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OPTIMIZATION OF DIAGNOSTICS OF EXUDATIVE TUBERCULOUS PLEURISY

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Abstract: Over the past decade, in most countries of the world, there has been an increase in the incidence of tuberculosis. The current epidemiological situation regarding tuberculosis remains tense in most countries of the world community. The reasons for the accumulation of fluid in the pleural cavity are different in genesis and mechanisms, which causes the difficulties of differential diagnosis of this pathology, recognized by most Russian and foreign authors. To diagnose tuberculous pleurisy, microbiological methods (microscopy and sputum culture), pleural biopsy (histological examination of the specimen and culture), X-ray methods, immunological methods, and polymerase chain reaction are used. One of the possible biochemical markers for diagnosing pleural effusion of tuberculous etiology can be the determination of adenosine deaminase (ADA) activity in pleural fluid. The enzyme A D A is present in the cytoplasm of cells of all mammalian tissues and plays an important role in their development and functioning. It is involved in purine metabolism and catalyzes the deamination of adenosine and 2-deoxyadenosine to inosine and deoxynosine, respectively.

Key words: tuberculous pleurisy, diagnosis, adenosine deaminase, diagnostic shortcomings

Relevance of the topic. Over the last decade, in most countries of the world, an increase in the incidence of tuberculosis has been noted (Erokhin V.V., 2003; Ubaidullaev A.M., Tillyashaikhov M.N., Parpieva N.N.). With the increasing incidence of tuberculosis, there has been an increase in the number of cases of tuberculous exudative pleurisy (Liam CK, 2000; Peto HM, 2009) . In terms of incidence, TEP ranks second among extrapulmonary

forms of tuberculosis (Kruijshaar ME et . al 2009). In 5-31% of cases, respiratory tuberculosis is complicated by exudative pleurisy (Ferrer J., 1977)

The current epidemiological situation regarding tuberculosis remains tense in most countries of the world community. According to the latest WHO data, in 2012, 8.6 million new cases of the disease and 1.3 million deaths associated with tuberculosis were registered worldwide [35]. A characteristic feature of the modern tuberculosis epidemic is the widespread distribution of drug-resistant strains of the pathogen. At the same time, the increase in the proportion of mycobacterium tuberculosis (MTB) with multidrug resistance (MDR) is alarming.

The first years of the 21st century were characterized by some stabilization of certain indicators of the prevalence of tuberculosis and the organization of anti- tuberculosis care to the population in Uzbekistan. In general, the situation with tuberculosis continues to remain very tense [34].

The worsening epidemiological situation of tuberculosis in Uzbekistan, as in other countries of the world, is due to an increase in the number of drug-resistant MBT strains [38].

The incidence of tuberculosis remains one of the main health problems. A common extrapulmonary manifestation of tuberculosis is pleurisy [3-9]. Tuberculous pleurisy (TP) develops when mycobacteria secrete an antigenic protein into the pleural cavity. This triggers a slow-type sensitization reaction that is not fully understood, and fluid accumulates in the pleural cavity.

The difficulties usually lie not in diagnosing pleurisy itself, but in determining its etiology for timely etiotropic treatment. The fact is that the presence of pleural effusion, in addition to tuberculosis, can be caused by pneumonia, malignant neoplasms, congestive heart failure, liver cirrhosis, nephrotic syndrome, infectious non-tuberculous lung disease, and diffuse connective tissue diseases.

In approximately 31% of patients, pulmonary tuberculosis is accompanied by pleural effusion, which is believed to be the result of a delayed-type hypersensitivity reaction in

response to the presence of mycobacterial antigens in the pleural cavity. Meanwhile, the clinical manifestations of tuberculous pleurisy are similar to those of pleurisy of other etiologies (due to malignant neoplasms in the lungs or an infectious process of non-tuberculous etiology). In this regard, differential diagnosis of tuberculous pleurisy is extremely important for timely etiotropic treatment [36].

Pathogenetic mechanisms of development of exudative tuberculous pleurisy. The reasons for the accumulation of fluid in the pleural cavity are different in genesis and mechanisms, which causes the difficulties of differential diagnosis of this pathology, recognized by most Russian and foreign authors. Tuberculosis is one of the most common causes of exudative pleurisy [16].

