

# Features of endobronchial pathology among patients with chemoresistant tuberculosis of lungs depending on a case of the previous disease

O. M. Raznatovska, V. M. Khlystun

Zaporizhzhia State Medical University, Ukraine

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**E-mail:**  
raxnatovskaya@  
gmail.com

**Objective** – to study character and features of endobronchial pathology among patients with chemoresistant tuberculosis (CRTB) of lungs depending on a case of the previous disease.

**Materials and methods.** Studying of endobronchial pathology was carried out in 79 patients with CRTB of lungs with lesion of mucosa of bronchi. The patients were divided into 2 groups depending on a case of the previous disease of tuberculosis: the 1<sup>st</sup> group included 35 patients with new cases (tuberculosis) of CRTB of lungs (middle age – 39.1±2.2 years), the second – 44 patients with repeated cases of CRTB of lungs (middle age – 39.5±1.7 years diagnosed for the first time). In both groups males prevailed: 23 (65.7 %) and 31 (70.4 %), respectively. Diagnostic fibre-optic bronchoscopy of a tracheobronchial tree was carried out on clinical base of the department of phthisiology and pulmonology of ZSMU at Municipal institution "Zaporizhzhia Regional Antituberculous Dispensary" by the applicant V. M. Khlystun. The criteria for including of patients into the study were: existence of resistance of micobacteria of tuberculosis to anti-microbacterial drugs among patients with new and repeated episodes of tuberculosis, pathology of the mucosa of bronchi confirmed at fiber-optic bronchoscopy. Serious associated diseases (HIV infection/AIDS, diabetes mellitus, etc.) were criteria of exclusion. The condition of mucosa of bronchi was studied under narcotic anaesthesia by fibrotic bronchoscopes of Olympus (Japan). Pathology of a bronchial tree was described according to classification of M. Shesterina, A. Kalyuk (1975). Results of the research are processed by modern methods of the analysis on the personal computer with use of a statistical package Statistica® for Windows 6.0 license program (StatSoft Inc., No. AXXR712 D833214FAN5).

**Results.** All patients with CRTB of lungs with endobronchial pathology, irrespectively of the case of the previous disease excreted micobacteria with prevalence of multirefractory strains of MBT and had infiltrative clinical form and destructive lesion of segmental bronchi of S<sub>1+2</sub>. Among patients with new cases of CRTB of lungs tuberculosis of bronchi prevailed and among patients with repeated cases of CRTB of lungs the nonspecific endobronchitis prevailed. Irrespective of the case of the previous disease, tuberculosis of bronchi was diagnosed mainly in combination with non-specific endobronchitis. Infiltrative tuberculosis of bronchial tubes (62.9 %) prevailed among patients with new cases of CRTB of lungs, and among with repeated – the frequency infiltrative and infiltrative fistulous was almost identical (27.5 % and 25 % respectively). The frequency of development of stenosis of the affected bronchial tube was seen in 1,6 times more often than in case of the repeated one (65.7 % against 40.9 % respectively). Non-specific endobronchitis among the patients with CRTB of lungs, irrespective of the case of the previous disease, preferentially one-sided localization also had a purulent character.

**Conclusions.** The obtained data demonstrated that it is necessary to apply both specific and non-specific methods of correction, pathology of mucosa of a tracheobronchial tree among the patients with CRTB of lungs, irrespectively of the case. At the same time this correction among the bigger part of patients, namely, with existence of the combined course of tuberculosis of bronchi and non-specific bronchitis demands simultaneous use of methods of correction of both pathologies.

**Ключові слова:**  
бронхоскопія,  
трахеобронхіальне  
дерево,  
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## Особливості ендобронхіальної патології у хворих на хіміорезистентний туберкульоз легень залежно від випадку попереднього захворювання

O. M. Разнатовська, В. М. Хлистун

**Мета роботи** – вивчити характер та особливості ендобронхіальної патології у хворих на хіміорезистентний туберкульоз (ХРТБ) легень залежно від випадку попереднього захворювання.

