the lack of detailed information on the role of an important factor IL-26 in the development of broncho-pulmonary pathology on the background of obesity determines the need for further study of its direct functions.*

Keywords: chronic obstructive pulmonary disease, obesity, systemic inflammation, interleukin-26.

Environmental pollution, smoking, both active and passive, poor nutrition with the use of high calorie foods, sedentary lifestyle, urbanization and population aging lead to the development and growth of civilization diseases, including chronic obstructive pulmonary disease (COPD) and obesity. More recent prevalence among the population leads to a high probability of their combined flow, which is a serious public health problem.

Obesity, especially the abdominal form, negatively affects the course of COPD. The main pathogenic mechanisms responsible for the development of COPD and obesity distinguish systemic inflammation [8,10,14,17,20,24]. However, despite the above, many questions in the pathogenesis and treatment of these diseases are controversial and they require further research.

The accumulation of adipose tissue is associated with the development of chronic inflammation, which is characterized by obesity as a chronic systemic, low intensity, not associated with infection [28]. Adipose tissue produces adypotsytokiny (adipocyte hormone structurally similar to cytokines), cytokines, acute phase reagents, prostaglandins and other mediators that enhance local and systemic inflammatory reactions [14,18,23,27]. It should be noted that most of the proinflammatory factors are expressed by macrophages that infiltrate adipose tissue, which significantly increased during obesity [4,26].

At the same time ability of adipose tissue to produce adypotsytokins with proinflammatory properties such as leptin and resistin increases and synthesis of inflammatory adypotsytokins and adiponectin decreases [2,16,23]. On the whole in the serum of people with obesity occurs the rise in markers of inflammation, including CRP, IL-6, TNF-α, IL-8, IL-18 receptor antagonist IL-1, haptoglobin, protein amyloid A [21].

Inflammation of adipose tissue is associated with the development of hypoxia. Because of a significant number of lipid deposition in adipocytes, their hypertrophy occurs. The vessels may not be sufficient to provide trophic adipocytes and vascular insufficiency consequently leads to hypoxia and apoptosis of cells. Hypertrophic adipocytes induce the production of chemokines, which promote the involvement of macrophages and T cells from peripheral blood. These macrophages produce TNF-α, IL-6 and other cytokines that are influencing the differentiation of adipocytes, prevent preadypotcytes maturation, thereby increasing the flow of lipids. As a result, increased fat mass and hypoxia, which leads to activation of transcription factor NF-κB (nuclear factor-kappa B - nuclear factor kappa B) and HIF-1 (hypoxia-inducible factor 1) in adipocytes, leading to chronic inflammation [4].

Despite the proven link obesity and systemic inflammation, the role of adipose tissue in the development of inflammation in patients with COPD is poorly understood.

However, there is evidence that the fat tissue may respond to proinflammatory mediators, originating in the lungs, producing systemic circulation through adyposytokiny and other mediators of inflammation. In animal studies varied inhaled irritants (such as bacteria, ozone and various allergens) activate adipose tissue, causing a selection of leptin, IL-6 and other immune adyposytokines that can affect pneumonia [23].

In persons with COPD under the influence of risk factors, primarily tobacco, especially those with a genetic predisposition to the disease (hereditary α 1-antitrypsin deficiency) develops neutrophilic inflammation which is characterized by an increase in neutrophils, macrophages and T-lymphocytes in different parts of the lungs. Because of inflammation almost all the cellular elements of the respiratory system (alveolar macrophages, epithelial and dendritic cells) are activated and secrete cytokines - factors chemotaxis of inflammatory cells or mediators of inflammation. Cytokines induce an inflammatory reaction and acute response, providing immunopathological effects on cells and tissues [6], ensuring consistency, harmony and perfection of the immune response [7].

Inflammation in COPD is not limited bronchopulmonary system, but goes beyond, extending to the systemic circulation. This is evidenced by increase in markers of inflammation (C-reactive protein, fibrinogen, proinflammatory cytokines IL-1, IL-6, IL-8, TNF-α) in pe-

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ripheral blood [5]. It should be noted that even during clinical remission COPD is observed increasing levels of inflammatory markers, indicating a chronic inflammatory process [9].

In particular, foreign and domestic researchers are interested in the study of the role of interleukin-26 (IL-26) in the development and maintenance of inflammation in the body in various diseases.

For the first time Knape with their colleagues described IL-26 as a new cDNA clone (sDNA) called the AK-155 [15,22,28].

IL-26 (AK-155), a protein homodimer, consists of 171 amino acid residue and has 25% identity and 47% similarity with homologous sequence IL-10 [12]. IL-26 belongs to a family of cytokines IL-10 [11,12,15,19,25], which includes IL-10, IL-19, IL-20, IL-22, IL-24, IL-26 [15, 22] and type III interferon (IFNγ), namely IL-28A, IL-28V, IL-29 [12]. The gene encoding the amino acid sequence of IL-26 is located on chromosome 12q15, between genes IFNG (IFN-γ) and IL-22 [11,12,15,19].

IL-26 is expressed by T cells, mononuclear cells, natural killer (NK), like macrophages synoviotsyts in rheumatoid arthritis [12,15,28]. The mechanisms that regulate the transcription of IL-26 are not exactly known. However, recent studies have demonstrated that IL-26 co-expressed with IL-17 and IL-22 using Th17 cells. There is the probability that the gene expression of IL-26 is under the action of IL-23, because it induces differentiation of Th17 cells, exacerbating expression of IL-17 and IL-22 [15,28].