Opinions about the course of tuberculous pleurisy in the available literary sources are ambiguous. Depending on the pathogenetic mechanisms of the development of tuberculous pleurisy, the authors noted various variants of the course of the disease . For example, the period of exudation can last from 10-15 days to 3 months. In some cases, an atypical and asymptomatic course of tuberculous pleurisy is noted. Clinical, laboratory and radiological data for pleurisy of different etiologies are often similar to each other and do not have pronounced clinical features, which makes their differential diagnosis difficult. In 7-13.4 %) patients the process becomes chronic [1-2 , 2-1 , 2-5].

There is insufficient knowledge of the processes of endotoxicosis (or systemic response to inflammation syndrome) in various forms of tuberculosis, including tuberculous pleurisy [41]. To assess the pathophysiological mechanisms of endogenous intoxication, the level of urea, creatinine and medium molecular peptides, molecules of average weight, trypsin-like and anti-trypsin activity, ammonia concentration are determined and the leukocyte intoxication index is calculated.

TEP is a pathological accumulation of fluid in the pleural cavity due to inflammatory processes in adjacent organs or layers of the pleura or when there is a violation of the

relationship between the colloid-osmotic pressure of the blood plasma and the hydrostatic pressure in the capillaries.

Mechanisms of fluid accumulation in the pleural cavity with pleurisy:

1. The permeability of the vessels of the parietal pleura increases, which leads to an increase in capillary hydrostatic pressure in the visceral and parietal pleura.

2. Increased amount of protein in the pleural cavity.

3. Decrease in oncotic pressure of blood plasma.

4. Decrease in intrapleural pressure (with atelectasis due to bronchogenic lung cancer, sarcoidosis).

5. Impaired outflow of pleural fluid through the lymphatic vessels.

Optimization of modern approaches to diagnosis and differential diagnosis of TEC. To diagnose tuberculous pleurisy, microbiological methods (microscopy and sputum culture), pleural biopsy (histological examination of the specimen and culture), X-ray methods, immunological methods, and polymerase chain reaction are used. However, making a diagnosis based on the results of the above tests is quite difficult, since only 10-35 % of cultures and 20-81% of molecular tests can detect MBT in pleural fluid, and infectious granulomas are detected in histological examination of samples only in 56-82% of cases.

Verification of tuberculous pleurisy can be achieved by detection of Mycobacterium tuberculosis during microscopic or cultural microbiological examination of pleural exudate or through morphological examination (detection of caseifying epitheliodine cell granulomas) of pleural biopsies. In the presence of tuberculous changes in the lungs, MBT are detected in the exudate using culture in 30-50% of cases, but only for a fairly long time (up to months). The greatest difficulties arise when there are no visible changes in the lungs. In a significant proportion of cases, the diagnosis of tuberculous pleurisy is based only on clinical data, which leads to a large number of errors and long diagnostic times.

The obvious extreme relevance of timely diagnosis and differential diagnosis of tuberculous pleurisy, primarily the creation of methods for quickly determining the etiology of pleurisy.

Due to the insufficient information content of traditional microbiological research for the etiological diagnosis of exudative pleurisy, the diagnostic significance of using molecular and immunological methods for studying pleural exudate, including determination of the content of interferon a-γ (IFN -γ), is discussed. Polymerase chain reaction (PCR) testing can play a significant role in the diagnostic process. However, even with this method, the study of pleural exudate is much less informative, since its sensitivity is about 17% compared to the study of pleural biopsies using PCR - up to 90%. Pleural exudate during tuberculosis infection is characterized by the dominance of T-lymphocytes, which, when interacting with MBT antigens, produce IF H- γ, and therefore its determination in the exudate can serve as a diagnostic marker of tuberculous pleurisy.

A high concentration of interferon a- γ in the pleural fluid (more than 300 pg/ml) in patients with active exudative pleurisy can serve as a reliable diagnostic sign of tuberculous etiology of the disease. Determination of the level of IF H- γ in pleural fluid can be effectively used in the early stages of diagnosing the etiology of exudative pleurisy for the timely use of specific anti-tuberculosis chemotherapy [16].

Acid-fast bacteria are detected only in 20%-30% of pleural fluid examinations and in 50%-80% of pleural biopsy specimens. Even when using polymerase chain reaction to detect mycobacteria, the sensitivity does not exceed 78% [33].