**Матеріали та методи.** Вивчили ендобронхіальну патологію у 79 хворих на ХРТБ легень з ураженням слизової оболонки бронхів. Хворі були поділені на 2 групи залежно від випадку попереднього захворювання на туберкульоз: одну групу становили 35 хворих із новими випадками ХРТБ легень (середній вік – 39,1±2,2 року), другу – 44 хворих із повторними випадками ХРТБ легень (середній вік – 39,5±1,7 року). В обох групах переважали особи чоловічої статі: 23 (65,7 %) та 31 (70,4 %) відповідно. Діагностичну фібробронхоскопію трахеобронхіального дерева хворим на ХРТБ легень здійснив на клінічній базі кафедри фтизіатрії та пульмонології ЗДМУ в КУ «Запорізький обласний протитуберкульозний диспансер» власноруч здобувач В. М. Хлистун. Критерій включення пацієнтів у дослідження: наявність резистентності мікобактерій туберкульозу (МБТ) до антимікобактеріальних препаратів у хворих із новими та повторними випадками захворювання на туберкульоз, наявність патології слизової оболонки бронхів, що підтверджена при фібробронхоскопії. Критеріями виключення були тяжкі супутні захворювання (ВІЛ-інфекція/СНІД, цукровий діабет тощо). Стан слизової оболонки бронхів вивчали під наркозною анестезією фібробронхоскопом фірми «Olympus» (Японія). Патологію бронхіального дерева описували за класифікацією Шестеріної та Калюк (1975). Результати дослідження опрацьовані сучасними методами аналізу на персональному комп’ютері з використанням статистичного пакета ліцензійної програми «Statistica® for Windows 6.0» (StatSoft Inc., № AXXR712 D833214FAN5).

**Результати.** Усі хворі на ХРТБ легень з ендобронхіальною патологією, незалежно від випадку попереднього захворювання, були бактеріовиділювачами з переважанням мультирезистентних штамів МБТ, інфільтративної клінічної форми та деструк-

тивного ураження сегментарних бронхів  $S_{1+2}$ . У хворих із новими випадками ХРТБ легень переважав туберкульоз бронхів, а в осіб із повторними випадками ХРТБ легень – неспецифічний ендобронхіт. Незалежно від випадку попереднього захворювання, туберкульоз бронхів діагностувався переважно в поєднанні з неспецифічним ендобронхітом. У хворих із новими випадками ХРТБ легень переважав інфільтративний туберкульоз бронхів (62,9%), а з повторними – частота інфільтративного та інфільтративно-норицевого була майже однаковою (27,5% та 25% відповідно). Частота розвитку стенозу ураженого бронха при нових випадках у 1,6 раза частіша, ніж при повторних (65,7% проти 40,9% відповідно). Неспецифічний ендобронхіт у хворих на ХРТБ легень, незалежно від випадку попереднього захворювання, – переважно однобічної локалізації та мав гнійний характер. За наявності деструктивного процесу в сегментарних бронхах ( $S_{1+2}$ ,  $S_6$ ,  $S_{1+2+6}$ ) туберкульоз цих бронхів супроводжував у 65,7% з 88,6% при нових випадках ХРТБ легень та у 47,7% з 90,9% – при повторних.

**Висновки.** Дані, що отримали, свідчать: у хворих на ХРТБ легень, незалежно від випадку захворювання, необхідно застосовувати методи корекції як специфічної, так і неспецифічної патології слизової оболонки трахеобронхиального дерева. При цьому корекція в переважній частині пацієнтів, а саме: з наявністю п оєднаного перебігу туберкульозу бронхів і неспецифічного бронхіту – потребує одночасного застосування методів корекції обох патологій.

## Особенности эндбронхиальной патологии у больных химиорезистентным туберкулезом лёгких в зависимости от случая предыдущего заболевания

Е. Н. Разнатовская, В. Н. Хлыстун

**Цель работы** – изучить характер и особенности эндбронхиальной патологии у больных химиорезистентным туберкулезом (ХРТБ) лёгких в зависимости от случая предыдущего заболевания.