Thus, despite the fact that the first gene IL-26 has been identified as a result of increased expression in the transformed herpes viral T cells apes [19], to date, gene IL-26 expressed it Th17 cells after klonotypuvannya T-helper cells, due to antigen - specific stimulation[15].

For cytokine IL-10 is typical common genetic and protein structure, the use of heterodimer homologous cytokine receptor family class II on target cells. However, despite that some biological effects of cytokines are different [12].

IL-26, like other cytokines in cell transmits a signal via the receptor complex. The active receptor complex of IL-26 - a heterodimer composed of two chains, such as IL-20 retseptor1 (IL-20R1) and IL-10 retseptor2 (IL-10R2) [11,15,25]. IL-20R1 is functioning as a specific ligand-binding chain for IL-26 and IL-10R2 for the completion of the active receptor complex. IL-26 initially binds to IL-20R1, forming a dual complex: IL-26 + IL-20R1, thus causing conformational changes that facilitate staffing chain IL-10R2, for completion of the ternary complex [15]. Fully assembled receptor complex undergoes conformational changes induced activation of receptor-associated tyrosine kinases, followed by a transitional reduction and phosphorylation of transcription factors STAT3 and STAT1 to a lesser extent in cells [1,11,15,25]. Thereby increasing the secretion of IL-10, IL-8 and expression of CD54 on the cell surface [1].

IL-10R2 is widely expressed on the surface of various tissues, while IL-20R1 on a limited number of tissues, including the skin, intestine and lung tissue in small amounts expressed also in the main (cerebellum, medulla of the brain) and the spinal cord [15, 25].

That is why the ability to respond to IL-26 carried a greater extent due to IL-20R1. It is also necessary to note that interleukins, belonging to the family of cytokines IL-10 - IL-10, IL-19, IL-20, IL-22, IL-24 does not transmit signals through a combination of IL-20R1 and IL-10R2 proteins thereby demonstrating that this receptor combination is unique and specific to IL-26 [25].

Biological activity of IL-26 is poorly understood. However, there is evidence that despite the similarity of IL-10, IL-26 does not inhibit production of inflammatory cytokines such as TNF-α, and IL-1 in monocytes or macrophages. This is due to the lack of recent expression of IL-26 binding chain - IL-20R1. Further studies have shown that IL-26 actually increases the regulation of the expression of several inflammatory cytokines, such as IL-6 and IL-8 in keratocytes and intestinal epithelial cells [15].

In response to invading infectious agent alveolar macrophages produce increased amounts of IL-26. It is believed that in the lung tissue it increases the pool of immune cells and stimulates receptor apparatus neutrophils, causing the latter to focus on bacterial invasion [13].

All the above mentioned shows that IL-26 is actively involved in the inflammatory process as proinflammatory cytokines. However, the lack of detailed information on the role of an important factor IL-26 in the development of broncho-pulmonary pathology on the background of obesity determines the need for further study of its direct functions.

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# КОМПЛЕКСНЕ ЛІКУВАННЯ ХВОРИХ НА ПРОСТАТИТ З ТОЧКИ ЗОРУ СУЧАСНИХ ВИМОГ*

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*Обследовано 118 больных, которые поступили в урологическую клинику по поводу простатитов. Из них у 63 был острый простатит, а у 55 больных – хронический. Наряду с общеклиническими проведены бактериологические обследованиями с целью определения микрофлоры в моче. При этом выявилось, что бактериурия положительной была у 96 больных (81,3%), и почти поровну между моно инфекцией (50 человек) и микс-инфекцией (46 человек). Кроме этого у 18 больных призведено исследование простатического сока. Выяснилось что основным источником инфекции была кишечная палочка, как моноинфекция - 20 человек (20,7%) и в составе микст-инфекции – в 25 случаях (26,1%). Второй причиной простатита были стафилоккоки эпидермальные и гемолитические, всего у 31 больного. Четко определены возможности воздействия препаратов на микрофлору. При этом превалируют ванкомицин, ликезалид, и антибиотики цефалоспоринового ряда. Для достижения стойкого успеха предлагается целый ряд фитосборов для включения их в комплексное лечение простатитов.*

Ключевые слова: комплексное лечение, простатит, антибиотики, фитосборы.

## Вступ.

Гострі та особливо хронічні запалення передміхурової залози (простатит) найчастіше зустрічаються в основному у осіб молодого віку. У осіб похилого віку та у дітей ця хвороба зустрічається рідше. Особливістю являється те, що ця патологія викликає цілий ряд змін з боку сечової та особливо статевої системи. Слід зазначити, що простатит може призвести до появи порушень з боку емоційного стану, зниженню працездатності, ураженню сексуальної сфери, еректильної функції, навіть до безпліддя [1,2,4,11]. А це все веде до виникненню цілого ряду проблем особливо у соціальній сфері то що. Спроби боротися з цим недугом почалися з того моменту, коли було вперше його діагностовано. Застосування різних препаратів таких як загальнозміцнюючих, імуностимулюючих, антизапальних дає короткочасний ефект. Хворі знову і знову повертаються до урологів за медичною допомогою.

На сьогодення пошуки різних антибіотиків, масажу простати, застосування фізіотерапевтичних процедур, також не призводять до бажаного результату. В зв'язку з цим автори все частіше почали застосовувати препарати рослинного походження в комплексній терапії простатитів [3,7,8,10]. Отримані результати дають основу для сподівання про більш успішне ліку-

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