Meanwhile, it is known that pleural fluid contains quite sensitive biochemical markers, determination of the concentration of which can significantly facilitate the differential diagnosis of TP [16]. Thus, in response to antigenic stimulation by Micobacterium tuberculosis, a cell-mediated immune response is activated in the body, an important part of which is the production of interferon- g (INF-g) by T lymphocytes . INF- g

is capable of enhancing the phagocytic activity of macrophages directed against mycobacteria, which causes its overproduction against the background of LT [34].

Differential diagnosis of TP usually includes invasive procedures such as pleural biopsy and thoracoscopy [11, 42]. These manipulations require special skills of medical staff and can worsen the patient's condition. The high cost and long time required to obtain results further reduce the effectiveness of pleural biopsy and bacteriological method, which are considered the "gold standard" of diagnosis [28]. The difficulty of diagnosing TP is complemented by the relatively low sensitivity of conventional methods.

Adenosine deaminase and its role in the diagnosis of tuberculous pleurisy. One of the possible biochemical markers for diagnosing pleural effusion of tuberculous etiology can be the determination of adenosine deaminase (ADA) activity in pleural fluid. The enzyme A D A is present in the cytoplasm of cells of all mammalian tissues and plays an important role in their development and functioning. It is involved in purine metabolism and catalyzes the deamination of adenosine and 2-deoxyadenosine to inosine and deoxynosine, respectively. There are several isoenzyme forms of ADA, among which the most important are ADA1 and ADA2. The ADA1 isoenzyme is found in all cells of the body, but in the highest concentration in lymphocytes and monocytes. The ADA2 isoenzyme is present only in monocytes and macrophages [3-6].

It was found that ADA activity and IFN- g concentration are increased in the pleural fluid of patients with TP [28, 31, 37]. However, as it turns out, the diagnostic value of these tests depends on the prevalence of tuberculosis in the population, as well as on the population itself. So, according to R. W. _ The slightly lower level of ADA activity among Asians calls into question the feasibility of its determination in this population for the diagnosis of tuberculosis [26].

ADA activity can be determined by the method described by Giusti G. _ and Galanti B .. This method is based on the Berthollet reaction of formation (with the participation of ammonia released from adenosine) of a colored indophenol complex and subsequent

spectrophotometric assessment of its concentration. Results were expressed in international activity units (IU). A unit of ADA activity was taken to be the amount of enzyme required for release under standard assay conditions of 1 mmol of ammonia per minute.

To separate the enzymatic activity of A D A 1 and A D A 2, 200 μmol/L of the selective inhibitor of ADA1 activity, erythro-9-(2-hydroxy-3-nonyl) -adenosine hydrochloride (Sigma , USA), was added to the incubation medium, after which determination of ADA2 activity. The concentration of interferon- g is determined by enzyme immunoassay using reagent kits from Vector-Best JSC (Novosibirsk, Russia). The range of measured concentrations was 0 – 2000 pg/ml, the sensitivity of the analysis was 20 pg/ml.

Optimization of treatment methods for tuberculous exudative pleurisy. The accumulated experience in treating patients with tuberculosis has convincingly shown the need to combine etiotropic and pathogenetic therapy to ensure recovery in a shorter time with better anatomical and functional results [25].

Currently, there is sufficient data on the effective use of natural and artificial proteinase inhibitors in the acute phase of pulmonary tuberculosis. The most widely used protein inhibitor in clinical practice is contrical. The use of contrical allows you to quickly eliminate the symptoms of intoxication, normalize blood counts, reduce the time of abacillation and closure of cavities, and reduce the development of pneumofibrosis [22, 36, 38]. However, when administered intravenously, the effect of proteinase inhibitors is short-lived due to rapid elimination by the kidneys, their sufficient concentration in the affected area is not ensured, and conditions may be created for increased blood clotting, thrombus formation, and the occurrence of phlebitis [21, 34, 39].

There is no information about the nature of the concomitant pathology, the function of external respiration, hemostasis indicators, or the immunological characteristics of the process. The state of the tracheobronchial tree in patients with tuberculous pleurisy, the relationship between the state of the tracheobronchial tree and the function of external

respiration have not been studied; there is no information about the state of the cardiovascular system in patients with TEP.