**Материалы и методы.** Изучили эндбронхиальную патологию у 79 больных ХРТБ лёгких с поражением слизистой оболочки бронхов. Больные были разделены на 2 группы в зависимости от случая предыдущего заболевания туберкулезом: одну группу составили 35 больных с новыми случаями ХРТБ лёгких (средний возраст –  $39,1 \pm 2,2$  года), вторую – 44 больных с повторными случаями ХРТБ лёгких (средний возраст –  $39,5 \pm 1,7$  года). В обеих группах преобладали лица мужского пола: 23 (65,7%) и 31 (70,4%) соответственно. Диагностическая фибробронхоскопия трахеобронхиального дерева больным ХРТБ лёгких проводилась на клинической базе кафедры фтизиатрии и пульмонологии ЗГМУ в КУ «Запорожский областной противотуберкулёзный диспансер» собственоручно соискателем В. Н. Хлыстуном. Критерии включения пациентов в исследование: наличие резистентности микобактерий туберкулёза (МБТ) к антимикобактериальным препаратам у больных с новыми и повторными случаями заболевания туберкулезом, наличие патологии слизистой оболочки бронхов, подтверждённой при фибробронхоскопии. Критериями исключения были тяжёлые сопутствующие заболевания (ВИЧ-инфекция/СПИД, сахарный диабет и другие). Состояние слизистой оболочки бронхов изучали под наркозной анестезией фибробронхоскопом фирмы «Olympus» (Япония). Патологию бронхиального дерева описывали по классификации М. Шестериной и А. Калюк (1975). Результаты исследования обработаны современными методами анализа на персональном компьютере с использованием статистического пакета лицензионной программы «Statistica® for Windows 6.0» (StatSoft Inc., № AXXR712 D833214FAN5).

**Результаты.** Все больные ХРТБ лёгких с эндбронхиальной патологией, независимо от случая предыдущего заболевания, были бактериовыделителями с преобладанием мультирезистентных штаммов МБТ, инфильтративной клинической формы и деструктивного поражения сегментарных бронхов  $S_{1+2}$ . У больных с новыми случаями ХРТБ лёгких преобладал туберкулёт бронхов, а у лиц с повторными случаями ХРТБ лёгких – неспецифический эндобронхит. Независимо от случая предыдущего заболевания, туберкулёт бронхов диагностировался преимущественно в сочетании с неспецифическим эндобронхитом. У больных с новыми случаями ХРТБ лёгких преобладал инфильтративный туберкулёт бронхов (62,9%), а с повторными – частота инфильтративного и инфильтративно-свищевого была почти одинаковой (27,5% и 25% соответственно). Частота развития стеноза поражённого бронха при новых случаях в 1,6 раза чаще, чем при повторных (65,7% против 40,9% соответственно). Неспецифический эндобронхит у больных ХРТБ лёгких, независимо от случая предыдущего заболевания, – преимущественно односторонней локализации и носит гнойный характер. При наличии деструктивного процесса в сегментарных бронхах ( $S_{1+2}$ ,  $S_6$ ,  $S_{1+2+6}$ ) туберкулёт этих бронхов сопровождал в 65,7% из 88,6% при новых случаях ХРТБ лёгких и в 47,7% из 90,9% – при повторных.

**Выводы.** Полученные данные свидетельствуют о том, что у больных ХРТБ лёгких, независимо от случая заболевания, необходимо применять методы коррекции как специфической, так и неспецифической патологии слизистой оболочки трахеобронхиального дерева. При этом коррекция у большей части пациентов, а именно: с наличием сочетанного течения туберкулёза бронхов и неспецифического бронхита – требует одновременного применения методов коррекции обеих патологий.

## Introduction

The relevance of the problem of increasing the efficiency of treatment the patients with chemoresistant tuberculosis (CRTB) of lungs is undoubtedly [1]. In recent years there has been pathomorphism not only of CRTB of lungs, but also the accompanying endobronchial pathology, which is the important reason of depression of efficiency of treatment of tuberculosis of lungs, especially when it is complicated with development of stenosis of the afflict bronchus [2]. It is established that existence of endobronchial pathology correlates with clinical laboratory data [3]. Therefore, well-

timed diagnostics and treatment of pathology of mucosa of bronchi are urgent. One of the main diagnostic methods of pathology of mucosa of a tracheobronchial tree is fibre-optic bronchoscopy (FBS) [4], as well as development of ways of treatment of the patients with CRTB of lungs with accompanying endobronchial pathology is very urgent as the efficiency of treatment of this category of patients remains low [5–8].

The purpose of work was to study character and features of endobronchial pathology among patients with CRTB of lungs depending on a case of the previous disease.