The issues of etiological diagnosis of exudative pleurisy have not been fully considered; there is no data on the indicators of adenosine deaminase in exudate, bronchoalveolar fluid and blood plasma in patients with tuberculous exudative pleurisy in the Perm region. Morphometry of the pleural layers was not carried out, and the relationship of morphological variants with the clinical characteristics and course of the disease was not studied.

The effectiveness of treatment of modern tuberculous exudative pleurisy in the immediate and long-term periods has not been studied. At the same time, due to the pronounced negative pathomorphosis of tuberculosis and the increase in drug resistance, a decrease in the effectiveness of treatment of tuberculous exudative pleurisy and an increase in the frequency of its chronicity should be expected. This urgently requires the development and implementation of new pathogenetic methods in the treatment plan for tuberculous exudative pleurisy, aimed at increasing immunological protection and sanitizing the tracheobronchial tree.

It is necessary to study and implement new ways of introducing specific chemotherapy drugs into the patient's body, optimizing the treatment of concomitant diseases, which would reduce the most expensive inpatient stage of the main course of treatment.

Based on the above, the need to study tuberculous exudative pleurisy during the period of continued growth in morbidity and mortality from tuberculosis is very urgent.

REFERENCES

1. Титоренко О.Т., Солдатов Н.В., Умаров А.М. и др. // Клиническая медицина, 1995, №1, С. 672-674

2. Тюхтин Н.С. Болезни плевры // Болезни органов дыхания // под ред. Н.Р. Палеева, М., 2000, С. 673-704
3. Тюхтин Н.С., Строгова Н.А., З.Д. Берлова «Клиническое значение определения общей антитриптической активности сыворотки крови и экссудата при туберкулезном плеврите // Проблема туберкулеза и болезни легких, 2009, №6, С. 37-40
4. Федосеев Г.Б. Синдромная диагностика внутренних болезней, СПб., 1996, Т. 3, С. 322-334
5. Худзик Л.Б., Арсеньев В.С., Савина Е.Н. и др. // Всесоюзный съезд фтизиатров, 10-й, Тезисы докладов, Киев, 1986, С. 213-214
6. Черниченко, Н.В. Динамика вентиляционной и газообменной функции при применении препарата сурфактанта у больных туберкулезом легких / Н.В. Черни¬ченко, Е.А. Шергина, О.В. Ловачева, В.В. Ерохин // Проблемы туберкулезаза и болезней легких. 2006. №6. - С. 6-10;
7. Чучалин, А.Г. Актуальные вопросы диагноза в пульмонологии / А.Г. Чучалин // Пульмонология. 2001. № 1. С. 6-11
8. Шахматов И.И. // Регионарное кровообращение нижних конечностей и тромбоз, Томск, 1983, С. 107-112
9. Якушев, М.Ф. Клинико-функциональные сопоставления у больных туберку¬лезным плевритом / М.Ф. Якушев, Л.В. Хабибулин // Проблемы туберкулеза. 2002. №8. С. 12-15
10. Aktogu S. Clinical spectrum of pulmonary and pleural tuberculosis: a report of 5,480 cases / S. Aktogu, A. Yorgancioglu, K. Cirak // Eur. Respir. J. - 1996. 9(10). P. 2031-2035
11. Amicosante M., Houde M., Guaraldi G., Saltini C. // International Journal Tuberculosis Lung Diseases, 1999, Vol. 6, №6, P. 736-740