**Ключевые слова:**  
бронхоскопия,  
трахеоброн-  
хиальное дерево,  
слизистая  
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**Table 1.** Distribution of patients with CRTB of lungs with endobronchial pathology in the presence of bacterioexcretion and destructive process, n (%)

Indicators	New cases, n=35		Repeated cases, n=44	
	abs.	%	abs.	%
Bacterioexcretion	35	100	44	100
Destructive process	31	88.6	40	90.9
- in segmentary bronchial tubes S <sub>1+2</sub>	21	60.0*	21	47.7*
- in a segmentary bronchial tube S <sub>6</sub>	6	17.2	11	25.0
- in segmentary bronchial tubes S <sub>1+2</sub> , S <sub>6</sub>	4	11.4	8	18.2

\*: reliable difference of the existence of destruction in segmentary bronchial tubes within one group p<0.05.

## Materials and methods

Studying of endobronchial pathology was carried out among 79 patients with CRTB of lungs with lesion of mucosa of bronchi. The patients were divided into 2 groups depending on a case of the previous disease of tuberculosis: the 1st group consisted of 35 patients with newly diagnosed cases (tuberculosis) of CRTB of lungs (middle age – 39.1±2.2 years), the second – of 44 patients with repeated cases of CRTB of lungs (middle age – 39.5±1.7 years diagnosed for the first time). In both groups males prevailed: 23 (65.7 %) and 31 (70.4 %) respectively. The repeated cases are recurrence of tuberculosis (RTV), treatment after a break (TAB), treatment after failure of chemotherapy (FTTB) and others (OTB). Among the patients with repeated cases of CRTB of lungs with RTV there were 25 people (56.8 %), OTB – 3 (6.8 %), TAB – 4 (9.1 %), FTTB – 12 (27.3 %). The groups were compared by age, gender and the main anthropometric indicators.

Diagnostic of FBS of a tracheobronchial tree among patients with CRTB of lungs was carried out on clinical base of the department of phthisiology and pulmonology of ZSMU at Municipal institution «Zaporizhzhia Regional Antituberculous Dispensary» by the applicant V. M. Khlystun.

The criteria of involving the patients into the research were: existence of resistance of micobacteria of tuberculosis (MBT) to anti-microbacterial drugs among patients with new and repeated cases of tuberculosis, existence of pathology of mucosa of bronchi confirmed at FBS. Serious associated diseases (HIV infection/AIDS, diabetes mellitus, etc.) were exception criteria.

The condition of mucosa of bronchi was studied under narcotic anaesthesia by fibrotic bronchoscopes made by Olympus (Japan). The pathology of a bronchial tree was described according to classification of M. Shesterina, A. Kalyuk (1975): at a specific lesion of bronchi the infiltrative mucosa lesions, infiltrative and fistulous tuberculosis and cicatrical stenosis of bronchus were determined. According to classification of non-specific inflammatory processes the endobronchitis was classified: according to the nature of process (catarral, purulent, hypertrophic, atrophic and hemorrhagic) and a process of localization (diffuse unilateral and bilateral, limited).

The results of the research were processed by modern methods of the analysis on personal computer with the use of a statistical package Statistica® for Windows 6.0 license program (StatSoft Inc., No. AXXR712 D833214FAN5). The normality of distribution of quantitative signs was analyzed by Shapiro-Wilk's test. The parameters had normal distribution. The comparison of indicators in groups was carried out with the use of Student's test. The difference on p<0.05 was

considered statistically significant. All tests were bilateral. For definition of reliable distinctions between quality indicators the non-parametric statistical criteria were used (the analysis of tables – criterion  $\chi^2$ ).

## Results and discussion

Bacterioexcretion was diagnosed among all patients (100 %) of both groups (*Table 1*). Existence of destructive process in lungs was registered almost with an identical frequency in both groups: among 88.6 % of patients with new cases of CRTB of lungs and among 90.9 % – with repeated one. In case of distribution of patients on existence of destructive process in sectional bronchial tubes of lungs (S<sub>1+2</sub>, S<sub>6</sub>) at the same time diagnostics of destruction in S<sub>1+2</sub> and S<sub>6</sub>) it was established that the frequency of their damage between the groups wasn't different. However it was established that in both groups the existence of destructive process prevailed in sectional bronchial tubes of S<sub>1+2</sub>: with new cases in 60 % against 17.2 % in S<sub>6</sub> (p<0.01) and 11.4 % in S<sub>1+2</sub>, S<sub>6</sub> (p<0.01), and with repeated – in 47.7 % against 25 % in S<sub>6</sub> (p<0.05) and 18.2 % in S<sub>1+2</sub>, S<sub>6</sub> (p<0.05).

By distribution of patients on a range of resistance of MBT to antituberculous drugs it has been found that in both groups different ranges of resistance of MBT had almost identical frequency and weren't authentically different: polyresistant tuberculosis (PRTB) was diagnosed among 3 (8.6 %) patients with new cases and among 1 (2.5 %) – with repeated cases, multiresistant tuberculosis (MRTB) – among 27 (77.7 %) and among 32 (72.5 %), respectively, expanded resistance (RRTB) – among 5 (14.3 %) and among 11 (25 %) respectively. Thus, in both groups the patients with MRTB prevailed: among 77.1 % with new cases of CRTB of lungs and among 72.5 % – with repeated one.

Studying of clinical forms among patients with CRTB of lungs with endobronchial pathology showed that the patients in both groups the infiltrative form prevailed: among 30 (85.7 %) with new cases and among 28 (63.6 %) – with repeated one. At the same time it was diagnosed among the patients with new cases 1.3 times more often (p<0.05). The focal form was established only by 1 patient (2.9 %) with a new case, and caseous pneumonia – only by 1 (2.3 %) with a repeated case. Between disseminated and fibrocavernous (FCT) forms a reliable difference between the groups was not revealed, but among patients with repeated cases they were registered more often: disseminated by 2.5 times (9 (20.5 %) against 3 (8.5 %)), and FCT by 4.6 times (6 (13.6 %) against 1 (2.9 %)).

Diagnostic FBS allowed to study visually the changes of mucosa of bronchi of a tracheobronchial tree (*Table 2*). It has been found that tuberculosis of bronchi (TB) prevailed among patients with new cases (77.1 % against 52.3 % with repeated cases p<0.05), and the persons with repeated cases had non-specific endobronchitis (47.8 % against 22.8 % with new cases p<0.05). Studying of features of the progress of TB among patients with CRTB of lungs depending on a case was carried out. It has been found that in both TB groups it was diagnosed mainly in combination with non-specific endobronchitis. So, among patients with new cases a combined progress was found among 24 (68.6 %) against 3 (8.6 %) with TB (p<0.05), and among patients with repeated cases – at 17 (38.6 %) against 6 (13.6 %) with TB (p<0.05).

As the Table 2 testifies, by nature of specific damage of bronchial tubes the infiltrative damages of a mucous membrane prevailed among patients with new cases, as in relation to repeated cases (62.9 % against 27.3 %;  $p < 0.05$ ) and rather infiltrative fistulous forms of this group (62.9 % against 14.3 %;  $p < 0.05$ ). The patients with repeated cases have progress of the infiltrative form of TB and infiltrative fistulous was almost identical (27.3 % and 25 % respectively). At the same time among patients with new cases a specific process in bronchial tubes was followed by stenosis more often by 1.4 times, than by repeated cases (65.7 % against 40.9 %;  $p < 0.05$ ).

Non-specific inflammatory damage of bronchial tubes was the following. With new cases of CRTB of lungs non-specific endobronchitis was diagnosed among patients in 91.4 %, irrespective of the fact, whether it was independent (22.8 %), or in combination with TB (68.6 %), and in all cases it had purulent character. Among patients with repeated cases of CRTB of lungs also, irrespective of the above specified, purulent endobronchitis (77.3 %) prevailed, which at the independent course of endobronchitis occurred by 18 people (40.9 %) and by a joint progress with TB occurred among 16 (36.4 %). Besides, among patients with repeated cases catarrhal endobronchitis was revealed by 1 (2.3 %), subatrophic – by 2 (4.5 %) and fibrinous – by 1 (2.3 %). By localization non-specific endobronchitis in both groups was mainly unilateral: among 82.9 % with new cases and among 72.7 % – with repeated one. By prevalence of endobronchitis in both groups, irrespective of a case, a reliable difference between diffusion and limited process wasn't found: 37.1 % and 54.3 %, respectively – among patients with new cases and 52.3 % and 34.1 %, respectively – with repeated cases.

By comparison of results of the research of simultaneous diagnostics of destructive process in segmental bronchi ( $S_{1+2}$ ,  $S_6$ ,  $S_{1+2+6}$ ) and tuberculosis of bronchi it has been found that among patients with new cases of CRTB of lungs this progress with a specific lesion of the corresponding bronchus occurred among 23 people (65.7 %) of 31 (88.6 %) and by repeated – among 21 (47.7 %) of 40 (90.9 %).