12. Amiri M. Evaluation of the combined use of polymerase chain reaction and adeno¬sine deaminase activity on the diagnosis of pleural tuberculosis / M. Amiri, S. Mansouri, S. Mirsaeidi // Europ. Resp. J. 2005. Suppl. 40, Vol. 26. P. 2657
13. Andreasyan N. A., Hairapetian, H. L., Sargisova, Y. G. et al. Activity of adenosine deaminase and its isoforms in pleural fluid in tuberculous pleuritis // Med. Sci. Monit. 2002. Vol. 8, N 10. P. CR708 – CR712;
14. Andreu J. Radiological manifestations of pulmonary tuberculosis / J. Andreu, J. Ca-ceres, E. Pallisa, M. Martinez-Rodriguez//Eur. J. Radiol. -2004. - 51(2). -P. 139-149
15. Arif R., Misbahul, I., Abrar, A. et al. Serum adenosine deaminase (ADA) level in the cases of tuberculous pleural effusion // Pakistan. J. Med. Res. 2002. Vol. 41, N 3, P. 110 – 116
16. Burgess L. Use of adenosine deaminase as a diagnostic tool for tuberculous pleurisy /L. Burgess,F. Maritz, I. LeRoux, et al. //Thorax.- 1995. - Vol. 50.-P. 672-674
17. Chalhoub M., Cruz A.A., Marcilio C. et al. // Rev. Assoc. Med. Bras., 1996, Vol. 42, №3, P. 139-146;
18. Chen M. L., Yu, W. C., Lam, C. W. et al. Diagnostic value of pleural fluid adenosine deaminase activity in tuberculous pleurisy // Clin. Chem. Acta. 2004. Vol. 341. P. 101 – 107
19. Chittiprol S. Plasma adenosine deaminase activity among HIVI Clade C seroposi¬tives: relation to CD4 T cell population and antiretroviral therapy / S. Chittiprol, P. Sat- ishchandra, R.S. Bhimasenaraoet. al. // Clin. Chim. Acta. - 2007. - Vol. 377. - №1-2. - P. 133-137
20. Dikensoy O. Increased pleural fluid adenosine deaminase in brucellosis is difficult to differentiate from tuberculosis / O. Dikensoy, M. Namiduru, S. Hocaoglu, B. Ikidag, A. Filiz A. // Respiration. - 2002. - 69(6). - P. 556-559
21. Ferre J. “Pleural tuberculosis” // Eur. Respir. J., 1997, Vol. 10, P. 942-947;

22. Giuisti G.Methodes of Enzymatic Analysis / G Giuisti // New York. - 1974. - №2. - P. 1092-1099
23. Giusti G., Galanti, B. // Methods of enzymatic analysis. 1984. Vol. 4. P. 315 – 323
24. Global Tuberculosis Report 2013, WHO, Geneva, Switzerland
25. GorgunerM., Cerci, M., Gorguner, I. Determination of adenosine deaminase activity and its isoenzymes for diagnosis of pleural effusions // Respirology. 2000. Vol. 5. P. 321 – 324
26. Hagmar L. Impact of lymphocyte chromosomal aberrations on human cancer risk: results from Nordic and Italian cohorts / L. Hagmar, U. Strornberg, S. Bonassi // Cancer Res. - 2004. - Vol. 64. - P. 2258-2263
27. Hiraki A., Aoe, K., Eda, R. et al. Comparison of six biological markers for the diagnosis of tuberculous pleuritis // Chest. 2004. Vol. 125. P. 987 – 989
28. Perez-Rodriquez E., Castro, D.J. The use of adenosine deaminase and adenosine deaminase isoenzymes in the diagnosis of tuberculous pleuritis // Current Opinion in Pulm. Med. 2000. Vol. 6. P. 259 – 266
29. Hiraki A., Aoe, K., Eda, R. et al. Comparison of six biological markers for the diagnosis of tuberculosis pleuritis // Chest. 2004. Vol. 125. P. 987 – 989
30. Hsu W.H., Chiang, CD, Chen, WT. et al. Diagnostic value of adenosine deaminase and gamma-interferon in tuberculous and malignant pleural effusions // Formosan Medical Association. 1989. Vol. 88(9). P. 879 – 82
31. Inase N. Adenosine deaminase-2 in the diagnosis of tuberculous pleuritis / N. Inase, S. Tominaga, M. Yasui, Y. Tsukada, M. Oukouchi, H. Miura // Kekkaku. - 2005. - 80(12).-P. 31-34
32. Kataria Y.P., Khurshid, I. Adenosine deaminase in the diagnosis of tuberculous pleural effusion // Chest. 2001. Vol. 120. P. 334 – 336
33. Khatami K. “Pleural tuberculosis, 2002, Vol. 13, P. 122-125

34.Khatami K. Pleural tuberculosis // semj. 2002. Vol.3 (3). P. 137 – 151;
35.Light R.W. Pleural diseases, 4-th. Edition, Philadelphia, 2001
36.Таганович А.Д., Саид М. Алинежад «Диагностические характеристики аденозиндезаминазного теста у больных туберкулезным плевритом – жителей Белорусии», Проблема туберкулеза и болезни легких, 2008, №8, С. 38-41
37.Малиев Б.М. Роль патологии трахеобронхиального дерева в эффективности ле¬чения туберкулеза легких / Б.М. Малиев, М.П. Грачева, ДЛ. Беляев, А.С. Габараев // Проблемы туберкулеза и болезней легких. 2007. №8. С. 19-25
38.Luis, V., David, A., Esther, S. J. et al. Tuberculous Pleurisy // Arch Intern Med. 1998. Vol. 158. P. 2017 – 2021
39.Hsu W.H., Chiang, CD, Chen, WT. et al. Diagnostic value of adenosine deaminase and gamma-interferon in tuberculous and malignant pleural effusions // Formosan Medical Association. 1989. Vol. 88(9). P. 879 – 82
40.Парпиева Н.Н., Мухтаров Д.З., Белоцерковец В.Г. и др. Функция легких и сердечно-сосудистой системы у больных с лекарственно-устойчивым туберкулезом легких // Вестник ассоциации пульмонологов Центральной Азии, 2007, №10, С. 70-74
41.Giusti G., Galanti, B. // Methods of enzymatic analysis. 1984. Vol. 4. P. 315 – 323
42.Global Tuberculosis Report 2013, WHO, Geneva, Switzerland
43.Akhtamovna K. N. Fibrotic Complications in the Lungs in Patients Who Have Had COVID-19 Pathogenesis of COVID-19 //European Journal of Life Safety and Stability (2660-9630). – 2021. – Т. 9. – С. 14-24.
44. Исомиддин Хайдарович Усмонов, Нозима Ахтамовна Кенжаева РОЛЬ МСКТ В ДИАГНОСТИКЕ БОЛЬНЫХ С COVID-19 // Scientific progress. 2021. №6. URL: https://cyberleninka.ru/article/n/rol-mskt-v-diagnostike-bolnyh-s-covid-19 (дата обращения: 22.10.2023).

45. Aslonov F. I., Rustamova S. A., Raxmonova K. M. Immunopatological aspects in patients with first detected pulmonary tuberculosis //World Bulletin of Public Health. – 2021. – T. 4. – C. 91-95.
46. Abdullayevna R. S. CLINICAL AND RADIOLOGICAL FEATURES OF NEWLY DETECTED PULMONARY TUBERCULOSIS IN PATIENTS WITH CONCOMITANT DISEASES //Intent Research Scientific Journal. – 2023. – T. 2. – №. 3. – C. 45-56.
47. Abdullaevna, R. S., & Rakhmanovich, M. B. (2023). Immunological Features of Pulmonary Tuberculosis in Patients with Drug Resistance. Scholastic: Journal of Natural and Medical Education, 2(4), 40-57.
48. Kh, Usmonov I., Bahodir R. Muazzamov, and Muhtor F. Jumaev. "Features of diagnostics and treatment of drug-resistant forms of pulmonary tuberculosis." International journal of pharmaceutical research 13.1 (2021): 2484-2489.
49. Муаззамов Б. Р., Муаззамов Б. Б., Медведева Н. В. ПРИМЕНЕНИЕ ИНТЕРАКТИВНЫХ ПЕДАГОГИЧЕСКИХ МЕТОДОВ ПРЕПОДАВАНИЯ ПРЕДМЕТА" ФТИЗИАТРИЯ" НА ПРИМЕРЕ ТЕМЫ" ДЕСТРУКТИВНЫЕ ФОРМЫ ТУБЕРКУЛЁЗА ЛЁГКИХ" //Новый день в медицине. –2019. –No. 3. – С. 45-50.
50. Рустамова С. А. и др. Изучение причин и факторов, способствующих развитию рецидивов туберкулеза органов дыхания //Медицинский альянс. – 2015. –No. 1. –С. 115-115.
51. Рустамова С. А. и др. Спектр лекарственной устойчивости и эффективность лечения впервые выявленных больных туберкулезом легких //Медицинский альянс. –2015. –No. 1.–С. 116-116.

52. Мухамедов К., Джурабаева М., Рустамова С. Частота встречаемости вирусных гепатитов среди впервые выявленных больных туберкулезом легких //Журнал проблемы биологии и медицины. –2014. –No. 3 (79). –С. 132-133.