Among 15 patients (42.8 %) with new cases of CRTB of lungs in the presence of destructive process in  $S_{1+2}$  in 9 (25.7 %) TB was diagnosed in  $S_{1+2}$  and among 6 (17.1 %) lesion of a top of a partial bronchus. Among all 6 (17.2 %) patients with destructors in  $S_6$  TB in  $S_6$  was found. In the presence of destruction in  $S_{1+2+6}$ , TB was diagnosed among 2 (5.7 %) of 4 people.

At repeated cases of CRTB of lungs the following picture was defined. In the presence of destructive process in  $S_{1+2}$  at 12 (27.3 %) TB was diagnosed in  $S_{1+2}$  and among 6 (13.6 %) lesion of a top of a partial bronchus. In the presence of destruction in  $S_6$  TB in  $S_6$  was found among 3 (6.8 %) of 11 patients.

## Conclusions

1. All patients with CRTB of lungs with endobronchial pathology, irrespectively of a case of the previous disease, were the persons discharging bacteria with prevalence of multirefractory strains of MBT, infiltrative clinical form and destructive lesion of segmental bronchi of  $S_{1+2}$ .

2. Among patients with newly diagnosed cases of CRTB of lungs the tuberculosis of bronchi prevailed and among

**Table 2.** Distribution of patients with CRTB of lungs according to the character of endobronchial pathologies, n (%)

Indicator	New cases, n=35		Repeated cases, n=44		p
	abs.	%	abs.	%	
TB	27	77.1	23	52.3	<0.05
TB infiltrative	22	62.9	12	27.3	<0.01
TB infiltrative fistulous	5	14.3	11	25.0	>0.05
With stenosis	23	65.7	18	40.9	<0.05
Endobronchitis	8	22.8	21	47.8	<0.05

patients with repeated cases of CRTB of lungs the non-specific endobronchitis prevailed. Irrespectively of a case of the previous disease, tuberculosis of bronchi was diagnosed mainly in combination with non-specific endobronchitis.

3. Among patients with new cases of CRTB of lungs the infiltrative tuberculosis of bronchial tubes (62.9 %) prevailed, and with the repeated one – frequency infiltrative and infiltrative fistulous was almost identical (27.5 % and 25 % respectively). The frequency of development of stenosis of the affected bronchial tube in new cases occurred by 1.6 times more often than in case of the repeated one (65.7 % against 40.9 % respectively).

4. Non-specific endobronchitis among patients with CRTB of lungs, irrespective of a case of the previous disease, is preferentially of one-sided localization and has purulent character.

5. In the presence of destructive process in segmental bronchi ( $S_{1+2}$ ,  $S_6$ ,  $S_{1+2+6}$ ) it was followed by tuberculosis of these bronchi in 65.7 % of 88.6 % of new cases of CRTB of lungs and in 47.7 % of 90.9 % – of the repeated ones.

6. The obtained data demonstrate that, irrespectively of a case, among patients with CRTB of lungs, it is necessary to apply correction methods, both of specific and non-specific pathology of mucosa of a tracheobronchial tree. At the same time this correction by the most part of patients, namely, with existence of the combined course of tuberculosis of bronchi and non-specific bronchitis, demands simultaneous use of methods of correction of both pathologies.

**Prospects of further scientific research.** Development and justification of additional methods of endobronchial therapy of pathology of mucosa of bronchi among patients with CRTB of lungs will entirely promote therapeutic actions among these patients with CRTB and increase the efficiency of treatment.

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**Information about authors:**

Raznatovska O. M., Associate Professor, MD, Professor,  
Department of Phthisiology and Pulmonology, Zaporizhzhia State  
Medical University, Ukraine.  
Khlystun V. M., Assistant, Department of Phthisiology  
and Pulmonology, Zaporizhzhia State Medical University, Ukraine.

**Відомості про авторів:**

Разнатовська О. М., д-р мед. наук, доцент, професор  
каф. фтизіатрії і пульмонології, Запорізький державний медичний  
університет, Україна.  
Хлистун В. М., асистент каф. фтизіатрії і пульмонології,  
Запорізький державний медичний університет, Україна.

**Сведения об авторах:**

Разнатовская Е. Н., д-р мед. наук, доцент, профессор  
каф. фтизиатрии и пульмонологии, Запорожский  
государственный медицинский университет, Украина.  
Хлыстун В. Н., ассистент каф. фтизиатрии и пульмонологии,  
Запорожский государственный медицинский университет,  
Украина.

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